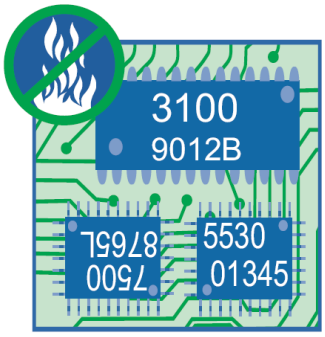
United States Environmental Protection Agency

FLAME RETARDANTS IN PRINTED CIRCUIT BOARDS

Chapter 4



FINAL REPORT

August 2015

EPA Publication 744-R-15-001

4 Hazard Evaluation of Flame Retardants for Printed Circuit Boards

This chapter summarizes the toxicological and environmental hazards of each flame-retardant chemical that was identified for potential functional use in printed circuit boards (PCBs) laminates. Evaluations of chemical formulations may also include associated substances (e.g., starting materials, by-products, and impurities) if their presence is specifically required to allow that alternative to fully function in the assigned role. Otherwise, pure substances were analyzed in this assessment. Users of the alternative assessments should be aware of the purity of the trade product they purchase, as the presence of impurities may alter the hazard of the alternative.

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 Section 4.4 and Section 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 4.8. Lastly, the collected data and hazard profile of each chemical are presented in Section 4.9.

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 Program 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 which DfE characterizes but does not assign criteria to and these 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 Program 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.

Endpoint Category	Endpoint	Definition
	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; the assessment is focused on effects in three groups of surrogate aquatic organisms (freshwater fish, invertebrates, and 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 alternative 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 4.9). 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 Program Alternatives Assessment Criteria for Hazard Evaluation* underwent internal and public 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 Program 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					
Carcinogenicity	*Known or presumed human carcinogen* (equivalent to Globally Harmonized System of Classification and Labeling of Chemicals (GHS) Categories 1A and 1B)	*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 Relationship (SAR)* (As described above)	–

Endpoint	Very High	High	Moderate	Low	Very Low
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	–
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Repeated-dose toxicity					
Oral (mg/kg/day)	–	<10	10–100	>100	–

Endpoint	Very High	High	Moderate	Low	Very Low
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.*				
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					

Endpoint	Very High	High	Moderate	Low	Very Low
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	–

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 located 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, by professional judgment, or from a computerized model, then the next-level designation was assigned (e.g., use of data from a structural analog that would yield a designation of Very High would result in a designation of high for the chemical in review). One exception is for the estimated persistence of polymers with an average molecular weight (MW) >1,000 daltons, which may result in a Very High designation.

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 the 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, biotransformation, and excretion 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 alternative 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[1].
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.

Toxicological Endpoint	Definition
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 or other stressor from human activities (e.g., application of pesticides, the discharge of industrial chemicals to air, land, or water, or the use of synthetic chemicals in consumer products.)

[1]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).

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 polymers differ from discrete chemicals in terms of how they are evaluated 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* (U.S. EPA, 1999b) on searching for existing chemical information. 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. These were supplemented by primary searches of scientific literature published after these secondary sources were released; this 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 U.S. Environmental Protection Agency (EPA) public databases (e.g., integrated risk information system (IRIS); the High Production Volume Information System) and confidential databases 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 4-2. For most alternatives assessed, high-quality secondary sources were not available; therefore a comprehensive search of the 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, the literature review focused primarily on the use of secondary sources, such as Agency for Toxic Substances and Disease Registry Toxicological Profiles or IRIS assessments. 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. 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 Relationship (QSAR)-based estimations from the EPA New Chemical Program's predictive methods; (2) analog data; (3) class-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 Program 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 (U.S. EPA, 2012c). Often analog data were used to support predictions from models. These approaches were described in the EPA Pollution Prevention (P2) Framework and Sustainable Futures (SF) program (U.S. EPA, 2005; 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 ACE acidity and basicity calculator website for dissociation constants) were used (ACE Organic 2013). 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 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, 2010c). The categories identify substances that share chemical and toxicological properties and possess potential health or environmental concerns (U.S. EPA, 2010a). 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 requirements 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 4.9. 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 without 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 preferred (Items 1 and 2 in the hierarchy list). Information from secondary sources such as Material Safety Data Sheets, or online databases (such as the National Library of Medicine's

Hazardous Substances Data Bank, 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 Polymers and Oligomers

The methodology and procedures used to assess polymers were slightly different than those used for oligomers, discrete compounds and simple mixtures. Although experimental data for polymers were identified using the literature search techniques discussed above in Section 4.2.1, in the absence of experimental data, estimates were performed using professional judgment as presented in the literature (U.S. EPA, 2010b). The polymers are a mixture of molecules with a distribution of components (e.g., different chain lengths) that depend on the monomers used, their molar ratios, the total number of monomeric units in the polymer chain, and the manufacturing conditions. To account for this variation, the average MW profile (also referred to as the number average molecular weight MW_n) was used in their assessment as the individual chains rarely have the same degree of polymerization and weight yet their physical, chemical, and environmental properties are essentially identical for the purposes of this assessment. The polymers evaluated as alternatives typically have average MWs ranging from >1,000 to <100,000 daltons.

For polymers with relatively low average MWs (i.e., those with average MWs generally less than 2,000), the alternative assessment also determined the amount of oligomers and unchanged monomers (starting materials) in the MW profile with MWs <1,000 daltons. Special attention was paid to materials that have a MW <1,000 daltons as these materials often have the highest hazard (potentially bioavailable substances) in the mixture. This type of assessment was similar to the evaluation of the hazards of impurities present in discrete chemical products. Methodological differences between the evaluation of discrete products and polymers are discussed in Section 4.3.

For the Alternatives Assessment, there were chemicals that are mixtures of low MW oligomers comprised of 2 or 3 repeating units. 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 by-products 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. 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 4.9. 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 Table 5-2.

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. Polymers and oligomers evaluated in this alternatives assessment were mixtures that contain a distribution of components and they may not have a unique MW (see also Section 4.2.3). To account for variation in these mixtures, the average MW or MW_n, determined experimentally (typically using high pressure liquid chromatography, viscosity, or light-scattering), was used in the assessment of polymers. The assessment of polymers also includes oligomers and unchanged monomers (starting materials) that have MW of <1,000 daltons as these were often the highest concern materials (bioavailable substances) in the mixture.

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 Chapter 5. 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 including polymers (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 1×10^{-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 1 x 10^{-4} mm Hg generally exist in the gas phase in the atmosphere. Substances with a vapor pressure between 1 x 10^{-4} and 1 x 10^{-8} mm Hg exist as a gas/particulate mixture. Substances with a vapor pressure less than 1 x 10^{-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 Earth's surface.

A maximum vapor pressure of 1 x 10^{-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, 2011e). The maximum vapor pressure of 1 x 10^{-8} mm Hg was also the default value reported for the vapor pressure of and other materials polymers with a MW >1,000 daltons (U.S. EPA, 2010b).

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 1 x 10^{-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: more than 10,000 mg/L was considered 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 less than 1 mg/L represents insoluble, noting that these guidelines might not match what is used elsewhere within the scientific literature for other disciplines. 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 un-dissolved 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 NES. An NES designation is equivalent to a low aquatic toxicity hazard designation for that endpoint.

While assessing the water solubility of a chemical substance, its potential to disperse in an aqueous solution was also considered. Ideally, a chemicals potential to disperse would be obtained from the scientific literature. In the absence of experimental data, the potential for dispersion 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 disperse 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 1×10^{-3} mg/L (U.S. EPA, 2011e). A water solubility of 1×10^{-3} mg/L is the default value used for discrete organics as well as non-ionic polymers with a MW >1,000 daltons according to information contained in the literature concerning polymer assessment (U.S. EPA, 2010b). This assignment is consistent with an analysis of the chemicals used in the development of the water solubility estimation program in EPA's EPISuite™ software. 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 4×10^{-7} mg/L (Meylan, Howard et al., 1996; U.S. EPA, 2011i). Given that water solubility decreases with MW, a default value of 1×10^{-3} mg/L is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons.

Octanol/Water Partition Coefficient (K_{ow})

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} 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. It 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 without data, that are not within the domain of EPISuite™ or that were expected to be insoluble in water (WS <1 x 10^{-3} mg/L), a minimum value of 10 was assigned for the log K_{ow} (U.S. EPA, 2011e). Insoluble chemicals that could be run through EPISuite™ software may use 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 ("training set") used in the development of the octanol/water partition coefficient estimation program in the EPISuite™ software. The training set for this model included 10,946 chemicals with a MW range 18-720 daltons and experimental log K_{ow} values 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. 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 non-flammable, 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 partitioning within environmental compartments and the amount of material removed by stripping in a sewage treatment plant. Henry's Law constant values less than 1×10^{-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 1×10^{-7} atm-m^3/mole) and values more than 1×10^{-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 1×10^{-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 (K_{oc})

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 unlikely to leach into ground water. 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, 2011e). A default K_{oc} of 30,000 was used for polymers and other materials with a MW >1,000 daltons.

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 4.3, 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 the importance of biodegradation 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 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 4.3. A default Very High persistence hazard designation was assigned for polymers and other materials with a MW >1,000 daltons according to information contained in the literature concerning polymer assessment (U.S. EPA, 2010b).

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 Table 4-2.

For acute mammalian toxicity the median lethal doses or concentrations 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, and not potency. The definitions applied in DfE criteria are based on International Agency for Research on Cancer 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 conclusions).

Similarly, the hazard designation for mutagenicity/genotoxicity was also based on the level of evidence rather than potency. Complete data requirements for this endpoint were 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 was considered and was evaluated using the developmental toxicity criteria, which are more stringent than the criteria for neurotoxicity, and thus designed to be 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[9] 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.

[9] 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).

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 U.S. EPA (1994). Public access to free validated quantitative SAR 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 subject matter 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.

Polymer Assessment

Estimates for polymers were obtained using information contained in the literature concerning polymer assessment based on the MW profile (U.S. EPA, 2010b). Those polymers with MW >1,000 were assessed using an appropriate representative structure that has a MW less than or equal to the average MW. For polymers with an average MW >1,000 daltons and a significant amount of low MW material <1,000 daltons, the low MW components were also assessed for their environmental fate and potential toxicity in order to identify any possible hazards for the most bioavailable fraction. Similarly, the presence of unreacted monomers requires that the assessment consider these components for polymers of any MW range. The properties for polymers with an average MW >1,000 with no low MW components were generally evaluated as a single high MW material for each of the properties described below. In general, polymers with an average MW >1,000 were not amenable to the available SAR estimation methods and based on the literature are assumed to have low to no bioavailability. Polymers with MW >1,000 that were not degradable or reactive are also typically not bioavailable. Polymers with an average MW >10,000 have potential for adverse effects due to lung overloading when respirable particles are present (less than ten microns). The potential for fibrosis or cancer are not assumed with high MW compounds. There may be exceptions to the rules of thumb outlined above and as such this guidance should not be held as absolute thresholds.

Polymers and oligomers with MWs <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 those employed for the evaluation of impurities or by-products 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.

4.5 Evaluating Environmental Toxicity and Fate 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 Aquatic Toxicity

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
- 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 reported in the alternatives assessment also included information on the species tested. Test data on other organisms (e.g., worms) were included in the assessment if data were readily available. These data would be evaluated using professional judgment to support hazard designations assigned using the three surrogate species; however, they were not used by themselves to assign a hazard designation as DfE criteria are not available. Poorly soluble substances where the water column exposures may not be adequate to describe sediment and particulate exposures will be identified by a footnote.

If an experimental or estimated effect level exceeded the known water solubility of a chemical substance, or if the log K_{ow} exceeded the estimated ECOSAR™ cut-off values for acute and chronic endpoints (which are class specific), NES were predicted for the aquatic toxicity endpoints. NES indicates that at the highest concentration achievable, 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.

EPA's ECOSAR™ estimation program uses chemical structure to estimate toxicity of a chemical substance using class-specific QSARs. ECOSAR™ automatically determines all of the classes that a chemical substance may belong to and, therefore, may provide a number of different ecotoxicity estimates for some or all of the species and durations estimated. Modeled results are dependent on the functional groups present on the molecule as well as the diversity of chemicals with experimental data that were used to build the models (their training set). The hazard profiles report every estimated value returned from ECOSAR™. Narcosis classes (neutral organics) are only provided for comparative purposes if class-specific QSARs are available; the latter will be used preferentially. If multiple class-specific QSARs are available, the hazard designation was based on the most conservative ECOSAR™ estimate, unless expert judgment suggested that an individual substance was better represented by a specific class based on analysis of the operative mode of action. However, if the chemical substance is not anticipated to lie within the domain of the class-specific estimates provided by ECOSAR or to undergo the same mode of action of the chemicals that appear in their training sets, then 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 but is also accessible through the EPA EPISuite™ program after it is installed; therefore the Estimations Program Interface (EPI) program was cited for the ECOSAR™ values in this report.

The QSARs for ECOSAR™ were built using experimental data for several chemical classes. For a chemical class to be defined within ECOSAR™, sufficient acute experimental data were required to build a QSAR for all three species included in the model. The equations in ECOSAR 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 estimates of toxicity to the general trophic levels they represent (fish, aquatic invertebrates, and aquatic plants). There were instances, however, where sufficient experimental data are 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 (Mayo-Bean, Nabholz et al., 2011).

An estimate of NES is the default value used for organics, oligomers, or non-ionic polymers with a MW >1,000 daltons in the assignment of aquatic toxicity hazard. In EPA's New Chemical program, aquatic toxicity is not predicted for chemicals with a MW >1,000 daltons as uptake has been found to decrease exponentially with MWs >600 daltons (Nabholz, Clements et al., 1993)

due to a decrease in passive absorption through respiratory membranes (Mayo-Bean, Nabholz et al., 2011).

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 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 BCFs are more commonly used to evaluate the bioaccumulation hazard. BCFs are defined as the ratio of the concentration of a chemical in an organism to the concentration of the chemical in the organism's surroundings; 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/BAF designations range from <100 for a Low designation to >5,000 for a Very High designation (see 4.1.2). 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 if 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 discrete 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 will use all available well-conducted studies when

evaluating bioaccumulation potential for materials with a MW >1,000, including environmental biomonitoring data on higher trophic levels.

In general, for polymers and other materials with a MW >1,000 daltons, the default bioaccumulation designation of Low was assigned, arising from their predicted limited bioavailability (U.S. EPA, 2010b). A more detailed analysis was performed for compounds at or near this bright line cutoff as well as for polymers with components where residuals <1,000 had the potential to be present.

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 estimated, and the resulting half-lives can be compared directly to DfE criteria. For commercial chemicals, hydrolysis tends to be a slower environmental removal process than biodegradation. Direct and indirect photolysis also represents other potential chemical degradation processes that are considered in the alternative assessment, and they are discussed later in this section.

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, and mineral oxides (such as phosphates for chemicals containing phosphorus). 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 generally assessed in sediment. For determining the persistence hazard, 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 (E_h). 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 as 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 percent. The 10-day window must occur within the 28-day length of the test. If the pass level of the test (60 percent for oxygen demand and CO_2 production; 70 percent for dissolved organic carbon disappearance) is 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 percent removal in 30 days would be expected to have a half-life >60 days and would be assigned a High persistence concern.

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 estimated 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. 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 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, which 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 indicate the potential for the material to partition to sediment, an anoxic compartment, then the results of the anaerobic probability model (Biowin 7) will also be 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 an important 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.

Chemicals that contain a metal were assigned a High persistence designation in the assessment, as these inorganic moieties are recalcitrant. In this instance, an ‘R’ footnote was added to the hazard summary table to indicate that the persistence potential was based on the presence of a recalcitrant inorganic moiety. The assessment process also included the evaluation of the potential chemical reactions of metal-containing and inorganic moieties to determine if they were potentially transformed to more or less hazardous forms.

Polymers with a MW >1,000 generally received a Very High persistence designation due to their lack of bioavailability.

4.6 Endocrine Activity

Chemicals included in DfE alternatives assessments were screened for potential endocrine activity, consistent with the *DfE Program Alternatives Assessment Criteria for Hazard*

Evaluation. **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 4.9. Data on endocrine activity were available for two of the alternatives included in this report. For chemicals without available data on endocrine activity, this was acknowledged with a "no data located" statement. When endocrine activity data were available, the data are summarized as a narrative. A unique hazard designation of Low, Moderate or High is not provided for this endpoint in Table 4-2, 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 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[10]. 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.

[10] 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.

To assess the data on endocrine activity, DfE applies the weight-of-evidence approach developed by the EDSP (U.S. EPA, 2011c). 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 endocrine, 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 Program Alternatives Assessment Criteria for Hazard Evaluation*, 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 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 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 U.S. 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 U.S. 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 U.S. 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 References

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4.8 Hazard Summary Table

Table 4-4. Screening Level Hazard Summary for Reactive-Flame Retardant Chemicals & Resins

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

♦ TBBPA has been shown to degrade under anaerobic conditions to form bisphenol A (BPA; CASRN 80-05-7). BPA has hazard designations different than TBBPA, as follows: MODERATE (experimental) for reproductive, skin sensitization and dermal irritation. [§] Based on analogy to experimental data for a structurally similar compound. [‡]The highest hazard designation of any of the oligomers with MW <1,000. [¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

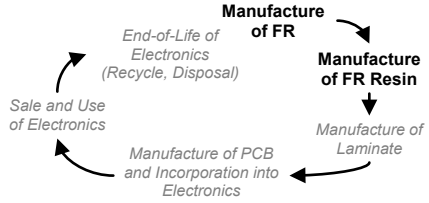
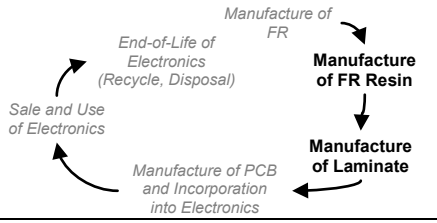
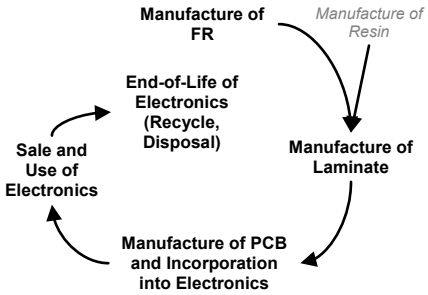
Chemical (for full chemical name and relevant trade names see the individual profiles in Section 4.9)	CASRN	Human Health Effects											Aquatic Toxicity		Environ-mental Fate		Exposure Considerations
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation	Availability of flame retardants throughout the life cycle for reactive and additive flame-retardant chemicals and resins
Reactive Flame-Retardant Chemicals																	
Tetrabromobisphenol A	79-94-7	L	M	L	L♦	M	L	L	L♦		M	L♦	VH	H	H	M	
DOPO	35948-25-5	L	*M*	L	*L*[§]	*M*	*M*	L	M		M	VL	L	*M*	*H*	*L*	
Fyrol PMP	63747-58-0	L	*L*[§]	*L*[§]	*M*[§]	*M*[§]	*M*[§]	*M*[§]	L		L	L	*H*[‡]	*H*[‡]	*VH*	*H*[‡]	
Reactive Flame-Retardant Resins																	
D.E.R. 500 Series[¥]	26265-08-7	*L*	*M*	*M*	*M*	*M*	*M*	*M*	H		*M*[‡]	*M*[‡]	*L*	*L*	*VH*	*H*[‡]	
Dow XZ-92547[¥]	Confidential	L	*M*[‡]	*M*[§]	*M*[‡]	*M*[‡]	*M*[‡]	*M*[‡]	H	*M*[‡]	VL	L	*L*	*H*	*VH*	*H*[‡]	

Table 4-5. Screening Level Hazard Summary for Additive Flame-Retardant Chemicals

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[R] Recalcitrant: Substance is comprised of metallic species (or metalloids) that will not degrade, but may change oxidation state or undergo complexation processes under environmental conditions. [§] Based on analogy to experimental data for a structurally similar compound. [¤]Concern linked to direct lung effects associated with the inhalation of poorly soluble particles less than 10 microns in diameter. [^] Depending on the grade or purity of amorphous silicon dioxide commercial products, the crystalline form of silicon dioxide may be present. The hazard designations for crystalline silicon dioxide differ from those of amorphous silicon dioxide, as follows: VERY HIGH (experimental) for carcinogenicity; HIGH (experimental) genotoxicity; MODERATE (experimental) for acute toxicity and eye irritation. [¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical (for full chemical name and relevant trade names see the individual profiles in Section 4.9)	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate		Exposure Considerations
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation	Availability of flame retardants throughout the life cycle for reactive and additive flame-retardant chemicals and resins
Additive Flame-Retardant Chemicals																	
Aluminum Diethylphosphinate[¥]	225789-38-8	L	*L*[§]	L	L	*M*[§]	*M*[§]	*M*[§]	L		L	VL	M	M	*H*[R]	*L*	
Aluminum Hydroxide[¥]	21645-51-2	L	*L*[§]	L	*L*[§]	L	M	*M*[§]	L		VL	VL	L	L	*H*[R]	*L*	
Magnesium Hydroxide[¥]	1309-42-8	L	L	L	L	L	*L*	L	L		M	L	*L*	*L*	*H*[R]	*L*	
Melamine Polyphosphate[1¥]	15541-60-3	L	*M*	*M*	*H*	*M*	*M*	*M*	*L*		L	VL	L	L	*H*	*L*	
Silicon Dioxide (amorphous)	7631-86-9	L[^]	L[^]	L[^]	L	L	*L*[§]	H[¤]	L		L[^]	VL	L	*L*	*H*[R]	*L*	

[1] Hazard designations are based upon the component of the salt with the highest hazard designation, including the corresponding free acid or base.

4.9 Hazard Profiles

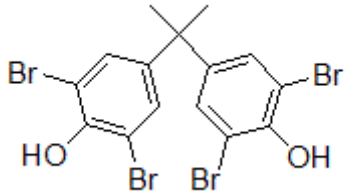
Tetrabromobisphenol A

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

♦ TBBPA has been shown to degrade under anaerobic conditions to form bisphenol A (BPA; CASRN 80-05-7). BPA has hazard designations different than TBBPA, as follows: MODERATE (experimental) for reproductive, skin sensitization and dermal irritation.

		Human Health Effects											Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Tetrabromobisphenol A	79-94-7	L	M	L	L♦	M	L	L	L♦		M	L♦	VH	H	H	M

Tetrabromobisphenol A



CASRN: 79-94-7

MW: 543.88

MF: $C_{15}H_{12}Br_4O_2$

Physical Forms: Solid
Neat: Solid

Use: Flame retardant

SMILES: Oc(c(cc(c1)C(c(cc(c(O)c2Br)Br)c2)(C)C)Br)c1Br

Synonyms: Tetrabromobisphenol A; TBBPA; TBBP-A; 4,4'-Isopropylidenebis(2,6-dibromophenol); 2,2-bis(3,5-dibromo-4-hydroxyphenyl) propane; 3,3',5,5'-tetrabromobisphenol-A; phenol, 4,4'-isopropylidinebis, (dibromo-); 4,4'-(1-methylethylidene)bis(2,6-dibromophenol); 2,2',6,6'-Tetrabromobisphenol A; 2,2-Bis(3,5-dibromo-4-hydroxyphenyl)propane; 2,2-Bis(4-hydroxy-3,5-dibromophenyl)propane

*Trade names:*BA-59P; F-2016; F-2400; F-2400E; FR-1524; Fire Guard FG2000; Firemaster BP 4A; Saytex RB-100; Saytex RB 100PC; Tetrabrom; Tetrabromodian; Bromdian

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v 4.11 was used to estimate physical/chemical and environmental fate values in the absence of experimental data. Measured values from experimental studies were incorporated into the estimations. TBBPA is produced by bromination of bisphenol A (BPA). (HSDB, 2013).

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: TBBPA-glucuronic acid conjugates (mono, di and a mixed glucuronide-sulfate conjugate); TBBPA-sulfate ester conjugates; tribromobisphenol A and glucuronide of tribromobisphenol A were identified as metabolites in experimental studies.

4-isopropyl-2,6-dibromophenol, 4-isopropylene-2,6-dibromophenol and 4-(2-hydroxyisopropyl)-2,6-dibromophenol were identified as major degradation products by UV light photolysis; other reported products include di- and tribromobisphenol A, dibromophenol, 2,6-dibromo-4-(bromoisopropylene)phenol, 2,6-dibromo-4-(dibromoisopropylene)phenol and 2,6-dibromo-1,4-hydroxybenzene. Polybrominated dibenzofurans (PBDF) and dibenzodioxins (PBDD) were identified by pyrolytic degradation. Debromination of TBBPA to tribrominated-BPA, dibrominated-BPA and BPA has been demonstrated in experimental anaerobic biodegradation studies. (Eriksson and Jakobsson, 1998; Eriksson et al., 2004; Ravit et al., 2005; EU, 2006; ACC, 2006b; Roper et al., 2007; Environment Canada, 2013; NTP, 2013)

Analog: None

Analog Structure: Not applicable

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

Risk Phrases: 50/53 - Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment (ESIS, 2012).

Hazard and Risk Assessments: Risk assessments were completed for TBBPA by the European Union in 2006 and Canada in 2013. (EU, 2006; Environment Canada, 2013).

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PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	179 (Measured)	Ashford, 1994; HSDB, 2013	Reported in a secondary source.
	181 Reported as a range 181-182°C (Measured)	EU, 2006	Study details and test conditions were not stated.
	178 (Measured)	EU, 2006	Reported in a secondary source. Details and test method were not stated.
	181 (Measured)	WHO, 1995; ACC, 2006b	The measurement was performed on a commercial product which was not 100% pure.
	178.35 Reported as 451.5 ± 0.5 K using differential scanning calorimeter (Measured)	Kuramochi et al., 2008	Adequate study details provided. Consistent with other reported values.
Boiling Point (°C)	316 Decomposes (Measured)	Stenger, 1978; WHO, 1995	TBBPA will decompose before boiling based on measurements on a commercial product, which may not have been 100% pure.
	>300 (Estimated)	EPI v4.11; EPA, 1999	Cutoff value for high boiling materials according to HPV assessment guidance.
Vapor Pressure (mm Hg)	$4.7x10^{-8}$ at 25°C Reported as $6.24x10^{-6}$ Pa (Measured)	BRE, 2009	Valid study with limited details reported.
	$<8.9x10^{-8}$ at 20°C Organisation for Economic Co-operation and Development (OECD) Guideline 104 "Vapor Pressure Curve" Spinning rotor gauge method; reported as $<1.19x10^{-5}$ Pa (Measured)	Lezotte and Nixon, 2001 (as cited in EU, 2006; ACC, 2006b)	Value reported is based on the limit of quantification of the method. The vapor pressure was below the limit of quantification of the method.
	$3.54x10^{-11}$ Reported as $4.72x10^{-9}$ Pa at 298K using Knudsen effusion method (Measured)	Kuramochi et al., 2008	Adequate study details provided.
	<1	WHO, 1995; Hardy and Smith,	Sufficient study details were not

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	(Measured)	1999	available to assess the quality of this study.
Water Solubility (mg/L)	4.16 (Measured)	Danish EPA, 1999	Limited study details provided.
	0.171 ±0.004 at pH 3.05 4.15 ±0.36 at pH 7.56 30.5 ±1.8 at pH 7.99 228 ±6 at pH 8.48 1,510 ±60 at pH 8.91 27,900 ±400 at pH 9.50 (Measured)	Kuramochi et al., 2008	Reported in a primary source; demonstrates the relationship between the pH conditions and the water solubility of TBBPA as an ionized and non-ionized compound.
	0.72 at 15°C 4.16 at 25°C 1.77 at 35°C (Measured)	WHO, 1995	Study details and test conditions were not available. The original study was in an unpublished report submitted to the WHO.
	0.082 at pH 7.6-8.1 (Measured)	Submitted confidential study (as cited in NOTOX, 2000)	The measured water solubility was dependent on the flow rates through the column. The cause of the flow rate dependency is unknown. The flow rate dependency is not caused by a failure to reach equilibrium, since higher flow rates gave higher solubility. The samples were centrifuged to remove dispersed TBBPA.
	0.148 at pH 5 1.26 at pH 7 2.34 at pH 9 (Measured)	Submitted confidential study (as cited in MacGregor and Nixon, 2002; EU, 2006)	Submitted confidential study. The samples were not assessed for the presence of colloidal material before analysis.
Log K_{ow}	4.54 (Measured)	EU, 2006	Reported in a secondary source.
	Generator column method used to evaluate D_{ow}: pH 3.05 = 6.53 ±0.12 (considered non-ionic form) pH 7.53 = 4.75 ±0.07	Kuramochi et al., 2008	Reported in a primary source; demonstrates the relationship between the pH conditions and the octanol-water partition coefficient (log K_{ow}) of TBBPA as an ionized

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	pH 8.12 = 3.00 ±0.03 pH 9.18 = 1.25 ±0.01 pH 10.19 = -0.293 ±0.020 pH 10.95 = -0.769 ±0.023 pH 11.83 = -1.22 ±0.00 (Measured)		and non-ionized compound.
	4.5 (Measured)	Danish EPA, 1999	Valid study reported in a secondary source.
	<4 (Measured)	EU, 2006	Reported in a secondary source. Study details and test conditions were not available.
	6.4 HPLC method (Measured)	EU, 2006	Reported in a secondary source. Limited study details available.
	3.25 (Measured)	EU, 2006	Reported in a secondary source.
	5.903 Reported as 5.90 ± 0.034; method based on USEPA Product Properties Test Guideline OPPTS 830.7560. (Measured)	MacGregor and Nixon, 2001 (as cited in EU, 2006)	Reported in secondary source.
	5.3 Reported as a range: 4.5-5.3 (Measured)	WHO, 1995	Study details and test conditions were not available.
Flammability (Flash Point)	Not flammable (Measured)	ICL, 2013	Reported in safety datasheet and based on its use as a flame retardant.
Explosivity	Dust Explosivity: Maximum Explosion Pressure (P_{max}) = 7.7 bar; Maximum Rate of Pressure Rise (dP/dt)max = 379 bar/s; K_{st} value = 103 bar.m/s (weak explosion) (Measured)	Churchwell and Ellis, 2007	Adequate supporting information provided.

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Pyrolysis	Under certain high temperature pyrolysis conditions, TBBPA can form and release brominated dibenzofurans (PBDF) and dibenzo-p-dioxins (PBDD). (Measured)	EU, 2006	Adequate.
	Purified TBBPA was pyrolyzed in open quartz tubes for 10 minutes resulting mainly in mono-, di-, tri- and tetra-PBDD and PBDF. The formation of PBDD and PBDF occurred at 0.02, 0.16, and 0.1% for 700, 800, and 900°C. (Measured)	WHO, 1995	Adequate.
pH			No data located.
pK_a	9.4 Method based on OECD Guideline 112. (Measured)	Lezotte and Nixon, 2002; EU, 2006; ACC, 2006b	Adequate guideline study.
	pK_{a1} = 7.5 pK_{a2} = 8.5 (Measured)	WHO, 1995; EU, 2006	Study details and test conditions were not available. Reported in a secondary source.
Particle Size			No data located.

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HUMAN HEALTH EFFECTS				
Toxicokinetics		**A laboratory study using human skin indicates TBBPA is not well absorbed dermally. The results indicated 0.73% of the applied dose penetrated through the skin. Oral administration to rats showed that TBBPA is rapidly metabolized and eliminated in the feces (>80%). TBBPA and metabolites were detected in plasma and traces of TBBPA and metabolites were detected in urine (glucuronic acid and sulfate ester conjugates). The estimated bioavailability following oral dosing is 1.6%. Human volunteers had no detectable TBBPA in plasma following ingestion of low doses; however, TBBPA metabolites (TBBPA-glucuronide, TBBPA-sulfate) were detected. TBBPA-glucuronide (25% of the administered dose) was the only metabolite detected in the urine. TBBPA has been detected in breast milk; although a study in pregnant rats indicates that there is no significant transfer of TBBPA or its metabolites to the fetus (total amount of radioactivity in the fetus was approximately 0.34% of the administered dose).**		
Dermal Absorption *in vitro*		Human split-thickness skin: Absorbed dose = 0.73% applied dose (14.06 µg/cm^2); Dermal delivery = 1.60% applied dose (32.05 µg/cm^2)	Roper, 2005; Roper et al., 2007	Sufficient study details reported in primary source.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Distribution of TBBPA and its conjugates was observed in pregnant rats fed 0, 100, 1,000 or 10,000 ppm from gestational day (GD) 0-16. Free-TBBPA detected in blood, liver and kidney of dams and amniotic fluid on GD10 and in the placenta and amniotic fluid in fetuses on GD16. Free-TBBPA was also found in the stomach of suckling pups from dams in the high dose group. Conjugated TBBPA was detected in the liver and kidney and suckling pups.	Fujitani et al., 2007	Insufficient study details; study is in Japanese with English abstract.
		Male rats exposed to TBBPA via i.v. injection (20 mg/kg), single oral bolus (2, 20 or 200 mg/kg) or repeated daily oral doses (20 mg/kg for 5-10 days). TBBPA is absorbed from the intestinal tract, but is extracted and metabolized by the liver to glucuronides that are exported into the bile.	Solyom et al., 2006	Sufficient study details reported in primary source.

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		Intravenous injection: half-life in blood was 82 minutes at a clearance rate of 2.44 mL/min. Major route of elimination was the bile/feces; 82% eliminated within 36 hours; 0.5% eliminated in the urine. Single oral bolus: 90-106% eliminated in feces within 72 hours; 2% in urine. Repeated dose: 85-98% eliminated in feces		
		In an intraperitoneal injection study in rats, peak concentrations of ^{14}C-TBBPA were found in all tissues within an hour; highest concentrations found in fat followed by the liver, sciatic nerve, muscles, and adrenals. A small amount of the administered dose was retained after 72 hours in fatty tissue and muscle (3-6% and 11-14%, respectively). It has also been observed that unmetabolized TBBPA is rapidly excreted in feces (51-95% of the administered dose) following single exposure (route not specified).	Birnbaum and Staskal, 2004	Adequate study details reported in a secondary source.
		The half-life of TBBPA was estimated to be 2 days in Swedish workers engaged in the recycling process.	Sjodin et al., 2003	Adequate study details reported in a secondary source.
		TBBPA was poorly absorbed in the gastrointestinal tract in rats following single oral administration. Approximately 95% of the administered dose was eliminated in feces and <1% was eliminated in urine within 72 hours. Levels in tissues were highest in the liver and gonads. The maximum half-life in	WHO, 1995	Summary information from an unpublished study.

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		any tissue was <3 days.		
		Placental transfer of hydroxylated BFRs was observed in rats orally dosed with test compounds (including TBBPA) on gestation days (GDs) 10-16. There were no associated developmental effects at the dose used in the study (25 mg/kg).	Buitenhuis et al., 2004	Sufficient study details reported in primary source.
		TBBPA has been detected in breast milk, although a study in pregnant rats indicates that there is no significant transfer of TBBPA or its metabolites to the fetus (total amount of radioactivity in the fetus was approximately 0.34% of the administered dose).	EU, 2006	Summary of various studies in a secondary source.
		Only an extremely small percentage of TBBPA particles are expected to be small enough (1-2 µm) to be deposited into the rat lung following inhalation. Particles that do not reach the alveolar region are expected to be exhaled. The remainder will deposit in the respiratory tract, will be swallowed and absorbed by the gastrointestinal tract (70% absorbed by gastrointestinal tract, <4% absorbed through the lungs).	EU, 2006	General information summarized in a secondary source.
		Recovery of TBBPA (measured as radioactivity) following single oral administration to rats: Feces: 90-95% Urine: <1% Tissues: 0.4% (Measured) Recovery of TBBPA (measured as radioactivity) following repeated oral administration to rats (1, 5 or 10 days): Feces: 82-98%	ACC, 2006b; Kuester et al., 2007	Sufficient study details reported in primary source.

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		Urine: <0.5% Tissues: <1% Unexcreted intestinal contents: 1-10%. The rats were sacrificed 24 hours after the last dose. (Measured) Following oral administration of ^{14}C-TBBPA to rats, 47% and 51% of the dose was excreted in the bile within 2 hours, primarily as 2 metabolites: TBBPA-glucuronide and TBBPA-diglucuronide. Estimated systemic bioavailability after oral dosing: 1.6%		
		In a single dose study in rats, TBBPA was rapidly metabolized following oral administration of 300 mg/kg. Primary metabolites were TBBPA-glucuronide and TBBPA-sulfate. Diglucuronide of TBBPA (a mixed glucuronide-sulfate conjugate of TBBPA), tribromobisphenol A, and the glucuronide of tribromobisphenol A were also present in low concentrations. A peak plasma concentration of 103 µmol/L was achieved within 3 hours with an elimination half-life of 13 hours. Fecal excretion of unchanged TBBPA was the major excretory pathway with (>80%).	Schauer et al., 2006 (as cited in ACC, 2006b)	Sufficient study details reported in primary source.
		In a single dose study in humans (3 males, 2 females), TBBPA was rapidly metabolized following oral administration via gel capsule of 0.1 mg/kg. Primary metabolites were TBBPA-glucuronide and TBBPA-sulfate. Only TBBPA-glucuronide was detected in the urine; approximately 25% of the administered	Schauer et al., 2006 (as cited in ACC, 2006b)	Sufficient study details reported in primary source.

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		dose was eliminated in urine.		
		In a single oral dose and bile-cannulated rat study, TBBPA was readily absorbed, metabolized and eliminated within 72 hours after dosing of male Sprague-Dawley rats. Excretion in oral dosing study: 91.7% in feces, 0.3% in urine. Residue in tissue was 2% of dose (Primarily large and small intestines). Excretion in bile-duct cannulated rat: 26.7% in feces, 71.3% in bile, <1% residue in tissues. Primary metabolites: Glucuronic acid and sulfate ester conjugates. Over 95% of extractable fecal ^{14}C was parent TBBPA.	Hakk et al., 2000 (as cited in ACC, 2006b; EU, 2006; NTP, 2013)	Sufficient study details reported in primary source.
		Rapid clearance of [^{14}C]-labeled TBBPA from the blood of male F344 or female Wistar Han rats; single oral or intravenous administration. T_{max} of ^{14}C in blood was observed at 32 ± 19 minutes in male rats (200 mg/kg fasted) and 114 ± 42 minutes in females (250 mg/kg nonfasted). Terminal half-lives were > 5 hours and systemic bioavailability was < 5%.	Knudsen et al., 2013 Kuester et al., 2007 (as cited in NTP, 2013)	Sufficient study details reported in NTP technical report.
		No accumulation of TBBPA in tissues of male Sprague-Dawley rats receiving 1,000 mg/kg for 14 consecutic ve days.	Kang et al., 2009 (as cited in NTP, 2013)	Sufficient study details reported in NTP technical report.
	Other	TBBPA was present in breast milk, and both maternal and fetal serum samples in two studies, indicating a possible risk of overexposure of newborns through breastfeeding.	Antignac et al., 2008; Cariou et al., 2008	Sufficient information in primary sources.
		In bile-cannulated rats, 71% of administered TBBPA was excreted in the	Birnbaum and Staskal, 2004	Sufficient information in review.

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		bile. Metabolites found in bile were a diglucuronide, a monoglucuronide, and a glucuronide-sulfate ester.		
Acute Mammalian Toxicity		**LOW: Experimental studies indicate TBBPA, administered orally to rats and mice at levels up to 50,000 and 10,000 mg/kg, respectively, and TBBPA administered dermally to rabbits at levels up to 10,000 mg/kg does not produce substantial mortality. Data from located inhalation studies are not sufficient to consider for the hazard designation.**		
Acute Lethality	**Oral**	Rat oral LD_{50} >50 mg/kg (range finding study in rats (2 rats/group) administered 0.5 - 50 mg/kg)	Sterner, 1967c	Limited study details reported in an unpublished study.
		Rat oral LD_{50} >2,000 mg/kg - >50,000 mg/kg	Doyle and Elsea, 1966; WHO, 1995; EU, 2006	Sufficient study details reported.
		Mouse oral LD_{50} 3,200 mg/kg - >10,000 mg/kg	Dean et al., 1978b (as cited in WHO, 1995; EU, 2006)	Limited information in secondary sources. Sufficient information in unpublished study.
		Rat oral LD_{50} >5,000 mg/kg	Mallory et al., 1981b (as cited in EU, 2006; ECHA, 2013)	Sufficient data in unpublished study conducted in accordance with good laboratory practices (GLP).
		Mouse oral LD_{50} >7,000 mg/kg	ECHA, 2013	Pre-dates standard guidelines and GLP; no analytical verification of test material; unequal amounts of vehicle administered; no vehicle control.
		Mouse oral LD_{50} >10,000 mg/kg	ECHA, 2013	Pre-dates standard guidelines and GLP; no analytical verification of test material; unequal amounts of vehicle administered; no vehicle control.
	Dermal	Rabbit dermal LD_{50} >2,000 mg/kg	WHO, 1995	Limited study details reported in a secondary source.
		Guinea pig dermal LD_{50} >1,000 mg/kg	WHO, 1995	Limited study details reported in a secondary source.
		Rabbit dermal LD_{50} >2 g/kg (2,000 mg/kg)	ECHA, 2013	Sufficient information in an unpublished study conducted in

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				accordance with GLP.
		Rabbit dermal LD_{50} >10,000 mg/kg	Doyle and Elsea, 1966 (as cited in EU, 2006; ECHA, 2013)	Sufficient study details reported in unpublished studies.
	Inhalation	Rat, mouse, guinea pigs 8-hour aerosol inhalation $LC_{50} \geq 0.5$ mg/L (whole-body, aerosol)	Sterner, 1967b (as cited in EC, 2000; EU, 2006)	Inadequate unpublished study, due to short observation period (2 days) and because the particle size of the aerosol was not measured.
		Rat 1 hour inhalation LC_{50} >57 mg/L (whole body, vapor)	ECHA, 2013	No GLP data; methodology predates or was not conducted according to standardized guidelines; no analytical verification of test compound concentrations.
		Rat 1-hour inhalation LC_{50} >1,267 ppm (whole-body)	Doyle and Elsea, 1966 (as cited in EU, 2006)	Inadequate, methodological deficiencies (lack of analysis of the test atmosphere and stability of the test compound) raise uncertainties as to the reliability of this study.
Carcinogenicity		**MODERATE: There is evidence of increased incidences of tumors of the uterus in female rats and interstitial cell adenoma of the testes in male rats orally exposed to TBBPA for up to 105 weeks. There were also increased incidences of tumors in male mice (hepatoblastoma and combined incidence of hepatocellular carcinoma or hepatoblastoma of the large intestine and hemangiosarcoma in all organs); however, there was no evidence of carcinogenicity reported in female mice. In addition, a marginal concern was estimated based on structure-activity relationships and functional properties. The mechanism of action of TBBPA carcinogenicity is not clearly understood. While there was some evidence of carcinogenicity in animals (in male and female rats and male mice, but not in female mice), there is inadequate evidence of carcinogenicity in humans.**		
	OncoLogic Results	Marginal; likely to have equivocal carcinogenic activity.	OncoLogic, 2008	Estimated by OncoLogic based on structure-activity relationships and functional properties.
	Carcinogenicity (Rat and Mouse)	2-year oral gavage carcinogenicity study; B6C3F1/N mice (50/sex/dose) were administered 0, 250, 500, or 1,000 mg/kg-day 5 days/week for up to 105 weeks. Survival was decreased at 1000 mg/kg-day, and therefore, effects are not reported	NTP, 2011; NTP, 2012; NTP, 2013	Sufficient study details reported.

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		for this dose. There was an increase in incidence of multiple hepatocellular adenomas in male mice in the 500 mg/kg-day dose group. Increased incidence of hepatoblastoma and combined incidence of hepatocellular carcinoma or hepatoblastoma were reported in male mice in the 250 mg/kg-day dose group when compared to controls. Also, a significant increased positive trend in the incidence of adenoma or carcinoma (combined) was seen in the large intestine in males. In addition, there was a significant trend for increased incidence of hemangiosarcoma in all organs in male mice. There was no evidence of carcinogenicity in female mice.		
		2-year oral gavage carcinogenicity study; Wistar Han rats (50 or 60/sex/dose) were administered 0, 250, 500, or 1,000 mg/kg-day 5 days/week for up to 105 weeks. There was a slight increase in incidence of interstitial cell adenoma of the testis in male rats (1/50 at 500 mg/kg-day; 3/50 at 1,000 mg/kg-day) as compared to controls (0/50). There was a significant increase in the incidences of adenomas and carcinomas of the uterus in female rats at 500 and 1,000 mg/kg-day compared to controls. There was also an increased combined incidence of adenoma, adenocarcinoma, and malignant mixed Mullerian tumor of the uterus at these dose groups (3/50, 7/50, 11/50, 13/50 in the 0, 250, 500, and 1,000 mg/kg-day	NTP, 2013	Sufficient study details reported.

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		groups, respectively).		
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	Negative in a tumor promotion study in male F344 rats exposed *in utero* and directly via drinking water for 2 weeks after weaning.	CCRIS, 2013	Limited study details reported in a secondary source.
Genotoxicity		**LOW: Experimental studies indicate that TBBPA is not genotoxic to bacterial, mammalian, or yeast cells *in vitro*. TBBPA was negative in a micronucleus test in mice *in vivo*.**		
	Gene Mutation *in vitro*	Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535, or TA1537, or *E. coli* strain WP2 *uvr*A/pKM101, with or without metabolic activation.	NTP, 2013	Sufficient study details reported in NTP technical report.
		Negative, several Ames assays in *Salmonella typhimurium* strains TA92, TA98, TA100, TA1535, TA1537 and TA1538 with and without metabolic activation. Positive controls responded as expected.	Brusick and Weir, 1976; Jagannath and Brusick, 1977; Simon et al., 1979; Curren et al., 1981; WHO, 1995; EC, 2000; Darnerud, 2003; EU, 2006	Sufficient information in secondary sources and unpublished reports.
		Negative, several gene mutation assays in yeast (*Saccharomyces cerevisiae* D3 and D4) with and without metabolic activation. Positive controls responded as expected.	Brusick and Weir, 1976; Jagannath and Brusick, 1977; Simon et al., 1979; WHO, 1995	Sufficient information in secondary sources and unpublished reports.
		Negative, induction of intragenic recombination in two *in vitro* mammalian cell assays. No information was provided regarding positive controls.	Simonsen et al., 2000; Darnerud, 2003	Limited data in secondary sources.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative, chromosomal aberration in human lymphocytes. Positive controls responded as expected.	Gudi and Brown, 2001 (as cited in EU, 2006)	Sufficient information in primary source.

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	Chromosomal Aberrations *in vivo*	No increases in micronucleated normochromatic erythrocytes in B6C3F1/N mice administered TBBPA via oral gavage for 3 months.	NTP, 2013; NTP, 2012	Sufficient study details reported in NTP technical report.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: Experimental studies indicate TBBPA, administered orally to rats, produces no adverse effects on reproductive performance or outcomes at levels up to 3,000 mg/kg-day. In some studies there were changes in testis weights at low doses; the significance of these changes on testicular function is unclear given the limitations of the studies.**		
	Reproduction/Developmental Toxicity Screen	In a dietary study, pregnant rats (8/group) were fed 0, 100, 1,000, or 10,000 ppm (~17, 149, and 1,472 mg/kg-day) TBBPA (>98% pure) on GD 10 until day 20 after delivery. There was no evidence of maternal toxicity during the study. Treatment with TBBPA did not affect the number of implantation sites. No other reproductive endpoint was assessed. NOAEL: 10,000 ppm (~1,472 mg/kg-day, highest dose tested) LOAEL: Not established	Saegusa et al., 2009	Sufficient study details reported in primary source, but limited reproductive data. Doses are TWA for mean intakes of TBBPA during GD 10-20, PND 1-9, and post natal days [PND10-20) estimated by the investigators.
		In a dietary study, rats (8-13 males and 6-10 females/group) were fed 0, 3, 10, 30, 100, 300, 1,000 and 3,000 mg/kg-day TBBPA (98% pure) for 11 weeks (males) or 2 weeks during premating and throughout pregnancy and lactation (females). Dosing continued in F_1 offspring after weaning until necropsy at approximately 6 weeks of age. Decreased body weight in dams at highest dose. No adverse effect on number of litters, number of implantation sites or number of	Van der Ven et al., 2008	Sufficient details provided in the primary source. Doses were estimated by the investigators. As stated in the study, dose-response analysis of effects based on external dosing (mg/kg-day) was done using a nested family of purely descriptive (exponential) models with the PROAST software. The method enables integrated evaluation of the complete data set. From the best fitted curve, indicated by

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		pups per litter. Increased testicular and pituitary gland weights in F_1 males (with BMDL values of 0.5 and 0.6 mg/kg-day). No other effect on F_1 gonads wes seen. Other reproductive-related effects in offspring were seen only at high doses (e.g., decrease in anogenital distance in females seen at day 7 only but not at day 4 or day 21; number of days until vaginal opening). BMDLs for these effects are 2736 and 2745 mgkg-day, respectively.		significance at the 5% level, a critical effect dose (CED) was calculated most often using a critical effect size of 10%; there has been some criticism of the modeling and methodology used for this study along (Banasik et al. 2009).
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	20-Week, 2-generation reproductive assay, rats (30/sex/group), administered TBBPA via oral gavage at 0, 10, 100 or 1,000 mg/kg-day. No effects on reproductive performance or outcomes. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	ACC, 2002	Sufficient details provided in primary source.
		2-generation drinking water study in mice administered TBBPA dissolved in water at a concentration of 200 µg/L. This provided a dose of 0.035 mg TBBPA/kg-day (reagent grade) based on body weight and daily water consumption (estimated by the investigators). In the parental generation, only females were exposed during gestation; In the F_1 generation,	Zatecka et al., 2013	Study is inadequate because only one dose level was tested. Unknown toxicological significance of alterations reported; therefore, study was not used for hazard classification.

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		pups were exposed to TBBPA during gestation, lactation, pre-pubertal and pubertal period, and up to adulthood. No adverse effect on progeny or sex ratio in either generation. Significantly reduced testicular weight, increased prostate and seminal vesicle weight. No visible abnormalities or pathological changes in the morphology of seminiferous tubules. Significantly increased number of apoptotic cells in the testes and increased expression pattern of genes encoding proteins important during spermatogenesis (F_1 generation).		
	Other	Male rats were administered 0, 10, 100 and 1,000 µg/kg (0, 0.01, 0.1, 1 mg/kg) TBBPA via subcutaneous injection on postnatal day (PND) 1-10. Increased preputial gland weight; decreased averages of preleptotene spermatocyte, pachytene spermatocyte and round spermatid; decreased cauda epididymal sperm reserves. These effects were not statistically different from controls.	Tada et al., 2005	Study in Japanese with English summary.

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Developmental Effects		**MODERATE: Based on several studies reporting potentially adverse effects in the range of moderate to high hazard designations with effects on kidney, liver, thyroid and brain endpoints. Some of the studies with effects in moderate to high hazard range have limitations in experimental design and/or statistical methods but cannot be completely dismissed. A number of studies indicate no effects up to relatively high oral or dietary doses of TBBPA. Based on this weight of evidence, a moderate hazard designation is assigned.** **Evidence of potential for moderate or high developmental toxicity:** **Nonstandard experimental studies indicate TBBPA, administered orally, produces adverse hepatic effects (very slight focal hepatocyte necrosis and enlargement of hepatocytes) at 140.5 mg/kg-day (NOAEL = 15.7 mg/kg-day) in mouse pups and kidney effects (polycystic lesions associated with the dilatation of the tubules) at 200 mg/kg-day (NOAEL = 40 mg/kg-day) in rats postnatally exposed from PND 4-21. Increased hearing latencies (most likely related to impairment of the development of the upper (apical) part of the cochlea) were reported in a dietary 1-generation study at a $BMDL_{10}$ of 8 mg/kg-day. There were also changes in plasma thyroid hormone levels (decreased TT4 at $BMDL_{10}$ of 30-60 mg/kg-day, and increased TT3 at $BMDL_{10}$ of 5 mg/kg-day) in rat fetuses. Alterations in pup development were observed following administration of TBBPA in the diet to pregnant rats at a dose of 10,000 ppm (NOAEL = 1,000 ppm). These effects included increase in interneurons in the dentate hilus-expressing reelin suggestive of aberration of neuronal migration. Cholinergic effects were observed in neonatal NMRI mice administered TBBPA at doses up to 11.5 mg/kg body weight (highest dose tested) on postnatal (PND) 10.** **Evidence of low developmental toxicity:** **Six oral exposure studies with rats and one with mice using standard exposure scenarios showed no effects in a range of endpoints including body weight, clinical signs, organ weights, alterations in development of the fetus, neonatal viability and growth, onset of puberty, estrous cycles, organ histology and brain morphometry at doses ranging from 1,000 to 10,000 mg/kg-day. Two studies with rats using oral exposure to relatively low doses (<10 mg/kg-day) of TBBPA showed no changes in thyroid and sperm endpoints.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

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	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	20-Week, 2-generation developmental neurotoxicity and neuropathology assay, rats, administered TBBPA via oral gavage at 0, 10, 100 or 1,000 mg/kg-day. Treatment with TBBPA did not induce significant alterations in F_1 or F_2 pups regarding body weight, clinical signs, survival to weaning, or organ weight data. F0 rats exhibited a decrease in T3 at 1000 mg/kg. Decreases in T4 were seen in F0 rats and in F1 offspring at 100 and 1000 mg/kg-day. NOAEL (developmental): 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	ACC, 2002	Sufficient study details provided in primary source.

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	Prenatal Development	In a nonstandard assay for gestational and lactational exposure, mice (6/group) were fed 0, 0.01, 0.1 or 1.0% TBBPA (99.1% pure) in the diet from GD 0 to postnatal day (PND) 27. Approximate daily doses were 15.7, 140.5 or 1,639.7 mg/kg-day for gestational period (GD0-17) and 42.1, 379.9 or 4,155.9 mg/kg-day for lactational period (PND0-21). No standard developmental effects. Very slight focal hepatocyte necrosis and enlargement of hepatocytes (female pups) were seen at 140.5 / 379.9 mg/kg-day and higher. NOAEL: 15.7 mg/kg-day during gestation and 42.1 mg/kg-day during lactation LOAEL: 140.5 mg/kg-day during gestation and 379.9 mg/kg-day during lactation based on very slight focal hepatocyte necrosis and enlarged hepatocytes	Tada and Fujitani, 2006	TWA doses can be estimated for the combined gestational and lactational periods as 32, 287, and 2,614 mg/kg-day for the 0.01, 0.1, and 1% dietary groups, respectively. The TWA developmental LOAEL would be 287 mg/kg-day. Study limitations include statistical deficiencies due to the failure to control for litter effects. Littermates were utilized as independent variables for the experimental and statistical analysis. The tendency of littermates to respond more similarly to one another than non-litter mates was not taken into account.
		In a dietary study, pregnant rats were fed 0, 100, 1,000, or 10,000 ppm (~17, 149, and 1,472 mg/kg-day) TBBPA on GD 10 until day 20 after delivery. Treatment with TBBPA did not result in maternal toxicity. Maternal exposure to TBBPA did not affect the number of live offspring, birth weight, anogenital distance (AGD) on postnatal day (PND) 1, neonatal viability and growth, or organ histology on PND 20, onset of puberty (males and females), estrous cycle, or organ histology and brain morphometry on post-natal week 11.	Saegusa et al., 2009	Sufficient details provided in primary source. Doses are TWA for mean intakes of TBBPA during GD 10-20, PND 1-9, and PND 10-20) estimated by the investigators.

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		NOAEL (developmental): 10,000 ppm (~1,472 mg/kg-day, highest dose tested) LOAEL: Not established		
		Pregnant rats (25/group) were orally administered 0, 100, 300 and 1,000 mg/kg TBBPA by gavage on gestation days (GDs) 0-19; sacrifices were conducted on GD 20. There were no toxicologically significant maternal effects and no adverse developmental effects. NOAEL (maternal and developmental): 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	MPI Research 2001 (as cited in EU, 2006)	Sufficiently detailed summary of results in secondary source.
		Pregnant rats were orally administered 0, 280, 830 and 2,500 mg/kg-day TBBPA by gavage throughout gestation. No toxicologically significant maternal effects were observed. There were no significant alterations in the development of fetuses examined on GD 20 or on pups monitored up to postnatal day (PND) 21. NOAEL (maternal and developmental): 2,500 mg/kg-day (highest dose tested) LOAEL: Not established	Noda et al., 1985 (as cited in EU, 2006)	Sufficiently detailed summary of results in secondary source.
		Pregnant rats (5/group) were orally administered 0, 30, 100, 300, 1,000, 3,000 and 10,000 mg/kg TBBPA by gavage on GDs 6-15. Sacrifices were conducted on GD 20. Maternal deaths occurred with the highest dose, but there were no adverse developmental effects. NOAEL (maternal): 3,000 mg/kg-day	Goldenthal et al., 1978 (as cited in EC, 2000; Simonsen et al., 2000)	Sufficiently detailed summary of results in primary source.

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		LOAEL (maternal): 10,000 mg/kg-day based on mortality NOAEL (developmental): 10,000 mg/kg-day (highest dose tested) LOAEL (developmental): Not established		
		Pregnant rats were orally administered ^{14}C-TBBPA (5 mg/kg) on gestation days (GDs) 10-16 and were sacrificed on GD 20. No effect on plasma total and free T4 levels in dams and fetuses and on maternal total and T3 levels. Significant increase (196%) in TSH levels in fetuses' plasma (but not in dams). TBBPA did not seem to bind to transthyretin (TTR) *in vivo*.	Darnerud, 2003	Limited scope study. Use of a single dose level precludes drawing firm conclusions.
	Postnatal Development	In a nonstandard assay for postnatal exposure, newborn rats (6/sex/group) were orally administered 0, 40, 200 and 600 mg/kg-day TBBPA (99.5% pure) by gavage from day 4-21 after birth and were sacrificed after the last dose. Kidney effects (polycystic lesions associated with dilatation of the tubules) evident at ≥ 200 mg/kg-day. NOAEL: 40 mg/kg-day LOAEL: 200 mg/kg-day (based on polycystic lesions, dilation of tubules in kidneys)	Fukuda et al., 2004	Sufficient details in primary source.
		Male rats were administered 0, 10, 100 and 1,000 µg/kg (0, 0.01, 0.1, 1 mg/kg) TBBPA via subcutaneous injection on postnatal days (PNDs) 1-10. Increased preputial gland weight; decreased averages of preleptotene spermatocyte,	Tada et al., 2005	Study in Japanese with English abstract.

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		pachytene spermatocyte and round spermatid; decreased cauda epididymal sperm reserves. These effects were not statistically different from controls. NOAEL: 1 mg/kg bw-day (highest dose tested) LOAEL: Not established		
		In 5-week old rats administered 0, 2,000 or 6,000 mg/kg-day TBBPA for 18 days, no adverse effects were observed. NOAEL: 6,000 mg/kg-day (highest dose tested) LOAEL: Not established	Fukuda et al., 2004	Sufficient study details reported in a primary study.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Pregnant Sprague Dawley rats were exposed to 0, 100, 1,000 or 10,000 ppm TBBPA in the diet from GD 10 through day 20 after delivery (weaning). Alterations in pup brain development on postnatal day (PND) 20 (increase in interneurons in the dentate hilus-expressing reelin suggestive of aberration of neuronal migration) in pups from the high dose group. NOAEL: 1,000 ppm (~80 mg/kg-day) LOAEL: 10,000 ppm (~800 mg/kg-day) based on alterations in pup brain development	Saegusa et al., 2012 (as cited in NTP, 2013)	Sufficient study details reported in NTP technical report. Doses were reported as ppm in the diet but were converted to mg/kg/day using EPA 1988 reference values for body weight and food consumption.
		Newborn rats (6/sex/group) were administered 0, 40, 300, or 600 mg/kg-day TBBPA (99.5% pure) by gavage on postnatal days (PNDs) 4 through 21. No	Fukuda et al., 2004	Qualitative observations only.

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		significant effects on a variety of reflexes tested on postnatal day 21. NOAEL: 600 mg/kg-day (highest dose tested) LOAEL: Not established		
		TBBPA administered to male neonatal NMRI mice at single oral doses of 0, 0.75, or 11.5 mg/kg body weight on postnatal (PND) 10; No neurotoxicity, changes in spontaneous motor behavior, or clinical signs of dysfunction; however, cholinergic effects were observed. NOAEL: 0.75 mg/kg LOAEL: 11.5 mg/kg (based on cholinergic effects)	Viberg and Eriksson, 2011 (as cited in NTP, 2013)	Sufficient study details reported in NTP technical report. Study limitations include statistical deficiencies due to the failure to control for litter effects.
		Sprague-Dawley rats administered TBBPA at doses of 0, 100, 1,000 or 10,000 ppm in a soy-free diet from GD 10 - postnatal day (PND) 20. Slight decrease in serum T3 concentrations in pups on PND 20; however, no evidence for developmental brain effects. NOAEL: 10,000 ppm (~1,472 mg/kg-day; highest dose tested) LOAEL: Not established	Saegusa et al., 2009	Sufficient study details reported in primary source.
		In a dietary study, rats (8-13 males and 6-10 females/group) were fed 0, 3, 10, 30, 100, 300, 1,000, or 3,000 mg/kg-day TBBPA (98% pure) for 11 weeks (males) or 2 weeks during premating and throughout pregnancy and lactation for females (doses estimated by the investigators). After weaning, dosing of	van der Ven et al., 2008; Lilienthal et al. (2008)	As stated in the study, dose-response analysis of effects based on external dosing (mg/kg-day) was done using a nested family of purely descriptive (exponential) models with the PROAST software. The method enables integrated evaluation of the complete data set.

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		F_1 continued for life. Neurobehavioral testing was conducted between postnatal days (PNDs) 50 and 140. Increase in hearing latencies were seen, with a $BMDL_{10}$ calculated to be 8 mg/kg-day. Other changes in auditory responses using other types of measures resulted in higher BMDL values. Changes in plasma thyroid hormone levels were seen, with decreased T4 at $BMDL_{10}$ of 30.8 mg/kg-day (males) and 16.1 mg/kg-day (females). Increased T3 levels were seen in female offspring, with a $BMDL_{10}$ of 2.3 mg/kg-day. Increases in pituitary gland and testis weights were seen in male F1 offpring (with BMDLs of 0.6 and 0.5 mg/kg-bw/day, respectively). Other offspring effcts (e.g., changes in body weight) were seen at much higher doses and not necessarily seen throughout the study.		From the best fitted curve, indicated by significance at the 5% level, a critical effect dose (CED, also referred as Benchmark Dose) was calculated most often using a critical effect size of 10%; there has been some criticism of the modeling and methodology used for this study along with noted study limitations not consistent with recommended study guidelines (Banasik et al. 2009; Strain et al. 2009; comparison with OPPTS 870.6855).
		20-Week, 2-generation developmental neurotoxicity and neuropathology assay, rats, administered TBBPA via oral gavage at 0, 10, 100 or 1,000 mg/kg-day. No significant neurobehavioral or neuropathological alterations in F_2 pups identified at various times up to postnatal day 60. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	ACC, 2002	Sufficient study details in primary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other			No data located.
Neurotoxicity		**LOW: An experimental study in rats produced no adverse neurotoxic effects in adults at levels up to 1,000 mg/kg-day. In an acute exposure study, TBBPA, administered orally to mice, resulted in neurobehavioral effects; these effects were not clearly dose-dependent. Although one study with limitations appears to result in neurobehavioral effects, a well-designed subchronic duration study did not identify any adverse neurological effects. Based on study quality, a Low hazard designation was assigned.**		
	Neurotoxicity Screening Battery (Adult)	In a 90-day study, rats (10-15/sex/dose) were administered daily doses of 0, 100, 300 or 1,000 mg/kg-day TBBPA via in corn oil. A detailed functional observational battery (FOB) was conducted pre-test and at week 12. Motor activity (MA) was also assessed at week 12. No neurobehavioral effect of treatment with TBBPA was evident. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	MPI Research, 2002 (as cited in EU, 2006)	Sufficient study details in secondary source.
		Male mice (14-15/group) were administered 0, 0.1, 5, or 250 mg/kg-day TBBPA (99% pure) by gavage 3 hours before a series of neurobehavioral tests (open field test, Y-maze test or training of contextual fear conditioning paradigm). No gross abnormalities. No significant differences in the number of rearing and grooming behaviors. Increased horizontal movement activities (5 mg/kg-day), increased freezing behavior in fear conditioning paradigm (0.1 or 5 mg/kg-day), increase in spontaneous alternation behavior in Y-maze test at the low dose, but no adverse effects occurred at higher doses. Elevated levels of TBBPA were detected in the striatum region of the brain	Nakajima et al., 2009	Sufficient details in primary source. Difficult to establish a NOAEL/LOAEL due to lack of dose-response relationships; acute study duration is not a standard methodology for a neurotoxicity screening study.

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		at lower doses (0.1 or 5 mg/kg-day). At the highest dose tested (250 mg/kg-day), there was non-specific accumulation of TBBPA in the brain.		
	Other	Potential for neurotoxic effects based on a structural alert for phenols (Estimated)	Professional judgment	Estimated based on a structural alert and professional judgment.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects	**LOW: Based on a weight of evidence indicating that effects occur at doses >100 mg/kg-day. Mice administered 500 mg/kg-day TBBPA for 3 months were reported to have increased liver weight and kidney effects in males (NOAEL=100 mg/kg-day). There was decreased serum alanine aminotransferase and sorbitol dehydrogenase activity at week 14 in male and female rats at 100 mg/kg-day following oral exposure for 3 months. Increased liver weights and decreased spleen weight were reported in male rats in the 500 and 1,000 mg/kg-day dose group, though no treatment-related histopathologic lesions were observed. Experimental studies indicate that TBBPA, administered orally to mice, produced effects on the liver (inflammatory cell infiltration) at ≥ 350 mg/kg-day (lowest dose tested). In a dietary study in mice, changes in hematology and clinical chemistry (decreased red blood cells, hemoglobin, hematocrit, serum triglycerides and total serum proteins) and decreased body weight gain occurred at 2,200 mg/kg-day (NOAEL: 700 mg/kg-day) while mortality was reported at the highest dose tested (7,100 mg/kg-day). In a 2-year oral gavage carcinogenicity study in mice, renal tubule cytoplasmic alteration and effects on the forestomach (ulcer, mononuclear cell cellular infiltration, inflammation, and epithelium hyperplasia) were observed at ≥ 250 mg/kg-day (lowest dose tested). Mean body weight was reduced by at least 10% in this study at 1,000 mg/kg-day. In a 2-year oral gavage carcinogenicity study in rats, mean body weight was reduced by at least 10% following exposure to ≥ 500 mg/kg-day and at 1,000 mg/kg-day. Thymus weight was reduced and liver weight was also increased in this study. Clinical signs of toxicity (excessive salivation and nasal discharge) were evident in rats following inhalation exposure at levels of 6 mg/L (NOAEC: 2 mg/L). Very slight dermal erythema was present in rabbits following application of 100 mg/kg-day TBBPA; however, this occurred in the absence of any systemic effects (NOAEL: 2,500 mg/kg-day).**		

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		3 month oral gavage study in F344/Ntac rats (10/sex/dose); rats were administered 0, 10, 50, 100, 500, or 1,000 mg/kg-day, 5 days/week for 14 weeks. Dose-related decrease in total thyroxine concentrations were reported on day 4 at the final week of the study at 500 and 1,000 mg/kg-day, but not consistently in the 100 mg/kg-day dose group in males and female rats. There was a small decrease in hematocrit levels, hemoglobin concentrations, and erythrocyte counts in female rats in the 500 and 1,000 mg/kg-day dose groups by week 14. There was also decreased serum alanine aminotransferase and sorbitol dehydrogenase activity at week 14 in males and females of the 100 mg/kg-day. Increased liver weights and decreased spleen weight were reported in male rats in the 500 and 1,000 mg/kg-day dose group. Although enzyme changes are seen at lower doses, it is uncertain if this is linked to any of the observed adverse endpoints. No treatment-related histopathologic lesions were observed. NOAEL: 100 mg/kg-day LOAEL: 500 mg/kg-day (based on decreased serum enzyme activity)	NTP, 2013	Sufficient study details reported in NTP technical report
		3 month oral gavage study in B6C3F1/N mice (10/sex/dose); Mice were administered 0, 10, 50, 100, 500, or 1,000 mg/kg-day, 5 days/week for 14 weeks. There was no mortality reported. Final mean body weight of treated mice in all	NTP, 2013	Sufficient study details reported in NTP technical report.

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		dose groups was similar to controls. Liver weights were significantly greater in male mice in the 500 and 1,000 mg/kg-day dose groups as compared to controls. Increased spleen weights and decreased kidney weights were reported in the male 1,000 mg/kg-day dose group. Increased incidence of renal tubule cytoplasmic alteration in the kidney at 500 and 1,000 mg/kg in male mice (greater severity at 1,000 mg/kg). NOAEL: 100 mg/kg-day LOAEL: 500 mg/kg-day (based on alterations in the kidneys in male mice)		
		In a 28-day dietary study, rats (25/sex/group) were fed a diet containing TBBPA at 0, 1, 10, 100 and 1,000 ppm (~ 0.07, 0.7, 7.2 and 75 mg/kg-day in males, and 0.07, 0.77, 7.4 and 72 mg/kg-day in females). No changes in general appearance, behavior, body weight or food consumption. No compound-related mortality, gross or microscopic lesions in the liver, kidneys, and thyroid. NOAEL: 1,000 ppm (75 or 72 mg/kg-day in males and females, respectively; highest dose tested) LOAEL: Not established	Sterner, 1967c (as cited in Wazeter et al., 1972); Simonsen et al., 2000; ACC, 2006b; EU, 2006; ECHA, 2013	Study limited by histological examination of only the liver, kidneys, and thyroid.
		28-day repeated-dose study, rat, diet, no treatment-related effects. NOAEL: ~ 98 mg/kg-day (0.1%, highest dose tested) LOAEL: Not established	Wazeter et al., 1972	Inadequate, the high dose was relatively low and failed to elicit toxicity.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In a 90-day repeated-dose study, rats were fed 0.3, 3, 30 or 100 mg/kg-day TBBPA in the diet. No toxicologically significant effects. NOAEL: ~ 100 mg/kg-day (highest dose tested) LOAEL: Not established	Quast et al., 1975	Sufficient details in a primary source. However, it was tested at relatively low doses.
		In a 14-day oral study, male mice (7-8/group) were dosed by gavage with 0, 350, 700 or 1,400 mg/kg-day TBBPA (99.1% pure) in olive oil. No clinical signs or mortality. Significant increase in absolute and relative liver weight in high-dose mice. Slight enlargement of hepatocytes at ≥ 700 mg/kg-day, inflammatory cell infiltration at ≥ 350 mg/kg-day, and focal necrosis of hepatocytes at 1,400 mg/kg-day. In treated mice the liver appeared swollen and the pancreas looked slightly enlarged and edematous. NOAEL: Not established LOAEL: 350 mg/kg-day (lowest dose tested)	Tada et al., 2007	Sufficient details in primary source.
		In a 14-day oral study, male rats (6/group) were administered 0, 200, 500 or 1,000 mg/kg TBBPA (98% pure) by gavage in corn oil. No significant adverse effects on body weight, clinical chemistry parameters, or enzymes' activities indicative of lipid peroxidation in the kidneys. NOAEL: 1,000 mg/kg-day (highest dose	Kang et al., 2009	Study of limited toxicological scope. There was no histological examination of the kidneys.

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		tested) LOAEL: Not established		
		B6C3F1 mice (10/sex/group) were fed TBBPA in the diet at 0, 71, 700, 2,200 or 7,100 mg/kg-day for 3 months. All animals receiving 7,100 mg/kg-day died, but no deaths occurred at lower doses. Decreased body weight gain at the two highest doses with no change in food consumption. Decreased red blood cells, hemoglobin, hematocrit, serum triglycerides and total serum proteins at 2,200 mg/kg-day. Increased spleen weight with blood observed outside the red pulp. No other organ weight or pathological changes. NOAEL: 700 mg/kg-day LOAEL: 2,200 mg/kg-day	IPCS, 1995; WHO, 1995; HSDB, 2013; NTP, 2013	Sufficient study details reported in a secondary source.
		In a 90-day repeated-dose study, rats were administered TBBPA via oral gavage at 0, 100, 300 or 1,000 mg/kg-day. No deaths. No effect on clinical signs, body/organ weight, histopathology, urinalysis, ophthalmology, or serum chemistries. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	MPI Research, 2002 (as cited in EU, 2006)	Sufficient details in a secondary source.
		10-day developmental study, rats orally gavaged with 0, 30, 100, 300, 1,000, 3,000 and 10,000 mg/kg TBBPA-day. Maternal clinical signs, mortality and reduced body weight gain at the high dose only (10,000 mg/kg-day). No effects at 3,000 mg/kg-day or less.	Goldenthal et al., 1978	Sufficient details in primary source.

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		NOAEL: 3,000 mg/kg-day LOAEL: 10,000 mg/kg-day		
		In an oral study, 5-week old rats were administered 0, 2,000 or 6,000 mg/kg-day TBBPA (99.5% pure) by gavage for 18 days. There were no changes in general behavior, body weight or kidney weight. Microscopic examination of the kidneys showed no abnormalities. NOAEL: 6,000 mg/kg-day (highest dose tested) LOAEL: Not established	Fukuda et al., 2004	Limited scope study; only the kidneys were examined.
		In a 28-day dietary study, rats (10/sex/group) were fed 0, 30, 100 and 300 mg/kg-day TBBPA (98% pure). Decreased circulating T4 and increased T3 levels in males (BMDLs = 48 and 124, respectively). No histopathological changes in the thyroid or pituitary gland.	Van der Ven et al., 2008	As stated in the study, dose-response analysis of effects based on external dosing (mg/kg-day) was done using a nested family of purely descriptive (exponential) models with the PROAST software. The method enables integrated evaluation of the complete data set. From the best fitted curve, indicated by significance at the 5% level, a critical effect dose (CED, also referred as Benchmark Dose) was calculated at a default critical effect size of 10%.
		2-year oral gavage carcinogenicity study; Wistar Han rats (50 or 60/sex/dose) were administered 0, 250, 500, or 1,000 mg/kg-day 5 days/week for up to 105 weeks. Survival was similar to controls. Decreased mean body weight (by at least 10% compared to controls) after week 25 in males in the 500 and 1,000 mg/kg dose	NTP, 2013	Sufficient study details reported in NTP technical report.

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		groups. At the 3-month interim sacrifice, there were no treatment-related lesions in either sex. However, thymus weight was decreased and liver weight was increased at 1,000 mg/kg. NOAEL: 250 mg/kg LOAEL: 500 mg/kg (based on decreased mean body weight in males)		
		2-year oral gavage carcinogenicity study; B6C3F1/N mice (50/sex/dose) were administered 0, 250, 500, or 1,000 mg/kg-day 5 days/week for up to 105 weeks. Reduced survival in males and females in the 1,000 mg/kg dose group. Decreased mean body weight (by at least 10% compared to controls) after week 25 in females at 1,000 mg/kg. Increase in the incidence of renal tubule cytoplasmic alteration in 250 and 500 mg/kg males. Significant increase in the incidences of ulcer, mononuclear cell cellular infiltration, inflammation, and epithelium hyperplasia in the forestomach in males at 500 mg/kg and in females at 250 and 500 mg/kg. NOAEL: Not established LOAEL: 250 mg/kg (based on effects in the forestomach in females)	NTP, 2013	Sufficient study details reported in NTP technical report.
		21-day repeated-dose study in rabbits with dermal application of 0, 100, 500 and 2,500 mg/kg TBBPA to the intact or abraded back 6 hours/day, 5 days/week. Very slight erythema (≥ 100 mg/kg-day). No compound-related changes in body	Sterner, 1967c (as cited in Goldenthal et al., 1979; Simonsen et al., 2000; EU, 2006; ECHA, 2013)	Sufficient details in secondary source.

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		weights, hematologic and biochemical parameters and urinalysis. No compound induced gross or microscopic lesions in any of the tissues examined. No compound-related organ weight variations occurred. NOAEL: 2,500 mg/kg-day (highest dose tested) LOAEL: Not established		
		In a 14-day inhalation study, rats (4/sex/group) were exposed whole-body to 0, 2, 6 or 18 mg/L TBBPA as dust 4 hours/day, 5 days/week. No significant effects on body weight gain, food consumption, hematology and clinical chemistry parameters or urinalysis. No deaths and no gross or microscopic lesions. Excessive salivation at 2 mg/L; excessive salivation, nasal discharge and lacrimation at ≥ 6 mg/L. NOAEC: 2 mg/L LOAEC: 6 mg/L	Sterner, 1967c (as cited in Wazeter et al., 1975; Simonsen et al., 2000; EC, 2000; ECHA, 2013)	No information regarding how the exposure atmosphere was generated or regarding analytical measurements of exposure concentrations.
Skin Sensitization		**LOW: TBBPA is not a skin sensitizer in humans or guinea pigs.**		
	Skin Sensitization	Non-sensitizing, human volunteers In a modified Draize Multiple Insult test.	Sterner, 1967c; Dean et al., 1978a; WHO, 1995; EC, 2000; EU, 2006; ECHA, 2013	Sufficient study details in secondary sources.
		Non-sensitizing, guinea pigs No irritation was elicited at either induction or challenge in the group exposed to TBBPA.	Mallory et al., 1981c (as cited in EU, 2006)	Sufficient study details in a primary source.
		Not sensitizing, guinea pigs Three treated animals showed a mild skin reaction at the induction site, no treated	Dean et al., 1978c (as cited in EU, 2006)	Sufficient study details in a primary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		animal showed a skin reaction at the challenge site.		
Respiratory Sensitization		**No data located**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Slight pain, conjunctivitis and corneal damage lasting for three days were reported in rabbits administered TBBPA in a 10% solution. In addition, moderate conjunctival erythema, clearing within 72 hours, was also reported following application of TBBPA to the eyes of rabbits.**		
	Eye Irritation	Application of the test material to the eye of rabbits produced no irritation in one rabbit, mild conjunctival erythema in eight rabbits, and moderate conjunctival erythema in the remaining three rabbits. Effects diminished in intensity or subsided completely during subsequent 72 hours.	Doyle and Elsea, 1966 (as cited in EU, 2006)	Sufficient details in primary source.
		Irritating, range-finding study in rabbits. Undiluted test material caused very slight immediate conjunctivitis (disappearing within 48 hours). TBBPA administered as 10% solution in water caused slight pain, conjunctivitis and corneal damage (lasting for 3 days and then returning to normal within a week).	EU, 2006	Sufficient details in secondary source.
		Non-irritating, rabbits	Sterner, 1967a (as cited in Mallory et al., 1981a; WHO, 1995; EU, 2006)	Sufficient study details in secondary sources.
Dermal Irritation		**LOW: Slightly irritating to rabbits in a 21-day dermal repeated dose study.**		
	Dermal Irritation	Irritating, rabbits 21-day repeated dermal toxicity assay with very slight dermal erythema persisting for 1-3 days.	Sterner, 1967c; Goldenthal et al., 1979; EU, 2006	Sufficient details in primary sources.
		Non-irritating, rabbits Undiluted test material was applied to intact and abraded skin.	Doyle and Elsea, 1966; Sterner, 1967c; Mallory et al., 1981d; EC, 2000; EU, 2006	Sufficient details in primary sources.

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		Non-irritating, human volunteers In a modified Draize Multiple Insult test.	Sterner, 1967c; Dean et al., 1978a; EC, 2000; EU, 2006	Sufficient details in primary source.
Endocrine Activity		**Both whole animal and *in vitro* studies indicate that TBBPA may exhibit thyroid endocrine activity. In a one-generation reproduction study in rats, TBBPA decreased circulating thyroxine (T4) and increased circulating T3 levels in males. TBBPA was negative for agonistic and antagonistic estrogenic responses following oral exposure and subcutaneous injection at doses up to 1,000 mg/kg-day in an uterotrophic assay with adult female ovariectomized mice. TBBPA has a high potency in competing with thyroxine (T4) for binding to transport protein transthyretin (TTR) in *in vitro* animal studies. In addition, TBBPA exhibited significant thyroid hormonal activity towards rat pituitary cell line GH3, which releases growth hormone in a thyroid hormone-dependent manner. TBBPA produced only mild effects during long-term treatment on larval development using the amphibian *Xenopus laevis*; however, short-term exposure revealed indirect evidence that TBBPA can function as a TH antagonist. There were no adverse effects on tail resorption in tadpoles that were microinjected with TBBPA during development. TBBPA did not induce Vitellogenin in immature rainbow trout after intraperitoneal injection.**		
		TBBPA did not exhibit thyroid hormonal activity in a thyroid hormone-responsive reporter assay using a Chinese hamster ovary cell line (CHO-K1) transfected with thyroid hormone receptor alpha1 or beta1. TBBPA showed significant anti-thyroid hormone effects on the activity of T3 in the concentration range of $3x10^{-6}$ to $5x10^{-5}$ M. In addition, TBBPA (in the concentration range of $1x10^{-8}$ to $1x10^{-6}$ M showed suppressive action on T3 enhancement of tadpole tail shortening.	Kitamura et al., 2005a	Sufficient study details reported in a primary source.
		One-generation reproduction study in Wistar rats fed TBBPA at doses of 0, 3, 10, 30, 100, 300, 1,000 and 3,000 mg/kg-day. Decreased circulating thyroxine (T4) and increased circulating T3 levels in males. BMDL: 31 (male) and 16 (female) mg/kg-day	Van der Ven et al., 2008	Sufficient study details summarized in a primary source.

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	There were no adverse effects on tail resorption in tadpoles microinjected with TBBPA at doses up to 60 µg at developmental stage 58 (hind limbs emerged; forelimbs formed, but not emerged).	HSDB, 2013	Sufficient study details summarized in a secondary source.
	TBBPA inhibited the binding of triiodothyronine (T3; $1x10^{-10}$ M) to thyroid hormone receptor in the concentration range of $1x10^{-6}$ M to $1x10^{-4}$ M. The thyroid hormonal activity of TBBPA was also examined using rat pituitary cell line GH3 cells. TBBPA enhanced the proliferation of GH3 cells and stimulated their production of growth hormone (GH) in the concentration range of $1x10^{-6}$ M to $1x10^{-4}$ M. TBBPA did not show antagonistic action (did not inhibit the hormonal activity of T3 to induce growth and GH production of GH3 cells). TBBPA enhanced the proliferation of MtT/E-2 cells (growth is estrogen-dependent).	Kitamura et al., 2002	Sufficient study details in a primary source.
	TBBPA gave a positive response in an *in vivo* uterotrophic assay using ovariectomized mice but was inactive for effects on the androgenic activity of 5alpha-dihydrotestosterone in mouse fibroblast cell line NIH3T3. TBBPA exhibited significant thyroid hormonal activity towards rat pituitary cell line GH3, which releases growth hormone in a thyroid hormone-dependent manner.	Kitamura et al., 2005b	Sufficient study details in a primary source.
	In a uterotrophic assay with adult female ovariectomized mice, TBBPA was administered by oral gavage and	Ohta et al., 2012 cited in Environment Canada, 2013	Sufficient study details in a secondary source.

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	subcutaneous injection daily for 7 days. TBBPA was negative for agonistic and antagonistic estrogenic responses by both routes of exposure at concentrations up to 1,000 mg/kg-day.		
	Positive for thyroid hormone agonist activity in a yeast two-hybrid assay incorporating human thyroid hormone with and without metabolic activation. Metabolic activation by rat liver S9 significantly increased the agonist/antagonist potential.	HSDB, 2013	Sufficient study details summarized in a secondary source.
	Negative for estrogenic activity in yeast two-hybrid assay. $REC_{10}(M) > 1x10^{-5}$ compared to $3x10^{-10}$ for E2.	Nishihara et al., 2000	Sufficient study details reported in a primary source.
	In vitro competition binding assays of T4 to TTR using human plasma samples; the competing potency of TBBPA was 5 times greater than T4.	Bergman et al., 1997	Sufficient study details reported in a primary source.
	The human adrenocortical carcinoma cell line (H295R cell line) was used to assess possible effects of TBBPA on the activity of adreno cortical enzyme CYP17. A maximum of 2-fold induction of CYP17 activity occurred after 24 hours of incubation. TBBPA was a potent inducer of CYP17 activity, causing 50% induction at the lowest concentration tested (0.01μM).	Canton et al., 2004	Sufficient study details reported in a primary source.
	In a 14-day oral study, male mice (7-8/group) were dosed by gavage with 0, 350, 700 or 1,400 mg/kg-day TBBPA (99.1% pure) in olive oil. No clinical signs or mortality. In treated mice the liver appeared swollen and the pancreas	Tada et al., 2007	Sufficient details in primary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	looked slightly enlarged and edematous. NOAEL: Not established LOAEL: 350 mg/kg-day (lowest dose tested)		
	Negative, thyroid hormone receptor (TR)-binding activity of TBBPA using a yeast two-hybrid assay; REC_{10}(M) >$3.0x10^{-4}$ compared to $2.1x10^{-8}$ for T3.	Kitagawa et al., 2003	Sufficient study details reported in a primary source.
	Hormonal effects of TBBPA were investigated *in vitro* on recombinant yeasts and *in vivo* on mosquitofish (*Gambusia affinis*). TBBPA had a weak androgenic activity with recombinant yeast systems carrying human androgen receptor (hAR). Following 60-days of exposure in mosquitofish, significant up-regulation of vitellogenin (Vtg), and estrogen receptor (ER-alpha and ER-beta) mRNAs was observed in the liver (500 nM of TBBPA). The lowest concentration (50 nM) markedly induced Vtg, ER-beta and AR-beta mRNA expression in the testes and significantly inhibited AR-alpha expression. TBBPA did not produce histopathological alterations in the liver or testis.	Huang et al., 2013	Sufficient study details reported in a primary source.
	TBBPA did not have anti-androgenic activity in a recombinant cell-based *in vitro* bioassay using the Chinese hamster ovarian cell line (CHO K1).	Roy et al., 2004	Sufficient study details reported in a primary source.
	In a transcriptional activation assay, TBBPA suppressed the thyroid replacement element (TRE) mediated transcriptional activity of T3 on the human HeLaTRDR4-luc cell line.	Sakai et al., 2003	Sufficient study details reported in a primary source.

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	ER-, DR-CALUX® and T4-TTR competitive binding assays; TBBPA did not show estrogenic/antiestrogenic or dioxin-like/anti-dioxin activity. TBBPA was more potent than to thyroxine (T4) in binding to transport protein transthyretin (TTR).	Legler et al., 2002	Sufficient study details reported in a primary source.
	Vitellogenin induction in immature rainbow trout after intraperitoneal injection of TBBPA was studied. Exposure to TBBPA did not induce vitellogenin synthesis.	Christiansen et al., 2000	Sufficient study details reported in a primary source.
	The estrogen-dependent human breast cancer cell line MCF-7 was used to characterize estrogen-like profiles of high volume chemicals. The EC_{50} for the displacement of radiolabeled 17 β-estradiol from the estrogen receptor = 2.5 (+/- 1.29) x 10^{-5}; Relative binding affinity (RBA) = 0.013.	Olsen et al., 2003	Sufficient study details reported in a primary source.
	Tadpoles were exposed to TBBPA at concentrations ranging from 2.5 to 500 µg/L for 21 days. Larval development was inhibited only at the highest concentration level. The TH receptor beta-mRNA was not affected. Conversely, short-term exposures to TBBPA slightly increased the expression of TH receptor beta- and basic region leucin zipper transcription factor b/Zip-mRNA but inhibited their T3-induced elevation in a dose-dependent manner indicating that TBBPA can function as a TH antagonist.	Jagnytsch et al., 2006	Sufficient study details reported in a primary source.
	Short (24 h) exposures of TBBPA modulated the expression of a number of TH target genes implicated in neural stem	Fini et al., 2012	Sufficient study details reported in a primary source.

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	cell function and neural differentiation. TBBPA also reduced cell proliferation in the brain of *Xenopus laevis* (African clawed frog).		
	Thyroid hormone (TH) disrupting activity of TBBPA was investigated in the rat pituitary cell line GH3. The effect of a strong antiestrogen, ICI (10^{-9} M), was also analyzed on E2 and TBBPA. TBBPA stimulated GH3 cell growth but could not counteract the inhibiting growth effect of 10^{-9} M ICI at the tested concentrations. These data indicate that the effect of TBBPA is TH-like and ER-mediated.	Ghisari and Bonefeld-Jorgensen, 2005	Sufficient study details reported in a primary source.
	In vitro bioassay with phenobarbital-induced rat liver microsomes. TBBPA and TBBPA-DBPE significantly increased TTR-binding potencies and E2SULT-inhibiting potencies after biotransformation. TBBPA-DBPE became a more potent AR-antagonist after biotransformation. TBBPA and TBBPA-DBPE enhanced GH3 cell proliferation in the T-Screen test.	Hamers et al., 2008	Sufficient study details reported in a primary source.
	TBBPA binded to crystal structures of the hormone-metabolizing enzyme, estrogen sulfotransferase (SULT1E1), and has the potential to cause endocrine disruption.	Gosavi et al., 2013	Sufficient study details reported in a primary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**The data located had limited experimental details. TBBPA inhibits expression of CD25, which is essential for proliferation of activated T lymphocyte cells, at concentrations ≥ 3 µM. In a disease challenge study, TBBPA administered to mice (1% in diet for 28 days; approximately 1,800 mg/kg-day) produced irregular changes in cytokine production and immune cell populations, which were suggested to cause exacerbation of pneumonia in respiratory syncytial virus-infected mice. Determination of significance of the response to RSV infection is limited by the study design having only one, particularly high, dose of TBBPA. In an *in vitro* study, TBBPA decreased the level of cell surface proteins, possibly interfering with NK cell function.**		
	Immune System Effects	TBBPA is immunotoxic in culture; inhibits expression of CD25 at concentrations at ≥ 3 µM; CD25 is essential for proliferation of activated T cells and is commonly used as a marker for T-cell activation.	Birnbaum and Staskal, 2004	Limited information in a secondary source.
		In a 90-day oral study in mice, there were no adverse effects at doses up to 700 mg/kg-day; however, 2,200 mg/kg-day produced increased spleen weight and reduced concentrations of red blood cells, serum proteins and serum triglycerides. NOAEL: 700 mg/kg-bw LOAEL: 2,200 mg/kg-bw	Tobe et al., 1986; WHO, 1995; Simonsen et al., 2000; Darnerud, 2003	Limited details in secondary sources.
		In vitro study in natural killer (NK) cells; TBBPA (5 µM) decreased the level of cell surface proteins, possibly interfering with NK cell function.	Hurd and Whalen, 2011 (as cited in NTP, 2013)	Sufficient study details reported in NTP technical report.
		TBBPA administered to mice as 1% in diet for 28 days. Irregular changes in cytokine production and immune cell populations were suggested to cause exacerbation of pneumonia in respiratory syncytial virus-infected mice.	Watanabe et al., 2010 (as cited in NTP, 2013)	Sufficient study details reported in NTP technical report.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class	Phenols, Poly		
Acute Aquatic Toxicity	**VERY HIGH: Based on measured LC_{50} values <1 mg/L in fish, daphnia and algae.**		
Fish LC_{50}	Freshwater fish (*Salmo gairdneri*) 96-hour LC_{50} = 0.40 mg/L (Experimental)	Calmbacher, 1978 (as cited in Simonsen et al., 2000)	Insufficient information in primary source.
	Freshwater fish (*Lepomis macrochirus*) 96-hour LC_{50} = 0.51 mg/L (Experimental)	EC, 2000	Insufficient information in secondary source.
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 0.54 mg/L: 144-hour LC_{50} = 0.49 mg/L; 144-hour NOEC = 0.26 mg/L; Flow-through test conditions; test concentrations: 0.63, 0.45, 0.32, 0.26, and 0.19 mg active substance/L (Experimental)	Suprenant, 1988 (as cited in EC, 2000; ECHA, 2013)	Sufficient study details in primary source.
	Freshwater fish (*Cyprinus carpio*) 96-hour LC_{50} = 0.71 mg/L 48-hour LC_{50} = 0.80 mg/L Static conditions; test concentrations: 0.42, 0.65, and 1.0 mg/L (nominal) (Experimental)	ECHA, 2013	Sufficient study details in a secondary source; GLP study following standard guidelines; however, no analytical verification of test compound concentrations.
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 710 µg/L (0.71 mg/L) (Experimental)	ECOTOX, 2012	Sufficient study summary reported in a secondary source.
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 1,040 µg/L (1.04 mg/L) (Experimental)	ECOTOX, 2012	Sufficient study summary reported in a secondary source.
	Freshwater fish (*Oncorhynchus mykiss*) 96-hour LC_{50} = 1.1 mg/L 96-hour NOEC <1.1 mg/L; flow-through conditions; test concentrations: 1.1 and 1.7 mg/L	Blankenship et al., 2003a; ECHA, 2013	Sufficient information in primary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(measured); 1.2 and 1.8 mg/L (nominal) (Experimental)		
	Freshwater fish (*Danio rerio*) 96-hour EC_{50} = 1.1 mg/L (*Danio rerio*) larvae 96-hour LC_{50} = 5.27 mg/L (Experimental)	Chow et al., 2013	Insufficient study details reported in a primary source. EC_{50} is based on hatching of zebrafish embryos. Inconsistent with most other LC_{50} values reported for this compound.
	Freshwater fish (*Danio rerio*) LC_{100} = 1.5 mg/L Exposure concentrations were 0, 0.002, 0.01, 0.05, 0.25, 0.75, and 1.5 mg/L; nearly 100% of animals survived at concentrations <1.5 mg/L, but some embryos were malformed at 0.75 mg/L (Experimental)	Hu et al., 2009	Sufficient information in primary source.
	Freshwater fish (*Lepomis macrochirus*) 96-hour NOEC = 0.1 mg/L (Experimental)	Simonsen et al., 2000	No study details in secondary source.
	Freshwater fish (*Salmo gairdneri*) 96-hour NOEC = 0.18 mg/L (Experimental)	Simonsen et al., 2000	No study details in secondary source.
	Freshwater fish (*Danio rerio*) 96-hour LC_{50} = 1.5 µg/L (0.0015 mg/L) (Experimental)	ECOTOX, 2012	Insufficient study summary reported in a secondary source.
	Freshwater fish (*Pimephales promelas*) 96-hour LC_{50} = 60 µg/L (0.06 mg/L) (Experimental)	ECOTOX, 2012	Insufficient study summary reported in a secondary source.
	Freshwater fish (*Pimephales promelas*) 96-hour NOEC = 0.26 mg/L (Experimental)	Simonsen et al., 2000	No study details in secondary source.
	Freshwater fish (*Oryzias latipes*) 48-hour LC_{50} = 8.2 mg/L (Experimental)	MITI, 1992 (as cited in EC, 2000)	No study details in secondary source.
	Freshwater fish 96-hour LC_{50}= 0.89 mg/L	ECOSAR v1.11	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Estimated) ECOSAR: Phenols, Poly		
	Freshwater fish 96-hour LC_{50} = 2.3 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	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}	*Daphnia magna* 48-hour EC_{50} = 0.60 mg/L (Experimental)	Waaijers et al., 2013	Sufficient study details reported in a primary source.
	Daphnia magna 48-hour LC_{50} = 0.96 mg/L; NOEC <0.32 mg/L (Experimental)	Morrissey et al., 1978; Simonsen et al., 2000; EC, 2000; Anonymous, 2003	Sufficient information in primary source.
	Daphnia magna 48-hour LC_{50} >0.9 - <1.2 µg/L (>0.0009 - <0.0012 mg/L) (Experimental)	ECOTOX, 2012	Sufficient details reported in a secondary source.
	Daphnia magna 24 and 48-hour LC_{50} >1.8 mg/L 48-hour NOEC = 1.8 mg/L flow-through test conditions Test concentrations: 1.2 and 1.8 mg a.i./L (nominal); average measured concentration: 1.2 and 1.8 mg a.i./L (Experimental)	Blankenship et al., 2003b; ECHA, 2013	Sufficient information in primary source. GLP study, following standard guidelines, with analytical verification of test compound concentrations.
	Daphnia magna 48-hour LC_{50} = 7,900 µg/L (7.9 mg/L) (Experimental)	ECOTOX, 2012	Sufficient details reported in a secondary source.
	Daphnia magna 48-hour LC_{50}= 2.6 mg/L (Estimated) ECOSAR: Phenols, Poly	ECOSAR v1.11	
	Daphnia magna 48-hour LC_{50} = 1.7 mg/L	ECOSAR v1.11	Narcosis classes (neutral organics)

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Estimated) ECOSAR: 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.
Other Invertebrate LC_{50}	Saltwater Mysid shrimp 96-hour LC_{50} = 0.86-1.2 mg/L (in 1, 5 or 10 day old shrimp, respectively) (Experimental)	Goodman et al., 1988 (as cited in EC, 2000)	Sufficient information in primary source.
Green Algae EC_{50}	Green Algae (*Skeletonema costatum*) 72-hour EC_{50} = 0.09 - 0.89 mg/L (Experimental)	Walsh et al., 1987; EC, 2000; Simonsen et al., 2000; ACC, 2006b	Limited details in secondary sources.
	Green Algae (*Skeletonema costatum*) 72-hour EC_{50} = 0.09 - 1.14 mg/L (Experimental)	Walsh et al., 1987; ACC, 2006b	Sufficient details in primary source.
	Green Algae (*Thalassiosira pseudonana*) 72-hour EC_{50} = 0.13-1.0 mg/L (Experimental)	Walsh et al., 1987 (as cited in ACC, 2006b)	Sufficient details in primary source.
	Green algae 96-hour EC_{50} = 1.6 mg/L (Estimated) ECOSAR: Phenols, poly	ECOSAR v1.11	
	Green algae 96-hour EC_{50} = 3.3 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	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**
Chronic Aquatic Toxicity	**HIGH: Based on experimental LOECs and/or NOECs <1.0 mg/L in fish and daphnia.**		
Fish ChV	Freshwater fish (*Pimephales promelas*) 35 day NOEC = 0.16 mg/L; LOEC = 0.31 mg/L; MATC = 0.22 mg/L Flow-through test conditions Test concentrations: 0.025, 0.05, 0.1, 0.2, and 0.4 mg a.i./L (nominal); 0.024, 0.04, 0.084, 0.16, and 0.31 mg a.i./L. (measured) (Experimental)	Surprenant, 1989; EC, 2000; ACC, 2006b; ECHA, 2013; Weltje et al., 2013	Sufficient information in secondary sources.
	Freshwater fish (*Platichthys flesus*) 105 day NOEC >0.8 µM (435 ng/mL or 0.000435 mg/L) Test concentrations: 0; 0.001; 0.01; 0.1; 0.2; 0.4 and 0.8 µM (0, 0.54, 5.4, 54.4, 109, 218, 435 ng/mL) No adverse effect on behavior, survival, growth rate, relative liver and gonad weight. Increased levels of thyroid hormone thyroxin (T4) with no signs of altered thyroid gland activity. (Experimental)	Kuiper et al., 2007a	Sufficient details in primary source.
	Zebra fish (*Danio rerio*) 28-day LC_{100} (embryonic exposure) = 0.8 mg/L Edema and hemorrhage, decreased heart rate, edema of the trunk, tail malformation Test concentrations: 0.27, 0.4, 0.54, 0.8, 1.6 mg/L (Experimental)	McCormick et al., 2010	Sufficient details in primary source.
	Freshwater fish (*Danio rerio*) 30-day partial life cycle test; LC_{100} = 1.5 µM (0.816 mg/L) Exposure to 0, 0.023, 0.094, 0.375 and 1.5 µM. Reduced egg production (all	Kuiper et al., 2007b	Sufficient study details reported in a primary source.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	exposure groups) and hatching ratios (all groups other than 0.375 µM). All larvae died in the high dose group (1.5 µM) and mortality was preceded by retardation of development. (Experimental)		
	Freshwater fish ChV = 0.33 mg/L (Estimated) ECOSAR: Phenols, poly	ECOSAR v1.11	
	Freshwater fish ChV = 0.30 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	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	*Daphnia magna* 21 day EC_{50} >0.96 mg/L 21-day NOEC = 0.38 mg/L 21-day MATC >0.3 <0.98 mg/L Flow-through test conditions. Test concentrations: 0.13, 0.25, 0.5, 1.0, 2.0 mg/L (nominal); 0.037 - 0.078, 0.068 - 0.13, 0.14 - 0.26, 0.19 - 0.29, 0.65 - 1.3 mg/L (measured) (Experimental)	ECHA, 2013	Sufficient study details in a secondary source. GLP study with analytical verification of test compound concentrations; methodology employed is well described and designed specifically to meet US EPA requirements.
	Daphnia magna 21 day EC_{50} >0.98 mg/L MATC = 0.54 mg/L Flow-through test conditions. Test concentrations: 0, 0.13, 0.25, 0.5, 1.0 and 2.0 (nominal) (Experimental)	Suprenant, 1989 (as cited in EC, 2000; ACC, 2006b)	Sufficient study details
	Daphnia magna ChV = 0.82 mg/L (Estimated) ECOSAR: Phenols, poly	ECOSAR v1.11	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnia magna ChV = 0.31 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	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: 0.31 mg/L (Estimated) ECOSAR: Phenols, poly	ECOSAR v1.11	
	Green algae ChV = 5.6 mg/L (Experimental)	Giddings, 1988	The effect level is greater than the water solubility of 4.16 mg/L; no effects at saturation (NES) are predicted.
	Green algae ChV = 1.5 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	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 (*Pseudokirchneriella subcapitata*) 96-hour EC_{50} >5.6 mg/L 96-hour NOEC = 5.6 mg/L; Static test conditions; Test concentrations: 0.60, 1.2, 2.4, 4.8, and 9.6 mg/L (nominal); Mean measured concentration: 0.34, 0.76, 1.5, 3.0, and 5.6 mg/L. (Experimental)	Giddings, 1988; Anonymous, 2003; ACC, 2006b; ECHA, 2013	Sufficient study details in secondary sources. The effect levels are greater than the water solubility of 4.16 mg/L; no effects at saturation (NES) are predicted.
ENVIRONMENTAL FATE			

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Transport		**Level III fugacity models incorporating available physical and chemical property data indicate that at steady state, TBBPA is expected to be found primarily in soil and to a lesser extent, sediment. TBBPA is expected to have low mobility in soil based on its calculated K_{oc}. Therefore, leaching of TBBPA through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives for a model river and lake indicate that it will have low potential to volatilize from surface water. In the atmosphere, TBBPA is expected to exist primarily in the particulate phase. Particulate phase TBBPA will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$1.47x10^{-10}$ at 298K (Measured)	Kuramochi et al., 2008	Based on the measured enthalpy of fusion and melting point used to calculate the sub-cooled liquid vapor pressure and infinite dilution activity coefficient.
		$<10^{-8}$ (Estimated)	EPI v4.11; EPA, 2012	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	$1.1x10^5$ at 6.8% organic carbon; $2.0x10^5$at 2.7% organic carbon; $2.3x10^6$ at 0.25% organic carbon (Measured)	Breteler et al., 1989	The K_{oc} values were calculated from the reported K_d values and the percent organic carbon for each sediment sample.
		TBBPA is shown to adsorb to soil based on laboratory soil mobility tests. TBBPA was not eluted from the soil column after 11 pore volumes were displaced. No quantitative values for the rate of soil migration were measured. (Measured)	Larsen et al., 2001 (as cited in ACC, 2006a; ACC, 2006b)	Nonguideline study reported in a secondary sources.
		>30,000 (Estimated)	EPI v4.11; EPA, 2004	Estimated value is greater than >30,000 using the K_{ow} method from KOCWIN v2.00; the high estimated soil adsorption coefficient is consistent with nonmobile compounds.
	Level III Fugacity Model	Air = 0% Water = 1.4% Soil = 64% Sediment = 35% (Estimated)	EPI v4.11	EPI v 4.11 was used to estimate environmental fate values in the absence of experimental data. Measured values (log K_{ow}) from experimental studies, were

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				incorporated into the estimations.
Persistence		**HIGH: Experimental aerobic and anaerobic biodegradation studies in soil and sediment indicate that the aerobic primary biodegradation half-life is less than 180 days, but not less than 60 days. Mineralization under both aerobic and anaerobic conditions in soil and sediment is low, indicating that persistent degradation products are formed. An experimental photolysis half-life of 24 minutes at pH 7.4 in water indicates that TBBPA may photolyze rapidly to 4-isopropyl-2,6-dibromophenol, 4-isopropylene-2,6-dibromophenol and 4-(2-hydroxyisopropyl)-2,6-dibromophenol; however, it is not anticipated to partition significantly to water. Although adequate experimental data are not available, degradation of TBBPA by hydrolysis is not expected to be significant as the functional groups present on this molecule do not tend to undergo hydrolysis. The atmospheric half-life for the gas phase reactions of TBBPA is estimated at 3.6 days, though it is expected to exist primarily as a particulate in air.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301C: Modified MITI Test (I) No biodegradation was observed according to a Japanese MITI test using TBBPA (100 mg/L) in activated sludge (30 mg/L) for 2 weeks. (Measured)	MITI, 1992; ACC, 2006a; ACC, 2006b; CERIJ, 2007	Guideline study reported in a secondary source.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	EPI v 4.11 was used to estimate environmental fate values in the absence of experimental data. Measured values (log K_{ow}) from experimental studies, were incorporated into the estimations.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	EPI v 4.11 was used to estimate environmental fate values in the absence of experimental data. Measured values (log K_{ow}) from experimental studies, were incorporated into the estimations.

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Soil	**Aerobic Biodegradation**	Study results: 50%/65-93 days Test method: Other Half-life values reported for two aerobic series using activated or digested sludge. An aerobic soil half-life of 65 days was calculated for TBBPA in the experiment with activated sludge and 93 days in the experiment with digested sludge. (Measured)	Nyholm et al., 2010	Adequate guideline study.
		Aerobic biodegradation of TBBPA was measured in three soil types. After 64 days, the amount of TBBPA in the soil ranged from 43.7 to 90.6%. 0.5 to 2.5% of the applied radioactivity was recovered as CO_2, suggesting only partial biodegradation. (Measured)	Fackler et al., 1989b (as cited in ACC, 2006a)	Nonguideline study reported in a secondary source.
		Study results: 17.5%/6 months Test method: Other A transformation study in soil calculated an aerobic DT_{50} of 5.3-7.7 days for the soil extracts. The disappearance appears to be predominantly due to binding to soil and not due to biodegradation. Insufficient material was extracted to identify the transformation products. After 6 months, 17.5-21.6% of the dose was mineralized in the aerobic soils. (Measured)	Schaefer and Stenzel, 2006c (as cited in Environment Canada, 2013)	DT_{50} values were calculated for the soil extracts; however, the majority of the material remained bound to soil and was not extracted. The non-extractable (bound) radioactivity or residues in the soil were not characterized as called for in the OECD guidelines. The abiotic degradation rate under sterile conditions was not estimated as called for in the OECD guidelines.
	Anaerobic Biodegradation	12-18% complete mineralization of TBBPA in different soil types observed after 4 months and 3-9% complete mineralization observed after six months in two separate series of anaerobic biodegradation experiments.	Schaefer and Stenzel, 2006c (as cited in Environment Canada, 2013)	Nonguideline studies reported in a secondary source. Full anaerobic conditions were not used throughout the duration of the study in soil.
		Study results: 50%/430 days Test method: Other Using a testing method similar to OECD	Nyholm et al., 2010	Adequate guideline study.

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		Test Guideline 307. (Measured)		
		Study results: >43.7%/64 days Test method: CO_2 Evolution Anaerobic biodegradation of TBBPA was measured in three soil types. After 64 days, the amount of TBBPA remaining in the soils ranged from 43.7 to 90.6%. Less than 0.5% applied radioactivity was recovered as CO_2, suggesting only partial biodegradation. (Measured)	Fackler et al., 1989b	Adequate guideline study.
		Study results: 100%/45 days Test method: Other Under anaerobic conditions the results initially reported TBBPA was mostly dehalogenated within 10 days, and complete dehalogenation to BPA was achieved after 45 days. The resulting BPA was not degraded anaerobically after 3 months. Di- and tribromobisphenol A were observed as intermediates. Under aerobic conditions, BPA was degraded to 4-hydroxybenzoic acid and 4-hydroxyacetophenone. (Measured)	Ronen and Abeliovich, 2000 (as cited in ACC, 2006a; ACC, 2006b)	Nonguideline study reported in a secondary report.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation	50%/84 days Half-lives of 48 to 84 days were determined in anaerobic natural river sediment/water test system using ^{14}C-TBBPA. Less than 8% applied radioactivity was recovered as CO_2, suggesting only partial biodegradation. (Measured)	Fackler et al., 1989a (as cited in ACC, 2006a; ACC, 2006b)	Adequate guideline study reported in a secondary source.
		TBBPA was reductively dehalogenated to BPA with tribromobisphenol A and	Ravit et al., 2005 (as cited in Environment Canada, 2013)	Adequate, nonguideline study.

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		dibromobisphenol A formed as intermediates in sediment samples through two species of salt marsh macrophyte. (Measured)		
		An anaerobic mineralization and transformation study in freshwater aquatic sediment systems calculated an anaerobic DT_{50} of 24-28 days for the whole system. Very little mineralization was observed. The transformation products included BPA and 3 (Measured)	Schaefer and Stenzel, 2006a; ACC, 2006b	Adequate nonguideline study.
		An anaerobic mineralization and transformation study in digester sludge calculated an anaerobic DT_{50} of 19 days. Very little mineralization was observed. The transformation products included BPA and 3 unidentified materials. (Measured)	Schaefer and Stenzel, 2006b	Adequate nonguideline study.
		Estuarine sediment; under methanogenic conditions half-life was estimated to be about 28 days. Under sulfate-reducing conditions half-life was estimated to be 40 days. (Measured)	Voordeckers et al., 2002 (as cited in ACC, 2006b)	Nonguideline study reported in a secondary source.
Air	**Atmospheric Half-life**	3.6 days assuming 12-hr day/sunlight (Estimated)	EPI v4.11	EPI v 4.11 was used to estimate environmental fate values in the absence of experimental data. Measured values (log K_{ow}) from experimental studies, were incorporated into the estimations.
Reactivity	**Photolysis**	50%/24 minutes Photolysis half-lives in water of 16, 24, and 350 minutes at pH values 10, 7.4, and 5.5, respectively, were measured under fluorescent UV radiation representing environmental wavelengths. Major	Eriksson et al., 2004 (as cited in ACC, 2006a; ACC, 2006b; NTP, 2013)	Adequate nonguideline study.

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		degradation products were 4-isopropyl-2,6-dibromophenol, 4-isopropylene-2,6-dibromophenol and 4-(2-hydroxyisopropyl)-2,6-dibromophenol. Other products include di- and tribromobisphenol A, dibromophenol, 2,6-dibromo-4-(bromoisopropylene)phenol, 2,6-dibromo-4-(dibromoisopropylene)phenol and 2,6-dibromo-1,4-hydroxybenzene. (Measured)		
		50%/33 hour Photolysis of TBBPA in the presence of UV light and hydroxyl radicals has also been reported; TBBPA was no longer detected after 5-6 days with an estimated 33 hour half-life. TBBPA decomposition produced 2,4,6-tribromophenol and other bromine containing compounds that were not fully identified. (Estimated)	Eriksson and Jakobsson, 1998 (as cited in ACC, 2006a; ACC, 2006b)	Reported in a secondary source.
		A study of TBBPA on silica gel was reported. The wavelength studied was too short to derive any environmental conclusions. (Measured)	WHO, 1995 (as cited in ACC, 2006a)	Study details and test conditions were not available. Reported in a secondary source.
		Reported half-lives in water of 6.6, 10.2, 25.9, and 80.7 days during summer, spring, fall and winter, respectively. (Measured)	WHO, 1995 (as cited in ACC, 2006a; NTP, 2013)	Study details and test conditions were not available. Reported in a secondary source.
	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.
Environmental Half-life		360 days (Estimated)	PBT Profiler v1.301; EPI v4.11	Half-life estimated for the predominant compartment (soil), as determined by EPI methodology. Measured values from experimental

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				studies, were incorporated into the estimations.
Bioaccumulation		**MODERATE: The measured fish BCF and estimated BAF values are greater than 100 but less than 1,000.**		
	Fish BCF	485 *Cyprinus carpio* BCF ranges of 30 to 341 and 52 to 485 were measured in carp during an 8-week study at concentrations of 80 µg/L and 8 µg/L, respectively. (Measured)	MITI, 1992 (as cited in HSDB, 2013)	Adequate guideline study reported in secondary source.
		300 *Pimephales promelas* A BCF of 1,200 was measured based on total ^{14}C radioactivity; however, extraction and thin layer chromatograph of the residue in the body of the fish determined that only 24.9% of the ^{14}C radioactivity was due to TBBPA, with the remainder due to metabolites, giving a BCF of 300 for TBBPA. Elimination half-life <24 hours for total ^{14}C radioactivity. (Measured)	Dionne et al., 1989; ACC, 2006b	Adequate nonguideline study reported in secondary source.
		170 *Lepomis macrochirus* Bluegill sunfish were exposed to ^{14}C-TBBPA for 28 days to 0.0098 mg/L (flow-through) followed by a 14-day withdrawal period. The bioconcentration factor (BCF) in edible tissue was 20 and 170 in visceral tissue. These BCF values were based on ^{14}C-residues and therefore represent the sum total of parent compound, any retained metabolites and assimilated carbon. (Measured)	ACC, 2006b	Adequate nonguideline study reported in secondary source.
		1,200 in Fathead minnows (*Pimephales promelas*) Reported for the BCF wet weight; BCF value for lipid weight = 24,000; 24 days	Geyer et al., 2000	The BCF value includes all the metabolites of the test substance, as well as the test substance, ^{14}C-labeled chemical was used.

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		uptake (Measured)		
		960 in Zebrafish; reported as BCF wet weight BCF value for lipid weight = 28,300; kinetic approach in outdoor experiment at pH 7.5. (Measured)	Geyer et al., 2000	Adequate nonguideline study reported in secondary source.
	Other BCF	<3,190 in *Chironomus tentans* BCF values of 243-511 (6.8% organic carbon sediment); 487-1,140 (2.7% organic carbon sediment) and 646-3,190 (0.25% organic carbon sediment). (Measured)	ACC, 2006b	Reported in a secondary source. This is nonguideline study using a non-standard test species and is not able to be evaluated with the assessment criteria.
		148 in Eastern oyster (Measured)	ACC, 2006b	Adequate nonguideline study reported in secondary source with limited study details.
	BAF	130 (Estimated)	EPI v4.11	EPI v 4.11 was used to estimate environmental fate values in the absence of experimental data. Measured values (log K_{ow} of 4.54) from experimental studies, were incorporated into the estimations.
	Metabolism in Fish			No data located.

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ENVIRONMENTAL MONITORING AND BIOMONITORING			
Environmental Monitoring	TBBPA has been detected in the air of electronic recycling plants, although its presence in the air of this facility likely arises from products where it was used as an additive flame retardant. Studies on the release of TBBPA from PCBs after disposal in landfills were not available but would likely be low due to the low levels of unreacted TBBPA. TBBPA was reported in air and marine sediment samples collected from several locations in the Arctic. TBBPA was reported in indoor dust and air, soil, and food in Europe and the United States. It has been reported in surface water in Japan, Germany, France, and the United Kingdom (Sellstrom and Jansson, 1995; Sjodin et al., 2001; Sjodin et al., 2003; PBS Corporation, 2006; Environment Canada, 2013).		
Ecological Biomonitoring	TBBPA was reported in eel, salmon, perch, pike, cod, whiting, starfish, whelk, hermit crab, bottlenose dolphin, bull shark, sharpnose shark, cormorant, harbour porpoise blubber, predatory birds, tern eggs and moss samples from Norway. (Environment Canada, 2013)		
Human Biomonitoring	TBBPA was detected in human umbilical cord, blood/serum, adipose, milk and hair samples (DeCarlo, 1979; Thomsen et al., 2002; Peters, 2005; NTP, 2013).		

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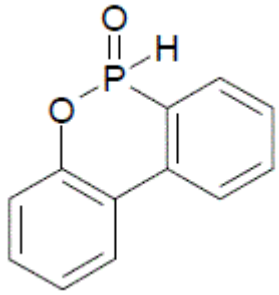
DOPO

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

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

		Human Health Effects											Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
DOPO	35948-25-5	L	*M*	L	*L*[§]	*M*	*M*	L	M		M	VL	L	*M*	*H*	*L*

DOPO



CASRN: 35948-25-5

MW: 216.18

MF: $C_{12}H_9O_2P$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: O=P1c2ccccc2c3ccccc3O1

Synonyms: DOP; DOPPO; 9,10-Dihydro-9-oxa-10-phosphaphenanthrene-10-oxide; 6H-dibenz[c,e][1,2]oxaphosphorin 6-oxide

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v 4.11 was used to estimate physical/chemical and environmental fate values in the absence of experimental data. Measured values from experimental studies were incorporated into the estimations. As described in the *DfE Program Alternatives Assessment Criteria for Hazard Evaluation*, stable degradation products of the alternatives are evaluated. Therefore the hydrolysis product of DOPO was evaluated in this assessment for endpoints typically obtained in the presence of water; based on a submitted guideline water solubility study reporting that 2-(2'-hydroxyphenyl)phenyl phosphonic acid is readily formed by deesterification of DOPO in water. Although there were no separate experimental studies available for the hydrolysis product, it was considered in the evaluation of the human health designations using structural alerts and professional judgment (ECHA, 2013).

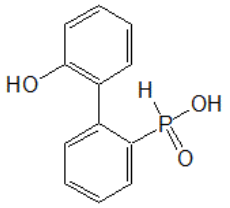
Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: [2-(2'-Hydroxyphenyl)phenyl]phosphonic acid by hydrolytic deesterification (ECHA, 2013)

Analog: [2-(2'-Hydroxyphenyl)phenyl]phosphonic acid (the hydrolysis product of DOPO)

Endpoint(s) using analog values: Endpoints typically obtained in the presence of water for [2-(2'-Hydroxyphenyl)phenyl]phosphonic acid, the hydrolysis product of DOPO

Analog Structure:



Structural Alerts: Phosphinate esters - environmental toxicity (aquatic toxicity); Organophosphorus compounds - neurotoxicity; Phenols (for the hydrolysis product) - neurotoxicity (EPA, 2010; EPA, 2012).

Risk Phrases: R43 - May cause sensitization by skin contact (ECHA, 2013).

Hazard and Risk Assessments: None located.

DOPO CASRN 35948-25-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	122 According to Organisation for Economic Co-operation and Development (OECD) 102 (Measured)	Chang et al., 1998 (as cited in ECHA, 2013)	Adequate guideline study.
	117 (Measured)	Chernyshev et al., 1972	Consistent with other measured values.
Boiling Point (°C)	359 (Extrapolated)	McEntee, 1987	The boiling point at 760 mmHg was extrapolated from the measured boiling point at reduced pressure using a computerized nomograph.
	200 at 760 mmHg pressure reported as 5 Torr (Measured)	International Resources, 2001	Value was obtained at a reduced pressure, no further study details reported.
	>300 at 5 mmHg (Estimated)	EPI v4.11; EPA, 1999	Estimated value is greater than the cutoff value, >300°C, according to HPV assessment guidance.
Vapor Pressure (mm Hg)	0.000022 at 25°C (Extrapolated)	McEntee, 1987	The vapor pressure was extrapolated from the measured boiling point at reduced pressure using a computerized nomograph.
	5 at 200°C (Measured)	International Resources, 2001	Value reported at an elevated temperature.
	0.000012 (Estimated)	EPI v4.11	
	$1.1x10^{-8}$ for [2-(2'-hydroxyphenyl)phenyl] phosphonic acid (Estimated)	EPI v4.11	This value is applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.

DOPO CASRN 35948-25-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Water Solubility (mg/L)	3,574 at 25°C according to OECD 105 study. DOPO is readily converted to [2-(2'-hydroxyphenyl)phenyl] phosphonic acid by deesterification in water; however, the rate of hydrolysis and pH conditions were not reported. (Measured)	ECHA, 2013	The reported water solubility is measured for the hydrolysis product of DOPO, in this guideline water solubility study.
	460 (Estimated)	EPI v4.11	
Log K_{ow}	1.87 (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions.
	1.33 for [2-(2'-hydroxyphenyl)phenyl] phosphonic acid (Estimated)	EPI v4.11	This value is applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
Flammability (Flash Point)	Not readily combustible solid EU Method A.10 Flammability (Solids). Fine powder sample melted to a clear liquid and no ignition was observed. (Measured)	ECHA, 2013	Guideline study reported in a secondary source.
	Flash point: 222°C Cleveland open tester (Measured)	ECHA, 2013	Nonguideline study reported in a secondary source.
Explosivity	Lower explosive limit: 980 g/m^3 Considered non explosive. Vertical tube test. (Measured)	ECHA, 2013	Nonguideline study reported in a secondary source.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	The substance does not contain functional groups that would be expected to ionize; although this compound hydrolyzes in aqueous conditions.

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
pK_a		Not applicable (Estimated)	Professional judgment	The substance does not contain functional groups that would be expected to ionize. Although this is compound hydrolyzes in aqueous conditions.
Particle Size				No data located.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Absorption of neat solid is expected to be negligible through skin. Absorption in solution is expected to be moderate through skin, and moderate through lungs and gastrointestinal tract.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**			No data located.
	Other	Absorption of neat solid negligible through skin. Absorption in solution moderate through skin. Absorption moderate through lungs and GI tract. (Estimated)	Professional judgment	Estimated based on physical/chemical properties
Acute Mammalian Toxicity		**LOW: Based on experimental oral and dermal LD_{50} data in rats. No inhalation data were located.**		
Acute Lethality	**Oral**	Mouse (male) oral LD_{50} = 6,490 mg/kg, Mouse (female) oral LD_{50} = 7,580 mg/kg	International Resources, 2001	Study details and test conditions were not available.
		Rat oral LD_{50} > 2,000 mg/kg; Observation period was 14 days. No deaths occurred.	ECHA, 2013	Sufficient information in secondary source. Study conducted in accordance with OECD Guideline 401 and good laboratory practices (GLP). Test substance was CASRN 35948-25-5 named Ukanol DOP 95 in study report. Primary reference not identified; purity of test substance not provided.
	Dermal	Rat dermal LD_{50} > 2,000 mg/kg (semi-occlusive). Observation period was 14 days. No deaths occurred.	ECHA, 2013	Sufficient information in secondary source. Study conducted in accordance with OECD guideline 402 and GLP. Test substance was CASRN 35948-25-5 named HCA in study report. Primary reference not

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				identified. Neat test substance (99.5% pure).
	Inhalation			No data located.
Carcinogenicity		**MODERATE: OncoLogic estimates a low concern for carcinogenicity for the organophosphates chemical class; However, there is uncertainty based on the lack of data and carcinogenic effects cannot be ruled out.**		
	OncoLogic Results	Low; although the structure of DOPO is not fully represented by the phosphate and phosphinate skeletons provided in the program. (Estimated)	OncoLogic, 2008	Estimated for the aryl phosphinate-type compound.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**LOW: Experimental studies indicate that DOPO was not mutagenic to bacteria or mammalian cells and did not cause chromosomal aberrations *in vitro*.**		
	Gene Mutation *in vitro*	Negative in Ames assay; in Salmonella typhimurium strains TA1535, TA97a, TA98, TA100, and TA102 with and without metabolic activation. Tested up to 5,024 µg/plate (purity >99%). Positive controls responded as expected.	ECHA, 2013	Sufficient study details reported in a secondary source. Study conducted in accordance with OECD guideline 471 and GLP. Test substance was CASRN 35948-25-5 named Ukanol GK-F in study report. Primary reference not identified.
		Negative in Ames assay in *Salmonella typhimurium* strains TA97, TA98, TA100, and TA102 and *Escherichia coli* WP2 *uvr* A pKM 101 with and without metabolic activation. Tested up to 5,000 µg/plate (purity, industrial grade). Positive controls responded as expected.	Hachiya, 1987 (as cited in ECHA, 2013)	Sufficient study details reported in a secondary source. Not GLP study, but adequate as supporting data.
	Gene Mutation *in vivo*			No data located.

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	Negative in Chinese hamster lung cells with and without activation. Tested up to 216 µg/mL (purity not provided). Positive controls responded as expected.	Ryu et al., 1994 (as cited in ECHA, 2013)	Sufficient study details reported in a secondary source. Study equivalent to OECD Guideline 473; not GLP study.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: Based on closely related analogs with similar structures, functional groups, and physical/chemical properties, as well as professional judgment.**		
	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.
	Other	Low potential for reproductive effects. (Estimated by analogy)	Professional judgment	Estimated based on analogy to a structurally similar compound and professional judgment.
Developmental Effects		**MODERATE: There is uncertain concern for developmental neurotoxicity based on the potential for cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment. There is an estimated Low potential for developmental effects based on closely related analogs with similar structures, functional groups, and physical/chemical properties, as well as professional judgment. There were no experimental data for the developmental or neurodevelopmental endpoints.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment. (Estimated)	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other	Low potential for developmental effects. (Estimated by analogy)	Professional judgment	Estimated based on analogy to a structurally similar compound and professional judgment.
Neurotoxicity		**MODERATE: There is uncertain potential for neurotoxic effects based on a structural alert for organophosphates. There is also uncertain potential for neurotoxic effects for the hydrolysis product of DOPO [2-(2'-hydroxyphenyl)phenyl] phosphonic acid based on the phenols structural alert and professional judgment.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Potential for neurotoxic effects based on a structural alert for organophosphates. (Estimated by analogy)	Professional judgment	Estimated based on a structural alert for organophosphates and professional judgment.
		Potential for neurotoxic effects based on a structural alert for phenols. Estimated for the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid. (Estimated by analogy)	Professional judgment	Estimated based on a structural alert for phenols and professional judgment for the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**LOW: Based on no significant effects on multiple endpoints in a 16-week dietary study in rats at doses up to 1,094 mg/kg-day.**		
		Male and female Wistar rats (20/sex/dose) were fed diets containing 0, 0.24, 0.6, or 1.5% HCA (0, 159, 399, or 1,023 mg HCA/kg-day to males; 0, 177, 445, or 1,094 mg HCA/kg-day to females) for 16 weeks (purity of test substance not provided). There were no significant effects on body weight, food consumption, hematology, limited clinical chemistry, urinalysis, organ weight, and gross and microscopic examination of major organs. NOAEL= 1,023 mg/kg-day (males), 1,094 mg/kg-day (females); highest dose tested LOAEL= Not established	ECHA, 2013	Sufficient information in secondary source; data lacking regarding detailed clinical observations and neurobehavioral examination. Study equivalent to OECD guideline 408. Study pre-dates GLP. Test substance identified as HCA in study report. Primary reference not identified.
Skin Sensitization		**MODERATE: Limited data were available to categorize this compound; however, because an SI of 4.2 was seen at a 5% concentration, this compound is considered to have a Moderate concern for skin sensitization. Because the test concentrations started a 5%, there is uncertainty as to if there would be skin sensitization at a concentration < 2% resulting in an SI of 3 which would warrant a High hazard designation.**		
	Skin Sensitization	Local lymph node assay conducted in female CBA/J Rj mice. HCA tested at 5, 10, and 25% (w/v); four mice/treatment group. Test substance >98% pure. Significant lymphoproliferative response was noted for HCA at concentrations of 10% (SI 4.4) and 5% (SI 4.2). SI for positive control was 16.6. HCA was a sensitizer under the conditions of the study.	ECHA, 2013	Sufficient information in secondary source. Study conducted in accordance with OECD guideline 429 and GLP. Test substance was CASRN 35948-25-5 named HCA in study report. Primary reference not identified.
		Risk phrase: R43: May cause sensitization by skin contact	ECHA, 2013	Reported in a secondary source.

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on moderate signs of eye irritation in rabbits that cleared in 7 days.**		
	Eye Irritation	Neat test material (0.1 mL) was instilled in left eye of 3 female albino rabbits. Eyes were monitored for up to 7 days. Moderate signs of eye irritation that cleared in 7 days were observed among the rabbits.	ECHA, 2013	Sufficient information in secondary source. Study conducted in accordance with OECD guideline 405 and GLP. Test substance was CASRN 35948-25-5 named Ukanol DOP in study report. Primary reference not identified.
Dermal Irritation		**VERY LOW: Based on no skin reactions in semi-occlusive test in rabbits.**		
	Dermal Irritation	Not irritating. Neat test material (0.5 mL) was applied in gauze patches to a clipped skin area of 3 female albino rabbits; patches were secured for 4 hours. Skin was examined from 1 to 72 hours after patch removal and skin washing. No skin reactions were noted at any time point.	ECHA, 2013	Sufficient information in secondary source. Study conducted in accordance with OECD guideline 404 and GLP. Test substance was CASRN 35948-25-5 named Ukanol DOP in study report. Primary reference not identified.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**Estimated by professional judgment to have low potential for immunotoxic effects based on closely related analogs with similar structures, functional groups, and physical/chemical properties.**		
	Immune System Effects	Low potential for immunotoxic effects. (Estimated by analogy)	Professional judgment	Estimated by analogy to a structurally similar compound and professional judgment.

DOPO CASRN 35948-25-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class	Phenols class; only the hydrolysis product [2-(2'-hydroxyphenyl)phenyl]phosphonic acid was assessed in ECOSAR because DOPO hydrolyzes in water based on data from a water solubility study		
Acute Aquatic Toxicity	**LOW: Based on experimental acute aquatic toxicity values > 100 mg/L in fish, daphnia, and algae. DOPO will hydrolyze in water; therefore only the hydrolysis product, [2-(2'-hydroxyphenyl)phenyl]phosphonic acid, was assessed in ECOSAR, which is represented by the phenols class.**		
Fish LC_{50}	Freshwater fish (*Danio rerio*) 96-hour LC_{50} >100 mg/L; 96-hour NOEC = 100 mg/L; The study was conducted under static conditions. (Experimental)	ECHA, 2013	Sufficient study details reported in a secondary source. Study was conducted in accordance with OECD guideline 203. GLP deviations were not considered critical. Primary reference not identified; test substance purity >99%; Test substance concentrations were kept within 20% of initial concentrations.
	Oryzias latipes 48-hour LC_{50} = 370 mg/L (95% CI, 280-500 mg/L) Limit test conducted under static conditions. (Experimental)	ECHA, 2013	Test substance purity not reported; sufficient study details reported in a secondary source. The study follows the methodology presented in the Japanese Industrial Standard JIS K 0102-1986 No 71. Primary reference not identified.
	96-hour LC_{50} = >100 mg/L (Estimated) ECOSAR: Phenols	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions.
	Fish 96-hour LC_{50} = >100 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by

DOPO CASRN 35948-25-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} >100 mg/L; 48-hour NOEC = 100 mg/L Limit test conducted under static conditions. Concentrations of test substance were stable during study. Test substance purity >99%. (Experimental)	ECHA, 2013	Sufficient study details reported in a secondary source. Study was conducted in accordance with OECD guideline 202. GLP deviations were not considered critical. Primary reference not identified.
	Daphnia magna 48-hour EC_{50} = 240 mg/L (unbuffered); no effect up to 289 mg/L when buffered to pH 7.5 Test conducted under static conditions. Test substance purity =98%. Concentrations of the test substance were measured at the beginning and end of the test. (Experimental)	Waaijers et al., 2013	Sufficient study details reported in a primary source, Study was conducted in accordance with OECD Guideline 202 and GLP.
	48-hour LC_{50} = 29 mg/L (Estimated) ECOSAR: Phenols	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions.
	48-hour LC_{50} = >100 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions. 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.

DOPO CASRN 35948-25-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	Green algae (*Desmodesmus subspicatus*) 72-hour ErC_{50} = 110 mg/L; 72-hour EbC_{50} = 100 mg/L; EyC_{50} = 98 mg/L; all nominal concentrations; concentrations of test substance were stable during study). EyC_{50} = biomass at the end of exposure period minus biomass at the start of the exposure period. Test substance purity >99%. (Experimental)	ECHA, 2013	Sufficient study details reported in a secondary source. Study was conducted in accordance with OECD guideline 201 and GLP. Primary reference not identified.
	96-hour EC_{50} = >100 mg/L (Estimated) ECOSAR: Phenols	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions.
	96-hour EC_{50} = >100 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions. 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	**MODERATE: Based on estimated chronic aquatic toxicity values for the primary degradation product [2-(2'-hydroxyphenyl)phenyl]phosphonic acid of 5.6 mg/L for daphnid. DOPO will hydrolyze in water; therefore only the hydrolysis product was assessed in ECOSAR, which is represented by the phenols class.**		
Fish ChV	Fish ChV = 12 mg/L (Estimated) ECOSAR: Phenols	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions.
	Fish ChV = 70 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimation is for the hydrolysis product; This compound hydrolyzes in aqueous conditions.

DOPO CASRN 35948-25-5			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			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 = 5.6 mg/L (Estimated) ECOSAR: Phenols	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions.
	Daphnid ChV = 34 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions. 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 = 68 mg/L (Estimated) ECOSAR: Phenols	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions.
	Green algae ChV = 54 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimation is for the hydrolysis product; this compound hydrolyzes in aqueous conditions. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**Under aqueous conditions, DOPO is expected to hydrolyze to [2-(2'-hydroxyphenyl)phenyl] phosphonic acid based on data from a water solubility study. Therefore, the transport and mobility of DOPO and the hydrolysis product of DOPO are evaluated. Level III fugacity models incorporating available physical and chemical property data indicate that at steady state DOPO and [2-(2'-hydroxyphenyl)phenyl] phosphonic acid are expected to be found primarily in soil and to a lesser extent, water. DOPO and [2-(2'-hydroxyphenyl)phenyl] phosphonic acid are expected to be highly mobile in soil based on an experimental K_{OC} value; these compounds have the potential to migrate from soil into groundwater. The estimated Henry's Law constant indicates that the hydrolysis product, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid will not significantly volatilize from water to the atmosphere. Volatilization from dry surfaces is also not expected. In the atmosphere, DOPO is expected to exist in both the vapor and particulate phase, based on its vapor pressure and [2-(2'-hydroxyphenyl)phenyl] phosphonic acid is expected to exist primarily in the particulate phase. Vapor-phase DOPO is expected to have limited potential for photodegradation. Particulates will be removed from air by wet or dry deposition.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ for [2-(2'-hydroxyphenyl)phenyl] phosphonic acid (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions. This value is applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
		5.4×10^{-8} (Estimated)	EPI v4.11	Estimated by the HENRYWIN Bond SAR model.
	Sediment/Soil Adsorption/Desorption - K_{oc}	36 According to OECD 121 (Measured)	ECHA, 2013	Adequate guideline study reported in a secondary source. This study was performed in acetonitrile and water; it is unclear if this value is for DOPO or the hydrolysis product since DOPO is expected to hydrolyze in water based on data from a water solubility study.
		120 (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions. This value is

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
	Level III Fugacity Model	Air = 0.3% Water = 18.9% Soil = 80.6% Sediment = 0.1% (Estimated)	EPI v4.11	
		Air = 0% Water = 16% Soil = 84% Sediment = 0.2% (Estimated) for [2-(2'-hydroxyphenyl)phenyl] phosphonic acid	EPI v4.11	This compound hydrolyzes in aqueous conditions. These values are applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
Persistence		**HIGH: The persistence designation of DOPO is High considering ultimate degradation based on an estimated environmental half-life of 75 days in soil. An intermediate, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid, is formed by hydrolysis of DOPO in aqueous environments. This primary degradation product is expected to resist further environmental degradation based on an estimated half-life of 75 days in soil. The rate of hydrolysis is expected to be dependent on pH, with increasing alkalinity resulting in increasing rates of hydrolysis. A guideline OECD 301B Ready Biodegradability study indicated that DOPO is not biodegradable under test conditions with activated sludge; however data from this protocol are insufficient to determine a persistence designation. QSARs of aerobic and anaerobic biodegradation estimate primary aerobic biodegradation in days-weeks and ultimate aerobic degradation in weeks-months for both DOPO and the hydrolysis product. DOPO is not expected to undergo direct photolysis by sunlight as it does not contain chromophores that absorb at wavelengths >290 nm. The atmospheric half-life for the gas phase reactions of DOPO is estimated at 1.8 days, though it is not anticipated to partition significantly to air.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test 0% degradation after 28 days using an activated sludge inoculum. (Measured)	ECHA, 2013	Adequate guideline study reported in a secondary source; this value is expected to apply to both DOPO and the hydrolysis product since DOPO is expected to hydrolyze in water based on data from a water solubility study.
		Days-weeks (Primary Survey Model)	EPI v4.11	This compound hydrolyzes in

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Weeks-months (Ultimate Survey Model) (Estimated)		aqueous conditions. These values are applicable to DOPO and for the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions. These values are applicable to DOPO and for the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions. These values are applicable to DOPO and for the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model)	EPI v4.11	
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.8 days (Estimated)	EPI v4.11	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	DOPO is readily converted to [2-(2'-hydroxyphenyl)phenyl]phosphonic acid by deesterification in water; however, the rate of hydrolysis and pH conditions were	ECHA, 2013	Summary statement reported in a modified OECD 105 guideline water solubility study; however, the rate of hydrolysis and pH conditions was

DOPO CASRN 35948-25-5				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		not reported. (Measured)		not reported.
		Phosphinate esters hydrolyze in water and their rate of hydrolysis is correlated to pH; increasing alkalinity results in increasing rates of hydrolysis. (Estimated)	EPA, 2010	Adequate summary statement from guidance document.
Environmental Half-life		75 days (Estimated)	PBT Profiler v1.301	Half-life estimated for the predominant compartment (soil), as determined by EPI methodology. This value is applicable to DOPO and for the hydrolysis product of DOPO, for [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
Bioaccumulation		**LOW: The bioaccumulation hazard designation is based on the estimated BCF and BAF values that are <100 for DOPO and the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl]phosphonic acid.**		
	Fish BCF	7.9 (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions.
		3.5 for [2-(2'-hydroxyphenyl)phenyl]phosphonic acid (Estimated)	EPI v4.11	This value is applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
	Other BCF			No data located.
	BAF	7.7 (Estimated)	EPI v4.11	This compound hydrolyzes in aqueous conditions.
		2.9 for [2-(2'-hydroxyphenyl)phenyl]phosphonic acid (Estimated)	EPI v4.11	This value is applicable to the hydrolysis product of DOPO, [2-(2'-hydroxyphenyl)phenyl] phosphonic acid.
	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, 2013).		

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Waaijers SL, Hartmann J, Soeter AM, et al. (2013) Toxicity of new generation flame retardants to Daphnia magna. Sci Total Environ 463-464:1042-1048.

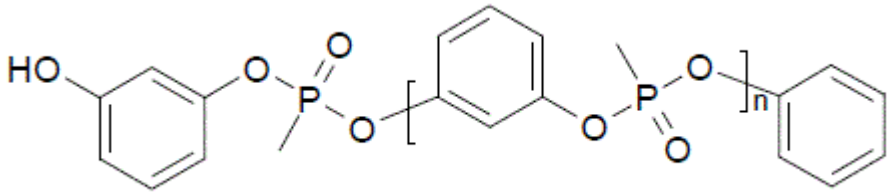
Fyrol PMP

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[§] Based on analogy to experimental data for a structurally similar compound. [‡] The highest hazard designation of any of the oligomers with MW <1,000.

		Human Health Effects										**Aquatic Toxicity**		**Environmental Fate**	
Chemical	**CASRN**	**Acute Toxicity**	**Carcinogenicity**	**Genotoxicity**	**Reproductive**	**Developmental**	**Neurological**	**Repeated Dose**	**Skin Sensitization**	**Respiratory Sensitization**	**Eye Irritation**	**Dermal Irritation**	**Acute**	**Chronic**	**Persistence**	**Bioaccumulation**
Fyrol PMP	63747-58-0	**L**	***L*[§]**	***L*[§]**	***M*[§]**	***M*[§]**	***M*[§]**	***M*[§]**	**L**		**L**	**L**	***H*[‡]**	***H*[‡]**	***VH***	***H*[‡]**

Fyrol PMP



Representative Structure

CASRN: 63747-58-0

MW: >1,000; with a significant percentage of components having MW <1,000

MF: $(C_{13}H_{13}O_3P \cdot C_6H_6O_2)_x$

Physical Forms: Solid
Neat: Solid

Use: Flame retardant

SMILES: c1(OP(C)(=O)Oc2cc(O)ccc2)cc(OP(C)(=O)Oc2ccccc2)ccc1 (n=1);
c1(OP(C)(=O)Oc4cc(OP(C)(=O)Oc3cc(O)ccc3)ccc4)cc(OP(C)(=O)Oc2ccccc2)ccc1 (n=2);
c1(OP(C)(=O)Oc5cc(OP(C)(=O)Oc3cc(OP(C)(=O)Oc4cc(O)ccc4)ccc3)ccc5)cc(OP(C)(=O)Oc2ccccc2)ccc1 (n=3);
c1(OP(C)(=O)Oc6cc(OP(C)(=O)Oc3cc(OP(C)(=O)Oc4cc(OP(C)(=O)Oc5cc(O)ccc5)ccc4)ccc3)ccc6)cc(OP(C)(=O)Oc2ccccc2)ccc1 (n=4)

Synonyms: Phosphonic acid, P-methyl-, diphenyl ester, polymer with 1,3-benzenediol; Phosphonic acid, methyl-, diphenyl ester, polymer with 1,3-benzenediol; 1,3-Benzenediol, polymer with diphenyl methylphosphonate; Diphenyl methylphosphonate-resorcinol copolymer; Aryl alkylphosphonate; Poly(m-phenylene methylphosphonate)
Trade Name: Fyrolflex PMP

CASRN 124933-95-5 was identified by literature searches based on name as a related alternative. CASRN 124933-95-5 has a slightly different structure, and no other applicable data were found for this CASRN.

Chemical Considerations: This alternative is a polymer consisting of oligomers with MWs above and below 1,000 daltons according to commercial product datasheets.
The oligomers with a MW >1,000, where n≥5, are assessed using the available polymer assessment literature.
The components with a MW <1,000 are evaluated with four representative structures, where n=1, 2, 3 and 4, as indicated in the SMILES entry. The low MW components are assessed with EPI v4.11 and ECOSAR v1.11 estimates due to an absence of publicly available experimental physical/chemical, environmental fate and aquatic toxicity values. A typical phosphorus content of 17.5% was reported from the commercial product literature. (Hsu, 2013; ICL, 2013).

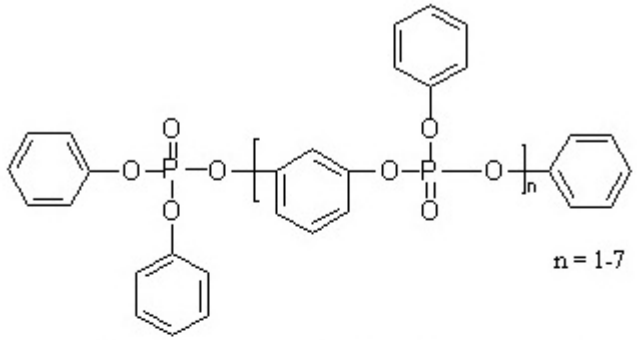
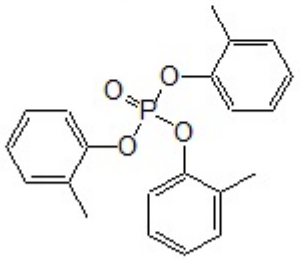
Polymeric: Yes
Oligomeric: This polymer is terminated with either resorcinol and/or phenyl groups based on the starting materials. The repeating units of this polymer are m-phenylene methylphosphonate. A representative structure for n=1 is identified in the SMILES section above.

Metabolites, Degradates and Transformation Products: None identified. Environmental degradation of Fyrol PMP has not been demonstrated in experimental studies. Degradation of Fyrol PMP by sequential dephosphorylation could produce phosphinates, phenol (CASRN 108-95-2) or resorcinol (CASRN 108-46-3). The importance of dephosphorylation relative to possible competing pathways has not been demonstrated in a published study. (Professional judgment)

Analog: Resorcinol bis-diphenylphosphate (RDP; CASRN 125997-21-9); tricresyl phosphate (TCP; CASRN 1330-78-5);and confidential analogs

Endpoint(s) using analog values: Carcinogenicity, genotoxicity, reproductive,

Analog Structure:

developmental, repeated dose	 Resorcinol bis-diphenylphosphate (RDP; CASRN 125997-21-9)  Phosphoric acid, tris(methylphenyl) ester (CDP; CASRN 1330-78-5) Representative structure
Structural Alerts: Phenols - neurotoxicity; Organophosphorus compounds - neurotoxicity. (EPA, 2012).	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).	
Hazard and Risk Assessments: None located.	

Fyrol PMP CASRN 63747-58-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	52 (Measured)	ICL, 2010	Reported in a material safety datasheet.
Boiling Point (°C)	>300 (Estimated)	EPA, 1999; EPI v4.11	Estimate based on four representative structures with MW <1,000. Also estimated for oligomers with MWs >1,000. Cutoff value according to HPV assessment guidance and cutoff value used for large, high MW solids.
Vapor Pressure (mm Hg)	$<10^{-8}$ for n=1-4 (Estimated)	EPA, 1999; EPI v4.11	Estimates based on the representative structures with MW <1,000. Cutoff value for nonvolatile compounds according to HPV assessment guidance.
	$<10^{-8}$ (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Cutoff value for large, high MW polymer components.
Water Solubility (mg/L)	8.4 for n=1 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1.
	0.1 for n=2 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=2.
	0.001 for n=3 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=3.
	$1.3x10^{-5}$ for n=4 (Estimated)	EPI v4.11; EPA, 1999	Estimates based on representative oligomer where n=4. Values are less than the cutoff value, <0.001 mg/L, for non-soluble compounds according to HPV assessment guidance.
	<0.001 for the n≥5 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Cutoff value for large, high MW non-ionic polymer components.
	<0.01% (Measured)	ICL, 2010	Reported in a material safety datasheet.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Log K_{ow}		3.4 for n=1 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1.
		4.4 for n=2 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=2.
		5.3 for n=3 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=3.
		6.3 for n=4 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=4.
Flammability (Flash Point)		Not flammable (Measured)	ICL, 2010	Reported in safety datasheet and based on its use as a flame retardant.
Explosivity		Not expected to form explosive mixtures with air. (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis				No data located.
pH				No data located.
pK_a				No data located.
Particle Size				No data located.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**No experimental data were located. Based on professional judgment, absorption is expected to be poor by all routes for the low MW (<1,000) fraction. There is no absorption expected for any route of exposure for the MW >1,000 components.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Absorption is expected to be negligible by all routes for the neat material and poor by all routes for the low MW fraction if in solution.	Professional judgment	Estimated based on professional judgment.
	Other			No data located.
Acute Mammalian Toxicity		**LOW: Experimental data indicates that the LD_{50} are >2,000 mg/kg when administered orally and dermally to rats. Experimental data for the analog, phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (CASRN 125997-21-9) indicates an LC_{50} > 4.14 mg/L.**		
Acute Lethality	**Oral**	Rat LD_{50} >2,000 mg/kg in a 75% DMSO solution	ICL, 2010	Reported in a material safety datasheet with limited study details.
	Dermal	Rabbit LD_{50} >5,000 mg/kg	ICL, 2010	Reported in a material safety

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				datasheet with limited study details.
	Inhalation	Rat inhalation LC_{50} > 4.14 mg/L	EPA, 2010	Estimated by analogy to Phosphoric trichloride, polymer with 1,3-benzenediol, phenyl ester (CASRN 125997-21-9)
Carcinogenicity		**LOW: Estimated based on analogy to tricresyl phosphate (TCP). There was no evidence of carcinogenicity in rats or mice following dietary exposure to a commercial mixture of TCP for 2 years. There were no experimental data located for this substance.**		
	OncoLogic Results			This polymer is not amenable to available estimation methods.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity	2-Year dietary study in Fischer 344/N rats (95/sex/concentration) Test substance concentrations: 0, 75, 150, 300 ppm (approximately 0, 3, 6, and 13 mg/kg bw-day for males and 0, 4, 7, and 15 mg/kg bw-day for females) Chronic toxicity: NOAEL = 13 mg/kg bw-day (males); 4 mg/kg bw-day for females LOAEL = 26 mg/kg bw-day (males) and 7 mg/kg bw-day (females) for cytoplasmic vacuolization of adrenal cortex No evidence of carcinogenic activity (Estimated by analogy)	NTP, 1994	Estimated based on analogy to tricresyl phosphate (TCP); study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of 18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
		2-Year dietary study in B6C3F1 mice (95/sex/concentration) Test substance concentrations: 0, 60, 125, 250 ppm (approximately 0, 7, 13, and 27 mg/kg bw-day for males and 0, 8, 18, and 37 mg/kg bw-day for females)	NTP, 1994	Estimated based on analogy to tricresyl phosphate (TCP); study details reported in a reliable primary source; test substance: Tricresyl phosphate (CASRN 1330-78-5) as a commercial product comprised of

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		chronic toxicity NOAEL = 18 mg/kg bw-day for females, not established for males LOAEL: 7 mg/kg bw-day (males) and 37 mg/kg bw-day (females) for ceroid pigmentation of adrenal cortex No evidence of carcinogenic activity (Estimated by analogy)		18% dicresyl phosphate esters (unconfirmed isomeric composition) and 79% tricresyl phosphate esters (21% confirmed as tri-m-cresyl phosphate, 4% as tri-p-cresyl phosphate, and no detectable tri-o-cresyl phosphate [<0.1%]).
	Other			No data located.
Genotoxicity		**LOW: Based on results from an Ames assay, analogy to RDP (CASRN 125997-21-9) and professional judgment. The test substance was reported to be negative for gene mutations in an Ames assay; however, there were no experimental chromosomal aberrations data for the test substance. The analog RDP did not cause gene mutations or chromosomal aberrations *in vitro* and did not produce an increase in micronuclei in mice *in vivo*.**		
	Gene Mutation *in vitro*	Negative, Ames assay	ICL, 2010	Reported in a material safety datasheet with limited study details.
		Negative in *Salmonella typhimurium* (strains not indicated) with and without metabolic activation at concentrations up to 5,000 µg/plate. No cytotoxicity was evident. (Estimated by analogy)	EPA, 2010; Pakalin et al., 2007	Estimated based on analogy. Guideline study. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
		Negative in *Escherichia coli* (strains not indicated) with and without metabolic activation at concentrations up to 5,000 µg/plate. No cytotoxicity was evident. (Estimated by analogy)	EPA, 2010; Pakalin et al., 2007	Estimated based on analogy. Guideline study. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
	Gene Mutation *in vivo*			No data located.

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	Negative in chromosomal aberration test (cultured human lymphocytes) with and without metabolic activation at concentrations up to 625 µg/mL. Cytotoxicity data not indicated. (Estimated by analogy)	EPA, 2010; Pakalin et al., 2007	Estimated based on analogy. Guideline study. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
	Chromosomal Aberrations *in vivo*	Negative in mammalian erythrocyte micronucleus test (Swiss mice) following a single oral dose of 5,000 mg/kg-bw. (Estimated by analogy)	EPA, 2010; Pakalin et al., 2007	Estimated based on analogy. Guideline study. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
		Negative in mammalian erythrocyte micronucleus test (mice) following single oral dose of 500 mg/kg-bw. (Estimated by analogy)	Submitted confidential study	Estimated based on analogy. Reported in a submitted confidential study for the analog RDP (CASRN 125997-21-9) conducted in accordance with GLP and OECD Guideline 474.
	DNA Damage and Repair			No data located.
	Other	Limited bioavailability expected for the high MW (>1,000) components. (Estimated for n ≥5 oligomers)	Boethling and Nabholz, 1997; Professional judgment	Based on polymer assessment literature.
Reproductive Effects		**MODERATE: Based on data for a confidential analog and professional judgment. There were no experimental data located for the substance Fyrol PMP. There is potential for reproductive toxicity based on data for a confidential analog reporting reduced litter size and weight at 250 mg/kg-day (NOAEL: 50 mg/kg-day) a An experimental study for the analog RDP indicated no adverse effects on reproductive performance or fertility parameters at doses up to 1,000 mg/kg-day (highest dose tested) in a two generation dietary study in parental rats. Developmental changes effecting the reproductive system were also reported in F_1 female rats at 250 mg/kg-day. In the absence of experimental data for this substance, and conflicting results for analogs, a conservative approach was used to assign a Moderate hazard designation.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity	Two generation dietary reproduction study in rats. Sprague-Dawley rats (30/sex/dose) were fed 0, 50, 500, or	EPA, 2010; Pakalin et al., 2007	Estimated based on analogy. Guideline study. Data are for a commercial polymeric mixture of

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Screen	1,000 mg/kg-day to the analog RDP in the diet for 10 weeks. There were no reproductive or systemic effects reported in parental rats at doses as high as 1,000 mg/kg-day. Developmental changes affecting the reproductive system (delayed vaginal opening and preputial separation) were reported in F_1 female rats at 500 and 1,000 mg/kg-day. This effect was considered by study authors to be secondary to reduction of body weight in F_1 generation during week 1 (treated animals had decreased body weights compared to controls during week 1, reportedly due to an initial aversion to taste of diet) Parental systemic and reproductive toxicity: NOAEL: ≥1,000 mg/kg-day (highest dose tested) LOAEL: Not established Offspring (developmental) reproductive toxicity: NOAEL(F_1 generation): 50 mg/kg-day LOAEL (F_1 generation): 500 mg/kg-day (for vaginal opening and preputial separation) (Estimated by analogy)		the analog RDP (CASRN 125997-21-9).

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction and Fertility Effects	Potential for reproductive toxicity; no pregnancies (1,000 mg/kg-day); reduced litter size and weight (250 mg/kg-day). NOAEL: 50 mg/kg-day LOAEL: 250 mg/kg-day (Estimated by analogy)	Professional judgment; Submitted confidential study	Estimated by analogy to confidential analog.
	Other	Limited bioavailability expected. (Estimated for n ≥5 oligomers)	Boethling and Nabholz, 1997; Professional judgment	Based on cutoff value for large, high MW non-ionic polymers.
Developmental Effects		**MODERATE: Based on analogy to RDP (CASRN 125997-21-9) and professional judgment. There were no experimental data for the substance Fyrol PMP. An experimental study for the analog RDP reported a NOAEL of 50 mg/kg-day in a two generation dietary reproduction study in rats. Adverse effects included delayed vaginal opening and preputial separation at a dose of 500 mg/kg-day. Though the changes are considered by the study authors to be secondary to reduced body weight in the F_1 generation, reported data were insufficient to determine if this was a secondary effect. No adverse developmental effects were observed in rabbits following oral administration of the analog RDP at doses up to 1,000 mg/kg-day. There were no data located for the developmental neurotoxicity endpoint. The analog RDP (CASRN 125997-21-9) has been shown to cause cholinesterase inhibition which may be an indicator of potential developmental neurotoxicity.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Two generation dietary reproduction study in rats. Sprague-Dawley rats (30/sex/dose) were fed 0, 50, 500, or 1,000 mg/kg-day to the analog RDP in the diet for 10 weeks. Vaginal opening and preputial separation were delayed at 500 and 1,000 mg/kg-day. This effect was considered by study authors to be secondary to reduction of body weight in F_1 generation during week 1 (treated animals had decreased body weights compared to controls during week 1, reportedly due to an initial aversion to taste of diet). NOAEL(F_1 generation): 50 mg/kg-day LOAEL (F_1 generation): 500 mg/kg-day (for vaginal opening and preputial separation) (Estimated by analogy)	EPA, 2010; Pakalin et al., 2007	Estimated based on analogy. Guideline study. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9); limited study details reported to determine if the developmental effect is secondary to reduced body weight in F1 rats.

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	Pregnant rabbits; oral gavage; gestation days (GDs) 6-28; 0, 50, 200 or 1,000 mg/kg-day test material containing the analog RDP No clinical signs of toxicity. No adverse effects on maternal food consumption, body weight gain or organ weights. No adverse effects on fetal body weights, viability, or any developmental endpoint measured. NOAEL (maternal and developmental toxicity): >1,000 mg/kg-day (highest dose tested) LOAEL: Not established (Estimated by analogy)	EPA, 2010; Environment Agency, 2009	Estimated based on analogy. Guideline study reported in a secondary source. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	There were no data located for the developmental neurotoxicity endpoint. As a result, there is uncertain potential for developmental neurotoxicity for this substance. The analog RDP (CASRN 125997-21-9) has been shown to cause cholinesterase inhibition which may be an indicator of potential developmental neurotoxicity. (Estimated)	Professional judgment	Estimated by analogy to RDP (CASRN 125997-21-9).
	Other	Limited bioavailability expected. (Estimated for n≥5 oligomers)	Boethling and Nabholz, 1997; Professional judgment	Based on cutoff value for large, high MW non-ionic polymers.

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Based on data for the analog RDP (CASRN 125997-21-9) and professional judgment. There were no experimental data for the substance Fyrol PMP. A study for the analog RDP reported a 28-day inhalation LOAEL of 0.5 mg/L for inhibition of plasma ChE in rats (NOAEL = 0.1 mg/L). The neurotoxicity criteria values are tripled for 28-day studies to correlate to the criteria values based on 90-day repeated dose studies; the LOAEL and NOAEL of 0.5 mg/kg-day and 0.1 mg/kg-day, respectively, lie within the MODERATE hazard range from 0.06 - 0.6 mg/L. There is also potential for neurotoxicity based on the presence of the phenol and organophosphorus structural alerts.**		
	Neurotoxicity Screening Battery (Adult)	28-day inhalation study in rats with the analog RDP (CASRN 125997-21-9); 0, 0.1, 0.5 and 2.0 mg/L (aerosol) Significant inhibition of plasma cholinesterase (ChE) (0.5 and 2.0 mg/L). No clinical signs suggestive of neurotoxic effect. ChE was not affected after study termination. NOAEL: 0.1 mg/L LOAEL: 0.5 mg/L (plasma ChE inhibition) (Estimated by analogy)	Environment Agency, 2009	Estimated based on analogy to RDP (CASRN 125997-21-9). Study details reported in a secondary source; study was not designed to assess all neurological parameters; criteria values are tripled for chemicals evaluated in 28-day studies; the LOAEL of 0.5 mg/kg-day falls within the Moderate hazard criteria (0.06-0.6 mg/L).
		28-day oral (gavage) study in mice with the analog RDP (CASRN 125997-21-9); 0, 500, 1,500, 5,000 mg/kg-day. Dose-related decrease in plasma ChE compared to controls, which was no longer apparent after the 60 day recovery period. No NOAEL/LOAEL determined. (Estimated by analogy)	Environment Agency, 2009	Estimated based on analogy. Study details reported in a secondary source; study was not designed to assess all neurological parameters; cannot rule out all neurotoxicity.
	Other	Limited bioavailability expected. (Estimated for n≥5 oligomers)	Boethling and Nabholz, 1997; Professional judgment	Based on cutoff value for large, high MW non-ionic polymers.
		Potential for neurotoxic effects based on a	EPA, 2012; Professional	Estimated based on a structural alert

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		structural alert for phenol and organophosphorus compounds.	judgment	for phenols and organophosphorus compounds and professional judgment.
Repeated Dose Effects		**MODERATE: Based on analogy to RDP (CASRN 125997-21-9), a confidential analog and professional judgment. There were no experimental data for the test substance Fyrol PMP. A 4-week inhalation exposure study in rats to 0.5 mg/L of the analog RDP as an aerosol resulted in alveolar histiocytosis (NOAEC = 0.1 mg/L- day). No other exposure-related gross or microscopic pathology was identified in any organ in this study. The repeated dose criteria values are tripled for 28-day studies to correlate to the criteria values based on 90-day repeated dose studies; this study lies in the MODERATE hazard range from 0.06 - 0.6 mg/L. There is also potential for liver toxicity based on a confidential analog (NOEL = 300 mg/kg-day).**		

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In a 4-week inhalation study Sprague-Dawley rats (10/sex/group) were exposed (aerosol, nose only) to 0, 100, 500 or 2,000 mg/m^3 (0, 0.1, 0.5, or 2 mg/L) of the analog RDP. No deaths or clinical signs of toxicity. Decreased body weight and food consumption in males. Significant inhibition of plasma cholinesterase in females at 500 and 2,000 mg/m^3 and in males at 2,000 mg/m^3. White foci in the lungs at 2,000 mg/m^3 and alveolar histiocytosis at 500 and 2,000 mg/m^3. Although lung changes are relevant, they were not considered to be a reflection of a specific toxic response to the analog RDP; these changes are characteristic of exposure to non-cytotoxic water-insoluble materials. No other gross or microscopic pathology in any organ. NOAEC: 100 mg/m^3 (0.1 mg/L) LOAEC: 500 mg/m^3 (0.5 mg/L; based on alveolar histiocytosis) (Estimated based on analogy)	EPA, 2010; Environment Agency, 2009	Estimated based on analogy. Guideline study reported in a secondary source. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
		28-day oral study, rats Potential for liver toxicity. NOEL: 300 mg/kg-day (Estimated based on analogy)	Submitted confidential study; Professional judgment	Estimated based on analogy to confidential analog.
		Limited bioavailability expected for the high MW (>1,000) components. (Estimated for n ≥5 oligomers)	Boethling and Nabholz, 1997; Professional judgment	Based on polymer assessment literature.
	Immune System Effects	Negative, oral gavage study in mice.	EPA, 2010	Estimated based on analogy.

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Female B6C3F1 mice (50/group) were exposed via oral gavage to 0, 500, 1,500, or 5,000 mg/kg-day of the analog RDP for 28 days. No deaths, clinical signs of toxicity, or effects on body or organ weights. No adverse histopathological changes or necropsy findings. No treatment-related changes in peritoneal cell numbers or cell types, peritoneal macrophage phagocytic activity or host susceptibility to infection. No adverse effect on splenic natural killer cell activity, lymphocyte blastogenesis, or antibody-forming cell function. There were significant decreases in erythrocyte cholinesterase activity and plasma pseudocholinesterase activity in all dose groups, but both enzyme activities returned to control levels at the end of the 60 day recovery period.		Guideline study reported in a secondary source. Data are for a commercial polymeric mixture of the analog RDP (CASRN 125997-21-9).
Skin Sensitization		**LOW: Negative for skin sensitization in guinea pigs.**		
	Skin Sensitization	Non-sensitizing, guinea pigs	Submitted confidential study	Adequate confidential study
		Not a sensitizer, Modified Buehler Method	ICL, 2010	Reported in a material safety datasheet with limited study details.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Fyrol PMP was mildly irritating to rabbit eyes.**		
	Eye Irritation	Mild, rabbits	ICL, 2010	Reported in a material safety datasheet with limited study details.
		Negative, rabbits	Submitted confidential study	Study details and test conditions were not available.

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Dermal Irritation		**LOW: Fyrol PMP was mildly irritating to rabbit skin.**		
	Dermal Irritation	Mild irritant, rabbit	ICL, 2010	Reported in a material safety datasheet with limited study details.
Endocrine Activity		**No experimental data were located to evaluate and determine if Fyrol PMP affects endocrine activity. However, resorcinol, a metabolite of the analog RDP (CASRN 125997-21-9) and a starting material in Fyrol PMP synthesis, is listed as a suspected endocrine disruptor by the EU.**		
		Resorcinol (CASRN 108-46-3) is listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors. (Estimated by analogy)	European Commission, 2012	Estimated by analogy. "Potential for endocrine disruption. In vitro data indicating potential for endocrine disruption in intact organisms. Also included effects in-vivo that may, or may not, be endocrine disruption-mediated. May include structural analyses and metabolic considerations".

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**The analog, RDP (CASRN 125997-21-9), had no effect on immunological parameters at doses up to 5,000 mg/kg-day (highest dose tested) in an oral gavage study in mice. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for immunotoxicity.**		
	Immune System Effects	Negative, oral gavage study in mice. Female B6C3F1 mice (50/group) were exposed via oral gavage to 0, 500, 1,500, or 5,000 mg/kg-day for the analog RDP for 28 days. No deaths, clinical signs of toxicity, or effects on body or organ weights. No adverse histopathological changes or necropsy findings. No treatment-related changes in peritoneal cell numbers or cell types, peritoneal macrophage phagocytic activity or host susceptibility to infection. No adverse effect on splenic natural killer cell activity, lymphocyte blastogenesis, or antibody-forming cell function. There were significant decreases in erythrocyte cholinesterase activity and plasma pseudocholinesterase activity in all dose groups, but both enzyme activities returned to control levels at the end of the 60 day recovery period.	EPA, 2010	Estimated based on analogy. Guideline study reported in a secondary source. Data are for the analog, a commercial polymeric mixture of RDP (CASRN 125997-21-9).
		Limited bioavailability expected for the high MW (>1,000) components. (Estimated for n ≥5 oligomers)	Boethling and Nabholz, 1997; Professional judgment	Based on polymer assessment literature.

Fyrol PMP CASRN 63747-58-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class	Phenols		
Acute Aquatic Toxicity	**HIGH: Based on estimated acute aquatic toxicity values for fish, daphnia, and green algae using the phenols SAR for a representative structure, where n=1, with a MW <1,000. The high MW components, with a MW>1,000 have low water solubility and are expected to have no effects at saturation (NES).**		
Fish LC_{50}	Freshwater fish 96-hour LC_{50}: 6.2 mg/L (ECOSAR class: Phenols)	ECOSAR v1.11	Estimate based on representative oligomer n=1.
	Freshwater fish 96-hour LC_{50}: n=2: 1.6 mg/L n=3: 0.39 mg/L n=4: 0.09 mg/L (ECOSAR class: Phenols) (Estimated)	ECOSAR v1.11	Estimates based on representative oligomers n=2 through n=4. The corresponding estimated effects exceed the water solubilities (0.1 mg/L for n=2, 0.001 mg/L for n=3, and 0.00001 mg/L for n=4) by more than 10x. NES are predicted for these endpoints.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50}: 3.5 mg/L (ECOSAR class: Phenols)	ECOSAR v1.11	Estimate based on representative oligomer n=1.
	Daphnia magna 48-hour LC_{50}: n=2: 1.4 mg/L n=3: 0.52 mg/L n=4: 0.18 mg/L (ECOSAR class: Phenols) (Estimated)	ECOSAR v1.11	Estimates based on representative oligomers n=2 through n=4. The corresponding estimated effects exceed the water solubilities (0.1 mg/L for n=2, 0.001 mg/L for n=3, and 0.00001 mg/L for n=4) by more than 10x. NES are predicted for

Fyrol PMP CASRN 63747-58-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			these endpoints.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
Green Algae EC_{50}	Green algae 96-hour EC_{50}: 14 mg/L (ECOSAR class: Phenols)	ECOSAR v1.11	Estimate based on representative oligomer n=1.
	Green algae 96-hour EC_{50}: n=2: 5.1 mg/L n=3: 1.7 mg/L n=4: 0.55 mg/L (ECOSAR class: Phenols) (Estimated)	ECOSAR v1.11	Estimates based on representative oligomers n=2 through n=4. The corresponding estimated effects exceed the water solubilities (0.1 mg/L for n=2, 0.001 mg/L for n=3, and 0.00001 mg/L for n=4) by more than 10x. NES are predicted for these endpoints.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
Chronic Aquatic Toxicity	**HIGH: Based on estimated chronic aquatic toxicity values for fish, daphnia, and green algae using the phenols SAR for representative structure, where n=1, with a MW <1,000. The high MW components, with a MW>1,000 have low water solubility and are expected to have no effects at saturation (NES).**		
Fish ChV	Freshwater fish ChV: 0.77 mg/L (ECOSAR class: Phenols)	ECOSAR v1.11	Estimate based on representative oligomer n=1.

Fyrol PMP CASRN 63747-58-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Freshwater fish ChV: n=2: 0.23 mg/L n=3: 0.06 mg/L n=4: 0.02 mg/L (ECOSAR class: Phenols) (Estimated)	ECOSAR v1.11	Estimates based on representative oligomers n=2 through n=4. The estimated effect for n=2 exceeds the water solubility of 0.1 mg/L, but not by 10x as required to be considered NES by ECOSAR. The chemical may not be soluble enough to measure the predicted effect. The corresponding estimated effects for n=3 and n=4 exceed the water solubilities (0.001 mg/L and 0.00001 mg/L, respectively) by more than 10x. NES are predicted for these oligomers.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
Daphnid ChV	Daphnia magna ChV: 0.67 mg/L (ECOSAR class: Phenols);	ECOSAR v1.11	Estimate based on representative oligomer n=1.
	Daphnia magna ChV: n=2: 0.27 mg/L n=3: 0.1 mg/L n=4: 0.03 mg/L (ECOSAR class: Phenols) (Estimated)	ECOSAR v1.11	Estimates based on representative oligomers n=2 through n=4. The estimated effect for n=2 exceeds the water solubility of 0.1 mg/L, but not by 10x as required to be considered NES by ECOSAR. The chemical may not be soluble enough to measure the predicted effect. The corresponding estimated effects for n=3 and n=4 exceed the water solubilities (0.001 mg/L and 0.00001 mg/L, respectively) by

Fyrol PMP CASRN 63747-58-0			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			more than 10x. NES are predicted for these oligomers.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
Green Algae ChV	Green algae ChV: 6.5 mg/L (ECOSAR class: Phenols)	ECOSAR v1.11	Estimate based on representative oligomer n=1.
	Green algae ChV: n=2: 2.4 mg/L n=3: 0.78 mg/L n=4: 0.25 mg/L (ECOSAR class: Phenols) (Estimated)	ECOSAR v1.11	Estimates based on representative oligomers n=2 through n=4. The corresponding estimated effects exceed the water solubilities (0.1 mg/L for n=2, 0.001 mg/L for n=3, and 0.00001 mg/L for n=4) by more than 10x. NES are predicted for these endpoints.
	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
ENVIRONMENTAL FATE			

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Transport		**The estimated negligible water solubility and estimated negligible vapor pressure indicate that this polymer is anticipated to partition predominantly to soil and sediment. The estimated Henry's Law Constant of $<10^{-8}$ atm-m^3/mole indicates that it is not expected to volatilize from water to the atmosphere. The estimated K_{oc} of >30,000 indicates that it is not anticipated to migrate from soil into groundwater and also has the potential to adsorb to sediment.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ for the n≥5 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	High MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization.
		$<10^{-8}$ for n=1-4 (Estimated)	EPI v4.11	
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 for n=1-4 (Estimated)	EPI v4.11; Professional judgment	Estimated value based on representative structures with MW <1,000. Cutoff value for nonvolatile compounds.
		>30,000 for the n≥5 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the n≥5 oligomers; cutoff value used for large, high MW polymers. High MW polymers are expected to adsorb strongly to soil and sediment.
	Level III Fugacity Model	Air = 0% Water = 4.8% Soil = 57% Sediment = 39% (Estimated) for n=1	EPI v4.11	Estimates based on a representative structure where n=1. No data located for the high MW component of the polymers.
Persistence		**VERY HIGH: Although experimental data are not available, the high MW components of this polymer (n≥5; MW>1,000) are expected to be recalcitrant to biodegradation. Estimated half-lives for ultimate aerobic biodegradation are >180 days for the n=1 oligomer, representing MW <1,000 components of the polymer. Degradation of this polymer by hydrolysis or direct photolysis is not expected to be significant as the functional groups present do not tend to undergo these reactions under environmental conditions. The atmospheric half-life is estimated to be <1 day; however, the polymer is not anticipated to partition significantly to air.**		
Water	**Aerobic Biodegradation**	Days-weeks (Primary Survey Model) Weeks-months (Ultimate Survey Model) (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1.
		Recalcitrant	Boethling and Nabholz, 1997;	High MW polymers are expected to

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		for n≥5 oligomers (Estimated)	Professional judgment	be non-biodegradable.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11; Professional judgment	Estimated value based on representative structures with MW <1,000. Also, the high MW polymer components are anticipated to be nonvolatile.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11; Professional judgment	Estimated value based on representative structures with MW <1,000. Also, the high MW polymer components are anticipated to be nonvolatile.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (Anaerobic-methanogenic biodegradation probability model) for n=1-4	EPI v4.11	Estimates based on representative oligomer where n=1-4.
		Recalcitrant for n≥5 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	High MW polymers are expected to be resistant to removal under anoxic conditions due to their limited bioavailability.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	<0.15 days (Estimated)	EPI v4.11	Estimated value based on four confidential representative structures with MW <1,000.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	This polymer does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	>1 year (Estimated)	Professional judgment	Given the limited solubility estimated for this material, hydrolysis is not anticipated to occur

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				to an appreciable extent.
		>1 year at pH 6 68 days at pH 7 6.8 days at pH 8 16 hours at pH 9 (Estimated for n=1)	EPI v4.11	Hydrolysis rates are expected to be pH-dependent and may be limited by the low water solubility of this compound. Under basic conditions, sequential dephosphorylation reactions may occur.
Environmental Half-life		>75 days Half-life estimated for representative structure where n=1; in the predominant compartment, soil, as determined by EPI and the PBT Profiler methodology (Estimated)	PBT Profiler v1.301; EPI v4.11	Half-life estimated for the predominant compartment, soil, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**HIGH: The estimated BCF and BAF for the low MW components (n=1-4; MW<1,000) result in a High bioaccumulation designation. The higher MW oligomers that may be found in the polymeric mixture (n≥5; MW>1,000) are expected to have Low potential for bioaccumulation based on their large size and low water solubility according to the polymer assessment literature and professional judgment.**		
	Fish BCF	6,600 for n=4 (Estimated)	EPI v4.11	Estimates based on representative structure where n=4.
		1,500 for n=3 (Estimated)	EPI v4.11	Estimates based on representative structure where n=3.
		360 for n=2 (Estimated)	EPI v4.11	Estimates based on representative structure where n=2.
		85 for n=1 (Estimated)	EPI v4.11	Estimates based on representative structure where n=1.
		<100 (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the oligomers with a MW >1,000. Cutoff value for large, high MW, insoluble polymers according to polymer assessment literature.
	Other BCF			No data located.
	BAF	$2.1x10^6$ for n=4 (Estimated)	EPI v4.11	Estimates based on representative structure where n=4.
		$3.2x10^4$ for n=3 (Estimated)	EPI v4.11	Estimates based on representative

Fyrol PMP CASRN 63747-58-0				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				structure where n=3.
		1,200 for n=2 (Estimated)	EPI v4.11	Estimates based on representative structure where n=2.
		170 for n=1 (Estimated)	EPI v4.11	Estimates based on representative structure where n=1.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		No data located.		

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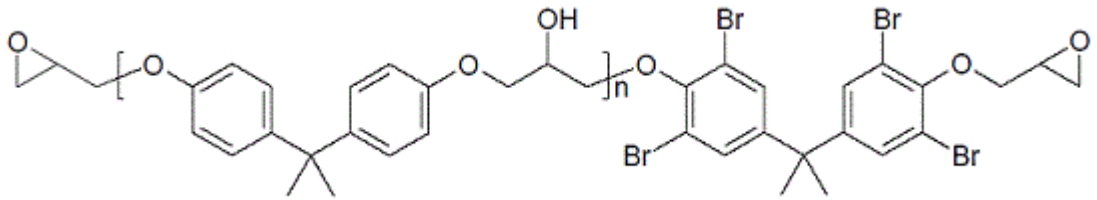
D.E.R. 500 Series

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

‡ The highest hazard designation of any of the oligomers with MW <1,000. ¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

		Human Health Effects										Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
D.E.R. 500 Series¥	26265-08-7	*L*	*M*	*M*	*M*	*M*	*M*	*M*	H		*M*‡	*M*‡	*L*	*L*	*VH*	*H*‡

D.E.R. 500 Series



CASRN: 26265-08-7

MW: Average MW 900 (Measured)

MF: $C_{39}H_{40}Br_4O_7$ as shown with n=1; MW=940

Physical Forms: Solid
Neat:

Use: Flame retardant

SMILES: O1CC1COc2ccc(cc2)C(C)(C)c3ccc(cc3)OCC(O)COc4c(Br)cc(cc4Br)C(C)(C)c5cc(Br)c(c(Br)c5)OCC6CO6 as shown with n = 1

Synonyms: Phenol, 4,4'(1-methylethylidene)bis[2,6-dibromo-, polymer with (chloromethyl)oxirane and 4,4'-(1-methylethylidene)bis[phenol] (The reaction product of TBBPA), bisphenol A, epichlorohydrin and tetrabromobisphenol A polymer; Brominated epoxy resin; Epichlorohydrin, tetrabromobisphenol A polymer
Trade names: D.E.R.® 500 series epoxy resin; D.E.R. 538; Epikote 1145-B-70; EPON Resin 1123 (polymer of tetrabromobisphenol A epoxy resin, bisphenol A diglycidyl ether, and epichlorohydrin)

The D.E.R. 500 series epoxy resin product literature also lists CASRN 40039-93-8, Phenol, 4,4'-(1-methylethylidene)bis[2,6-dibromo-, polymer with 2-(chloromethyl)oxirane; or Bisphenol A diglycidyl ether, brominated. This compound is a very close structural analog to Phenol, 4,4'(1-methylethylidene)bis[2,6-dibromo-, polymer with (chloromethyl)oxirane and 4,4'-(1-methylethylidene)bis[phenol] (CASRN 26265-08-7).

Chemical Considerations: The D.E.R. 500 Series of polymers consist of components with MWs above and below 1,000 daltons.
The low MW components (MW <1,000) are expected to be present at levels requiring their assessment. The MW <1,000 components are assessed with EPI v4.11 and ECOSAR v1.11 estimates due to an absence of publicly available experimental physical/chemical, environmental fate and aquatic toxicity values. These include the n=1 component as shown in the SMILES entry and the n=0 component, as represented by the discrete organic 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2).
The n≥2 oligomers have a MW >1,000 and are assessed using the available polymer assessment literature.

Polymeric: Yes
Oligomeric: This is a tetrabromobisphenol A (TBBPA)-based epoxy resin; the oligomers are produced by reacting epichlorohydrin with bisphenol A (BPA) and TBBPA (Dow, 2009).

Metabolites, Degradates and Transformation Products: None identified (Professional judgment)

Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable

Structural Alerts: Polyhalogenated aromatic hydrocarbons: immunotoxicity; epoxy groups/epoxides: dermal sensitization, cancer, reproductive effects, developmental toxicity (EPA, 2012; EPA, 2010).
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).
Hazard and Risk Assessments: None identified.

D.E.R. 500 Series CASRN 26265-08-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated)	EPI v4.11; EPA, 1999	Estimates based on a representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture with a MW <1,000. Also estimated for oligomers where n≥2 with MWs >1,000. Cutoff value according to HPV assessment guidance and cutoff value used for large, high MW solids.
Vapor Pressure (mm Hg)	$<10^{-8}$ for MW <1,000 components (Estimated)	EPI v4.11; EPA, 1999	Estimates based on representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. Cutoff value for nonvolatile compounds according to HPV assessment guidance.
	$<10^{-8}$ for the n≥2 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Cutoff value for large, high MW polymers.
Water Solubility (mg/L)	$3.3x10^{-5}$ for a component (Estimated)	EPI v4.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
	$1.7x10^{-9}$ for n=1 (Estimated)	EPI v4.11; EPA, 1999	Estimates based on representative oligomer where n=1. Values are less than the cutoff value, <0.001 mg/L, for non-soluble compounds according to HPV assessment guidance.
	<0.001	Boethling and Nabholz, 1997;	Cutoff value for large, high MW

D.E.R. 500 Series CASRN 26265-08-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	for the n≥2 oligomers (Estimated)	Professional judgment	non-ionic polymers.
Log K_{ow}	7.4 for a component (Estimated)	EPI v4.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
	11 for n=1 (Estimated)	EPI v4.11; EPA, 1999	Estimates based on representative oligomer where n=1. Estimated value is greater than the cutoff value, >10, according to methodology based on HPV assessment guidance.
	No data located; for n≥2 oligomers (Estimated)		Polymers with a MW >1,000 are outside the domain of the available estimation methods.
Flammability (Flash Point)	Not flammable (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
Particle Size			No data located.

D.E.R. 500 Series CASRN 26265-08-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**No experimental data were located. Based on professional judgment, absorption is expected to be poor by all routes for the low MW (<1,000) fraction. There is no absorption expected for any route of exposure for the large MW >1,000 components.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Absorption is expected to be poor by all routes for the low molecular weight fraction. There is no absorption expected for any route of exposure for the large, high molecular weight (>1,000) fraction. (Estimated)	Professional judgment	Estimated based on professional judgment.
	Other			No data located.
Acute Mammalian Toxicity		**LOW: Estimated based on experimental data for a component of D.E.R., professional judgment and by analogy to structurally similar polymers. The large MW components, with a MW >1,000, are expected to have limited bioavailability and therefore have low potential for acute mammalian toxicity. There was no data located regarding the inhalation route of exposure.**		
Acute Lethality	**Oral**	Rat oral LD_{50} > 2,000 mg/kg	ECHA, 2014	Study details reported in a secondary source; test substance identified as F-2200HM (CASRN 3072-84-2) a component of the polymeric mixture; purity: 100%; conducted according to OECD 423.
		Rat oral LD_{50} = 7,160 mg/kg	Ash and Ash, 2009	Limited study details reported in a secondary source; data are for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
		Rat oral LD_{50} >3,663 mg/kg (Estimated by analogy)	Submitted confidential study; Professional judgment	Based on closely related confidential analogs with similar structures, functional groups, and physical/chemical properties.
	Dermal	Rat LD_{50} >2,000 mg/kg (Estimated by analogy)	ECHA, 2014	Estimated based on analogy; Study details reported in a secondary

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				source for the test substance bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a very close structural analog.
		Rabbit LD_{50} >2,000 mg/kg (Estimated by analogy)	Submitted confidential study; Professional judgment	Based on closely related confidential analogs with similar structures, functional groups, and physical/chemical properties.
	Inhalation			No data located.
Carcinogenicity		**MODERATE: There is uncertainty due to lack of data for this substance. In addition, there is potential for carcinogenicity based on a structural alert for epoxy groups/epoxides though this concern may be mitigated by the high molecular weight; carcinogenic effects cannot be completely ruled out.**		
	OncoLogic Results			Not amenable for OncoLogic modeling.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	There is potential for carcinogenicity based on a structural alert for epoxy groups/epoxides; however, the concern may be mediated by the high molecular weight. (Estimated)	Professional judgment; EPA, 2010	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**MODERATE: There is uncertainty regarding the potential for genotoxicity due to the lack of sufficient data for this substance. Conflicting results were reported for gene mutations; the test substance was reported to be negative for gene mutations in one study, while there were positive results for gene mutations in Ames and mouse lymphoma assays. There were also mixed results for sister chromatid exchanges for analogs. There was no experimental chromosomal aberrations data for the test substance located. Genotoxic effects cannot be completely ruled out; an estimated Moderate hazard designation was assigned.**		
	Gene Mutation *in vitro*	Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 and *E. coli* strain WP2 *uvrA* pKM101 with and without metabolic activation.	Willett, 1991	Study details reported in the primary source. Test substances reported as Epikote 1145-B-70.
		Negative, *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and *E. coli* strain WP2 *uvrA* pKM101 with and without metabolic activation. (Estimated by analogy)	ECHA, 2014	Estimated based on analogy; study details reported in a secondary source for the test substance bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a very close structural analog; conducted according to OECD 471.
		Positive, Ames assay (Estimated by analogy)	Submitted confidential study	Limited study details reported in a confidential study submitted to EPA. Estimated based on a confidential analog.
		Positive, mouse lymphoma test (Estimated by analogy)	Submitted confidential study	Limited study details reported in a confidential study submitted to EPA. Estimated based on a confidential analog.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative, chromosomal aberration test in human lymphocytes with and without metabolic activation (Estimated by analogy)	ECHA, 2014	Estimated based on analogy; study details reported in a secondary source for the test substance bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a very close structural analog; conducted according to OECD 473.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Positive, chromosomal aberration test in human lymphocytes (Estimated by analogy)	Submitted confidential study	Limited study details reported in a confidential study submitted to EPA. Estimated based on a confidential analog.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**MODERATE: There is potential for reproductive toxicity for the low MW oligomers of the polymer (<1,000) based on a structural alert for epoxy groups/epoxides.**		
	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.
	Other	There is potential for reproductive toxicity based on a structural alert for epoxy groups/epoxides. (Estimated)	Professional judgment; EPA, 2010	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
Developmental Effects		**MODERATE: There is potential for developmental toxicity for the low MW oligomers of the polymer (<1,000) based on a structural alert for epoxides.** **There were no data located for the developmental neurotoxicity endpoint.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	No data was located for the developmental neurotoxicity endpoint.		No data located.
	Other	There is potential for developmental toxicity based on a structural alert for epoxy groups/epoxides (Estimated)	Professional judgment; EPA, 2010	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
Neurotoxicity		**MODERATE: There is potential for neurotoxicity for the lower MW components based on professional judgment.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Potential for neurotoxicity (Estimated)	Professional judgment	Estimated based on the lower MW components and professional judgment.
Repeated Dose Effects		**MODERATE: Estimated to have potential for immunotoxicity based on a structural alert for polyhalogenated aromatic hydrocarbons and liver effects for the lower MW components. A 28-day oral study in rats for a very close structural analog, bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8) indicated effects in males (reduced body weight gain) at a dose of 1,000 mg/kg bw-day (NOAEL = 300 mg/kg bw-day).**		
		Potential for liver effects (Estimated)	Professional judgment	Estimated based on the lower MW components and professional judgment.
		Potential for immunotoxicity based on structural alert for polyhalogenated aromatic hydrocarbons. (Estimated)	Professional judgment; EPA, 2012	Estimated based on structural alert for polyhalogenated aromatic hydrocarbons and professional judgment.
		28-day oral (gavage) study in male and female Wistar rats; 30, 300 and 1,000 mg/kg bw-day Reduced body weight gain in males at	ECHA, 2014	Study details reported in a secondary source for the test substance bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a

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		1,000 mg/kg bw-day. Microscopic liver changes (centrilobular hypertrophy) and metabolic blood chemical changes (increases in alanine aminotransferase, aspartate aminotransferase or bile acids) in males at 300 and 1,000 mg/kg bw-day were not considered to be adverse health effects. NOAEL = 300 mg/kg bw-day (males) LOAEL = 1,000 mg/kg bw-day (males, based on reduction in body weight gain)		very close structural analog. Conducted according to GLP and OECD guideline 407.
Skin Sensitization		**HIGH: Positive for skin sensitization in guinea pigs. In addition, there is an estimated potential for skin sensitization based on a structural alert for epoxy groups/epoxides.**		
	Skin Sensitization	Strong sensitizer, guinea pigs, maximization test. 19/20 test animals showed positive responses 24 hours after removal of challenge patches and 16 continued to have positive response at 48 hours.	Willett, 1990	Adequate primary source; Test substance reported as Epikote 1120-B-80.
		Not sensitizing, mouse local lymph node assay (LLNA)	ECHA, 2014	Estimated based on analogy; Study details reported in a secondary source for the test substance bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a very close structural analog.
		There is potential for skin sensitization based on a structural alert for epoxy groups/epoxides. (Estimated)	Professional judgment	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**MODERATE: Estimated based on mixed results for studies using the component F-2200HM (2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2)). The structural analog, bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), was not an eye irritant in rabbits.**		
	Eye Irritation	Mildly irritating in rabbit eyes; reported eye irritation was resolved within 72 hours.	ECHA, 2014	Study details reported in a secondary source; test substance identified as the component F-2200HM (2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2)); purity: 100%; conducted according to OECD 404.
		Eye irritant	Ash and Ash, 2009	Reported in a secondary source with limited details for the component 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2).
Dermal Irritation		**MODERATE: Estimated based on mixed results for studies using the component F-2200HM (2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2)).**		
	Dermal Irritation	Not a skin irritant in rabbits	ECHA, 2014	Study details reported in a secondary source; test substance identified as the component F-2200HM (2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2)); purity: 100%; conducted according to OECD 404.
		Skin irritant	Ash and Ash, 2009	Limited study details reported in a secondary source for the component 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2).
Endocrine Activity		**No data located.**		
				No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Estimated to have potential for immunotoxicity based on a structural alert for polyhalogenated aromatic hydrocarbons.**		
	Immune System Effects	Potential for immunotoxicity based on structural alert for polyhalogenated aromatic hydrocarbons. (Estimated)	Professional judgment; EPA, 2012	Estimated based on structural alert for polyhalogenated aromatic hydrocarbons and professional judgment.
ECOTOXICITY				
ECOSAR Class		Epoxides, Poly		
Acute Aquatic Toxicity		**LOW: Non-ionic polymers with a MW >1,000 and negligible water solubility are estimated to display no effects at saturation (NES). These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Guidance for the assessment of aquatic toxicity hazard leads to a low potential for those materials that display NES. The estimated acute toxicity values for fish, daphnid, and algae for the low MW components of the polymer (<1,000) also suggest no effects at saturation (NES).**		
Fish LC_{50}		NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
		Freshwater fish 14-day LC_{50}= 0.008 mg/L (Estimated) ECOSAR: Epoxides, Poly	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$mg/L by more than 10x. NES are predicted for these endpoints.
		Freshwater fish 96-hour LC_{50} = $1x10^{-5}$ mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$mg/L by more than 10x.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			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.
	Freshwater fish 14-day LC_{50} = 0.08 mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. NES: The log K_{ow} of 7.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $3.26x10^{-5}$mg/L by more than 10x. NES are predicted for these endpoints.
	Freshwater fish 96-hour LC_{50} = 0.008 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2). NES: The log K_{ow} of 7.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $3.26x10^{-5}$mg/L by more than 10x. NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			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}	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
	Daphnia magna 48-hour LC_{50}= 0.00065 mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. NES are predicted for these endpoints.
	Daphnia magna 48-hour LC_{50}=$1.28x10^{-5}$ mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. 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

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			narcosis.
	Daphnia magna 48-hour LC_{50} = 0.036 mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. NES: The log K_{ow} of 7.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. NES are predicted for these endpoints.
	Daphnia magna 48-hour LC_{50} = 0.007 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2). NES: The log K_{ow} of 7.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0. In addition, the estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. 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 EC_{50}	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.

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	Green algae 96-hour EC_{50} = 0.00027 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 6.4. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. 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 EC_{50} = 0.041 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. NES: The log K_{ow} of 7.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 6.4. In addition, the estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. 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

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**LOW: Non-ionic polymers with a MW >1,000 and negligible water solubility are estimated to display NES. These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Guidance for the assessment of aquatic toxicity hazard leads to a low potential for those materials that display NES. The estimated chronic toxicity values for fish, daphnid, and algae for the low MW components of the polymer (<1,000) also suggest no effects at saturation (NES).**		
Fish ChV	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
	Freshwater fish ChV = $2.7x10^{-5}$ mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. 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.
	Freshwater fish ChV =$2.5x10^{-6}$ mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of

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			8.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. 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.
	Freshwater fish ChV = 0.0008 mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. The estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by 10x. NES are predicted for these endpoints.
	Freshwater fish ChV = 0.0013 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2). The estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. 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

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			specific mode of action relative to narcosis.
Daphnid ChV	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
	Daphnia magna ChV: = $3.2x10^{-5}$ mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. NES are predicted for these endpoints.
	Daphnia magna ChV = $1.2x10^{-5}$ mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimate based on representative oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log Kow of 8.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. 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.
	Daphnia magna ChV = 0.002 mg/L (Estimated) ECOSAR: Epoxides, poly	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2). The

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			estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. NES are predicted for these endpoints.
	Daphnia magna ChV = 0.003 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. The estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. 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.
	21-day EC_{50} >23 µg/L Considered effects on *Daphnia magna* immobility and reproduction Static conditions; 1.9, 3.8, 7.5, 15, 30 µg/L (nominal concentration). (Estimated by analogy)	ECHA, 2014	Reported for bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a close structural analog. Study was conducted in accordance with OECD Guideline 211; *Daphnia magna* Reproduction Test and GLP. The estimated effect exceeds the water solubility by 10x. NES are predicted for these endpoints.
Green Algae ChV	NES (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES for the MW >1,000 components.
	Green algae ChV: 0.00044 mg/L	ECOSAR v1.11	Estimate based on representative

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	(Estimated) ECOSAR: Neutral Organic SAR		oligomer n=1. NES: The log K_{ow} of 11 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0. In addition, the estimated effect exceeds the water solubility of $1.68x10^{-9}$ mg/L by more than 10x. 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 ChV = 0.033 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR v1.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. The estimated effect exceeds the water solubility of $3.26x10^{-5}$ mg/L by more than 10x. 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.
	72-hour EC_{50} >30 µg/L	ECHA, 2014	Reported for bisphenol A diglycidyl

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		Considered effects on area under the growth curve, yield and growth rate relative to the negative control group in *Pseudokirchneriella subcapitata* Static conditions; 1.8, 3.9, 7.6, 15, 24, 30 µg/L (nominal concentration). (Estimated by analogy)		ether, brominated (CASRN 40039-93-8) a close structural analog. Study was conducted in accordance with OECD Guideline 201 (Alga, Growth Inhibition Test) and GLP. The estimated effect exceeds the water solubility by 10x. NES are predicted for these endpoints.
ENVIRONMENTAL FATE				
Transport		**The estimated negligible water solubility, the estimated negligible vapor pressure and the estimated K_{OC} of >30,000 indicate the components of this polymer are anticipated to partition predominantly to soil and sediment and these components are not anticipated to migrate from soil into groundwater. The estimated Henry's Law constant values of $<10^{-8}$ atm-m^3/mole indicate that the polymer components are not expected to volatilize from water to the atmosphere.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ for MW <1,000 components by Bond SAR Method. (Estimated)	EPI v4.11; Professional judgment	Estimates based on representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. Cutoff value for nonvolatile compounds.
		$<10^{-8}$ for the n≥2 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	High MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 for MW <1,000 components (Estimated)	EPI v4.11; Professional judgment	Estimates based on representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. Cutoff value for nonmobile compounds.
		>30,000 for n≥2 (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the n=2 oligomers; cutoff value used for large, high MW polymers. High MW polymers are expected to adsorb strongly to

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				soil and sediment.
		215,000 for n=1 >430,000 for n=2 and 3 Reported for components of the mixture. According to OECD Guideline 121; Estimation of the Adsorption Coefficient on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC). (Estimated by analogy)	ECHA, 2014	Adequate guideline study reported for bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8). The three components in this study are close structural analogs to the components of D.E.R. 500 Series (CASRN 26265-08-7).
	Level III Fugacity Model	Air = 0% Water = 3.3% Soil = 88% Sediment = 8.4% (Estimated)	EPI v4.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
		Air = 0% Water = 3% Soil = 60% Sediment = 37% (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1.

D.E.R. 500 Series CASRN 26265-08-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**VERY HIGH: Experimental data are not available. Estimated half-lives for ultimate aerobic biodegradation are >180 days for the n=1 oligomer and 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), representing MW <1,000 components of the polymeric mixture. Polymeric components with a MW >1,000 are expected to have negligible water solubility and poor bioavailability to microorganisms indicating that neither biodegradation nor hydrolysis are expected to be important removal processes in the environment. Although debromination by photodegradation of polybrominated benzenes has been observed, this process is not anticipated to lead to ultimate removal of the polymer. The estimated degradation half-life by hydrolysis is also expected to be >1 year. Degradation of this polymer by direct photolysis is not expected to be significant as the functional groups present do not tend to undergo these reactions under environmental conditions. The atmospheric half-life is estimated to be <2 days; however, the polymer is not anticipated to partition significantly to air.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test -2.4% degradation after 28 days in activated sludge. (Estimated by analogy)	ECHA, 2014	Adequate guideline study reported for bisphenol A diglycidyl ether, brominated (CASRN 40039-93-8), a very close structural analog.
		Months (Primary Survey Model) Recalcitrant (Ultimate Survey Model) (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1 and 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
		Recalcitrant for the n=2 oligomers (Estimated)	Boethling and Nabholz, 1997	Estimated for the n≥2 oligomers; high MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization.
		Microbial toxicity/inhibition: Water-leachates of the polymer inhibited bacterial growth by 8%. (Measured)	Willett, 1990	The study was performed on water-leachates of the polymer, and not on the polymer itself. Given the low water solubility of the polymer, it is not anticipated to be present in the leachate.

D.E.R. 500 Series CASRN 26265-08-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Not probable (Estimated)	Holliger et al., 2004	The estimated value addresses the potential for ultimate biodegradation. However, there is potential for primary anaerobic biodegradation of the lower MW (<1,000) haloaromatic compounds by reductive dehalogenation.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	1.4 hours (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1. This compound is anticipated to exist as a solid particulate in the atmosphere, degradation by gas-phase reactions are not expected to be important removal processes.
		0.6 days (Estimated)	EPI v4.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric

D.E.R. 500 Series CASRN 26265-08-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				mixture. This compound is anticipated to exist as a solid particulate in the atmosphere, degradation by gas-phase reactions are not expected to be important removal processes.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment	Bromine substituents may be susceptible to photolysis in the environment; however, this is expected to be a relatively slow process for a high MW brominated epoxy polymer and is not anticipated to result in the ultimate degradation of this substance.
	Hydrolysis	50%/>1 year at pH 7 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1 and for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture. The estimated hydrolysis rate is for the epoxide functional group; hydrolysis is not expected to be an important fate process for other parts of the polymer.
Environmental Half-life		>180 days for the n≥2 oligomers (Estimated)	Professional judgment	Estimated for the n≥2 oligomers; the substance is a high MW polymer and is not anticipated to be assimilated by microorganisms. Therefore, biodegradation is not expected to be an important removal process. It is also not expected to undergo removal by other degradative processes under environmental conditions.
		>1 year in soil; for the n=1 oligomer (Estimated)	PBT Profiler v1.301	Half-life estimated for the n=1 oligomer for the predominant

D.E.R. 500 Series CASRN 26265-08-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				compartment, soil, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**HIGH: The estimated BCF and BAF for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture and BAF for the n=1 component are >1,000 resulting in a High bioaccumulation designation. The higher MW oligomers that may be found in this mixture (n≥2) are expected to have Low potential for bioaccumulation based on their large size and low water solubility according to the polymer assessment literature and professional judgment.**		
	Fish BCF	8,400 for a component (Estimated)	EPI v4.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
		100 for n=1 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1.
		<100 for the n≥2 oligomers (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the n≥2 oligomers. Cutoff value for large, high MW, insoluble polymers according to polymer assessment literature.
	Other BCF			No data located.
	BAF	$9.7x10^6$ for a component (Estimated)	EPI v4.11	Estimated for 2,2',6,6'-tetrabromobisphenol A diglycidyl ether (CASRN 3072-84-2), a component of the polymeric mixture.
		69,000 for n=1 (Estimated)	EPI v4.11	Estimates based on representative oligomer where n=1.
	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, 2013).		

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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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[§] Based on analogy to experimental data for a structurally similar compound. [‡] The highest hazard designation of any of the oligomers with MW <1,000. [¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical	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
Dow XZ-92547[¥]	Confidential	L	*M*[‡]	*M*[§]	*M*[‡]	*M*[‡]	*M*[‡]	*M*[‡]	H	*M*[‡]	VL	L	*L*	*H*	*VH*	*H*[‡]

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	CASRN: Confidential CASRN
	MW: >1,000; with a significant percentage of components having MW <1,000
	MF: Confidential MF
	Physical Forms: Solid **Neat:**
	Use: Flame retardant
SMILES: Confidential SMILES notations for representative structures of the MW <1,000 components	
Synonyms: Reaction product of an epoxy phenyl novolak with DOPO	
Chemical Considerations: This alternative is a polymer consisting of components with MWs above and below 1,000 daltons. Lower MW components are expected to be present at a level requiring their assessment. The components with a MW <1,000 are evaluated as four proprietary representative structures. In general, the representative structures are different combinations of epoxy phenyl novolak and DOPO. These are assessed with EPI v4.11 and ECOSAR v1.11 estimates due to an absence of publicly available experimental physical/chemical, environmental fate and aquatic toxicity values. The oligomers with a MW >1,000 and are assessed using the available polymer assessment literature.	
Polymeric: Yes **Oligomeric:** This polymer contains oligomers that are formed by the reaction of an epoxy phenyl novolak with DOPO.	
Metabolites, Degradates and Transformation Products: None	
Analog: None **Endpoint(s) using analog values:** Not applicable	**Analog Structure:** Not applicable
Structural Alerts: Phosphinate esters - environmental toxicity; Epoxy groups/epoxides - dermal sensitization, cancer, reproductive effects, developmental toxicity; Organophosphorus compounds - neurotoxicity. (EPA, 2010; EPA, 2012).	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).	
Hazard and Risk Assessments: None located.	

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	89 (Measured)	Submitted confidential study	Adequate, measured value from submitted study.
Boiling Point (°C)	>300 (Estimated)	EPI v4.11; EPA, 1999	Estimate based on four representative structures with MW <1,000. Also estimated for oligomers with MWs >1,000. Cutoff value according to HPV assessment guidance and cutoff value used for large, high MW solids.
Vapor Pressure (mm Hg)	$<10^{-8}$ (Estimated)	EPA, 1999; EPI v4.11	Estimates based on four confidential representative structures with MW <1,000. Cutoff value for nonvolatile compounds according to HPV assessment guidance.
	$<10^{-8}$ (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Cutoff value for large, high MW polymer components.
Water Solubility (mg/L)	0.62 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 1 with MW <1,000.
	0.0023 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 2 with MW <1,000.
	$7.7x10^{-6}$ (Estimated)	EPI v4.11; EPA, 1999	Estimates based on confidential representative structure 3 with MW <1,000. Estimated value is less than the cutoff value, <0.001 mg/L, for non-soluble compounds according to HPV assessment guidance.
	0.0082 (Estimated)	EPI v4.11; EPA, 1999	Estimates based on confidential representative structure 4 with MW <1,000.
	<0.001 (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Cutoff value for large, high MW non-ionic polymer components.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Log K_{ow}	3.7 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 1 with a MW <1,000.
	5.3 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 2 with a MW <1,000.
	7 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 3 with a MW <1,000.
	4.8 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 4 with a MW <1,000.
Flammability (Flash Point)	Not flammable (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable (Estimated)	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
Particle Size			No data located.

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Based on the physical/chemical properties of this polymer, the higher MW fraction (>1,000) is estimated to have limited bioavailability. Based on the physical/chemical properties, absorption is expected to be negligible by all routes for the neat material and poor by all routes for the low molecular weight fraction if in solution.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Absorption is expected to be negligible by all routes for the neat material and poor by all routes for the low MW fraction if in solution. (Estimated)	Professional judgment	Estimated based on professional judgment.
	Other			No data located.
Acute Mammalian Toxicity		**LOW: Based on experimental data that reported LD_{50} >2,000 mg/kg when administered orally and dermally to rats. There were no data located for the inhalation route of exposure. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for acute toxicity.**		
Acute Lethality	**Oral**	Estimated to have a low potential for acute toxicity for the high MW component. Limited bioavailability expected. (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on cutoff value for large, high MW non-ionic polymer components.
		Rat, oral LD_{50} >2,000 mg/kg.	Submitted confidential study	Limited study details reported in a confidential study.
	Dermal	Rat, dermal LD_{50} >2,000 mg/kg.	Submitted confidential study	Study details reported in a confidential study.
		Rat, dermal LD_{50} >2,000 mg/kg.	Submitted confidential study	Limited study details reported in a confidential study.
	Inhalation			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Carcinogenicity		**MODERATE: There were no experimental data located for this substance. Carcinogenic effects cannot be ruled out; therefore, uncertainty due to lack of data for this substance results in a Moderate designation. In addition, there is an estimated potential for carcinogenicity based on a structural alert for epoxy groups/epoxides and for the low MW components (MW < 1,000). The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for carcinogenicity.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)			No data located.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other	Potential for carcinogenicity based on a structural alert for epoxy groups/epoxides. (Estimated)	Professional judgment; EPA, 2010	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
		Potential for carcinogenicity for the low MW components. (Estimated)	Professional judgment	Estimated for the low MW components based on professional judgment.
		Estimated to have a low potential for carcinogenicity for the high MW component. Limited bioavailability expected. (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on professional judgment and the cutoff value for large, high MW non-ionic polymer components.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**MODERATE: Estimated based on positive gene mutation results for a confidential analog of the low MW components (MW < 1,000) reported in a submitted confidential study. There were no gene mutation or chromosomal aberrations data located for this substance. Negative results for mutagenicity and chromosomal aberrations *in vitro* were reported in experimental data for the analog DOPO (CASRN 35948-25-5). In the absence of data for this substance and conflicting results reported for two analogs, a conservative approach is used to assign a Moderate designation. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for genotoxicity.**		
	Gene Mutation *in vitro*	There is potential for mutagenicity for the low MW components. Positive in Ames assay. (Estimated by analogy)	Professional judgment; Submitted confidential study	Estimated based on experimental data for a confidential analog for the low MW components; reported in a submitted confidential study and professional judgment.
		Negative in Ames assay in *Salmonella typhimurium strains* TA97, TA98, TA100, and TA102 and *Escherichia coli* WP2 uvr A pKM 101 with and without metabolic activation. Tested up to 5,000 µg/plate (purity, industrial grade). Positive controls responded as expected. (Estimated by analogy)	ECHA, 2013	Estimated based on analogy to DOPO (CASRN 35948-25-5). Sufficient study details reported in a secondary source. Non-GLP study, but adequate as supporting data.
		Negative in Ames assay; in *Salmonella typhimurium* strains TA1535, TA97a, TA98, TA100, and TA102 with and without metabolic activation. Tested up to 5,024 µg/plate (purity >99%). Positive controls responded as expected. (Estimated by analogy)	ECHA, 2013	Estimated based on analogy to DOPO (CASRN 35948-25-5). Sufficient study details reported in a secondary source. Study conducted in accordance with OECD guideline 471 and GLP. Test substance was CASRN 35948-25-5 named Ukanol GK-F in study report. Primary reference not identified.
	Gene Mutation *in vivo*			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	Negative in Chinese hamster lung cells with and without activation. Tested up to 216 µg/mL (purity not provided). Positive controls responded as expected. (Estimated by analogy)	ECHA, 2013	Estimated based on analogy to DOPO (CASRN 35948-25-5). Sufficient study details reported in a secondary source. Study equivalent to OECD Guideline 473; not a GLP study.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other	Estimated to have a low potential for genotoxicity for the high MW component. Limited bioavailability expected. (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on professional judgment and the cutoff value for large, high MW non-ionic polymer components.
Reproductive Effects		**MODERATE: There is an estimated potential for reproductive toxicity based on a structural alert for epoxy groups/epoxides and an estimated potential for male reproductive toxicity for the low MW components (MW < 1,000) based on professional judgment. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for reproductive toxicity.**		
	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.
	Other	There is potential for reproductive toxicity based on a structural alert for epoxy groups/epoxides. (Estimated)	Professional judgment; EPA, 2010	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
		There is potential for male reproductive toxicity for the low MW components. (Estimated)	Professional judgment	Estimated for the low MW components based on professional judgment.
		Estimated to have a low potential for	Boethling and Nabholz, 1997;	Estimated for the high MW

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		reproductive effects for the high MW component. Limited bioavailability expected. (Estimated)	Professional judgment	component (MW >1,000) based on professional judgment and the cutoff value for large, high MW non-ionic polymer components.
Developmental Effects		**MODERATE: There is an estimated potential for developmental toxicity based on a structural alert for epoxy groups/epoxides and an estimated potential for developmental toxicity for the low MW components (MW < 1,000) based on professional judgment. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for developmental toxicity. There is uncertain concern for developmental neurotoxicity based on the potential for cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment. No experimental data were located for this substance.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Uncertain concern for developmental neurotoxicity based on the potential for cholinesterase (ChE) inhibition in dams that may result in alterations of fetal neurodevelopment.	Professional judgment	Estimated based on a structural alert for organophosphates for the neurotoxicity endpoint.
	Other	There is potential for developmental toxicity based on a structural alert for epoxy groups/epoxides. (Estimated)	Professional judgment; EPA, 2012	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
		Estimated to have a low potential for developmental effects for the high MW component. Limited bioavailability	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on professional judgment and the cutoff

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		expected. (Estimated)		value for large, high MW non-ionic polymer components.
Neurotoxicity		**MODERATE: There is an estimated potential for neurotoxicity based on a structural alert for organophosphorus compounds and professional judgment. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for neurotoxicity. There were no experimental data located for this substance.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	There is potential for neurotoxicity based on the structural alert of organophosphorus compounds. (Estimated)	Professional judgment; EPA, 2012	Estimated based on a structural alert for organophosphorus compounds and professional judgment.
		Estimated to have a low potential for neurotoxicity for the high MW component. Limited bioavailability expected. (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on professional judgment and the cutoff value for large, high MW non-ionic polymer components.
Repeated Dose Effects		**MODERATE: There is an estimated potential for repeated dose effects for the low MW components (<1,000) for the inhalation and dermal routes of exposure. Experimental data for the analog DOPO (CASRN 35948-25-5) indicated a Low hazard designation with a reported NOAEL of 1,023 mg/kg-day (highest dose tested) in a 16-week dietary study in rats. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for repeated dose effects. There were no experimental data located for this substance.**		
		There is potential for repeated dose effects for the low MW component for the inhalation and dermal routes of exposure.	Professional judgment	Estimated for the low MW component based on professional judgment.
		Male and female Wistar rats (20/sex/dose) were fed diets containing 0, 0.24, 0.6, or 1.5% HCA (0, 159, 399, or 1,023 mg HCA/kg-day to males; 0, 177, 445, or 1,094 mg HCA/kg-day to females) of the analog DOPO for 16 weeks (purity of test substance not	ECHA, 2013; Professional judgment	Estimated based on analogy to DOPO (CASRN 35948-25-5). Sufficient information in secondary source; data lacking regarding detailed clinical observations and neurobehavioral examination. Study equivalent to OECD guideline 408.

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		provided). There were no significant effects on body weight, food consumption, hematology, limited clinical chemistry, urinalysis, organ weight, and gross and microscopic examination of major organs. NOAEL: 1,023 mg/kg-day (males), 1,094 mg/kg-day (females); highest dose tested LOAEL: Not established (Estimated based on analogy)		Study pre-dates GLP. Test substance identified as HCA in study report. Primary reference not identified.
		Estimated to have a low potential for repeated dose effects for the high MW component. Limited bioavailability expected. (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on professional judgment and the cutoff value for large, high MW non-ionic polymer components.
Skin Sensitization		**HIGH: Positive for skin sensitization in guinea pigs; reported in a submitted confidential study for the low MW components (MW < 1,000). In addition, there is an estimated potential for skin sensitization based on a structural alert for epoxy groups/epoxides.**		
	Skin Sensitization	Sensitizing, guinea pigs	Submitted confidential study	Data reported in a submitted confidential study.
		Positive for skin sensitization for the low MW component.	Submitted confidential study	Data reported in a submitted confidential study for the low MW component.
		There is potential for skin sensitization based on a structural alert for epoxy groups/epoxides. (Estimated)	Professional judgment; EPA, 2012	Estimated based on a structural alert for epoxy groups/epoxides and professional judgment.
Respiratory Sensitization		**MODERATE: There is an estimated potential for respiratory sensitization for the low MW component (MW < 1,000) based on professional judgment.**		
	Respiratory Sensitization	There is potential for respiratory sensitization for the low MW component. (Estimated)	OSHA, 1999; Professional judgment	Estimated based presence of epoxides and professional judgment for the low MW component.

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Eye Irritation		**VERY LOW: Based on a submitted confidential study, the polymer did not produce eye irritation in rabbits.**		
	Eye Irritation	Negative, rabbits	Submitted confidential study	Limited study details reported in a confidential study.
Dermal Irritation		**LOW: Negative for skin irritation in rabbits reported in a submitted confidential study. One study reported positive results for skin irritation, but did not contain adequate study details for assessment.**		
	Dermal Irritation	Positive for skin irritation for the low MW component.	Submitted confidential study	Inadequate study details reported in a submitted confidential study for the low MW component.
		Negative, rabbits	Submitted confidential study	Data reported in a submitted confidential study.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**Estimated to have a low potential for immunotoxic effects based on expert judgment. The higher MW components of this polymer (MW >1,000) are expected to have limited bioavailability and have low potential for immunotoxicity.**		
	Immune System Effects	Low potential for immunotoxic effects for the low MW component. (Estimated)	Expert judgment	Estimated based on expert judgment.
		Estimated to have a low potential for immunotoxic effects for the high MW component. Limited bioavailability expected.	Boethling and Nabholz, 1997; Professional judgment	Estimated for the high MW component (MW >1,000) based on professional judgment.
ECOTOXICITY				
ECOSAR Class		Epoxides, mono; Esters (Phosphinates)		
Acute Aquatic Toxicity		**LOW: Based on estimated acute aquatic toxicity values for fish, daphnia, and green algae, which all exceed the water solubility. No Effects at Saturation (NES) are predicted for these endpoints.**		
Fish LC_{50}		NES (Estimated)	Professional judgment	Estimations for the oligomers with a high MW; limited bioavailability and low water solubility suggest there will be NES.
		Freshwater fish 96-hour LC_{50}:	ECOSAR v1.11	Estimations for confidential

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	1.7 mg/L (ECOSAR class: Esters, phosphinate); 10.4 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)		representative structure 1. The estimated values exceed the water solubility (0.62 mg/L). The chemical may not be soluble enough to measure the 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.
	Freshwater fish 96-hour LC_{50}: 0.87 mg/L (ECOSAR class: Epoxides, mono); 0.74 mg/L (ECOSAR class: Esters phosphinates); 0.49 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 2. NES: The log K_{ow} of 5.3 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; 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.
	Freshwater fish 14-day LC_{50}: 0.13 mg/L (ECOSAR class: Epoxides, poly); Freshwater fish 96-hour LC_{50}: 0.28 mg/L (ECOSAR class: Esters phosphinates);	ECOSAR v1.11	Estimations for confidential representative structure 3. NES: The log K_{ow} of 6.9 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0 or 6.0; NES are predicted for these endpoints.

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Freshwater fish 96-hour LC_{50}: 0.021 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)		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.
	Freshwater fish 96-hour LC_{50}: 1.7 mg/L (ECOSAR class: Epoxides, mono); 1.1 mg/L (ECOSAR class: Esters phosphinates); 1.5 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 4. The estimated values exceed the water solubility (0.0082 mg/L). The chemical may not be soluble enough to measure the 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.
Daphnid LC_{50}	NES (Estimated)	Professional judgment	Estimations for the oligomers with a high MW; limited bioavailability and low water solubility suggest there will be NES.
	Daphnid 48-hour LC_{50}: 1.2 mg/L (ECOSAR class: Esters, phosphinate); 6.9 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 1. The estimated values exceed the water solubility (0.62 mg/L). The chemical may not be soluble enough to measure the predicted effect. Narcosis classes (neutral organics) are provided for comparative

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			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}: 0.69 mg/L (ECOSAR class: Epoxides, mono); 0.56 mg/L (ECOSAR class: Esters phosphinates); 0.38 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 2. The log K_{ow} of 5.3 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; 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.
	Daphnid 48-hour LC_{50}: 0.071 mg/L (ECOSAR class: Epoxides, poly); 0.24 mg/L (ECOSAR class: Esters phosphinates); 0.019 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 3. NES: The log K_{ow} of 6.9 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; 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.

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnid 48-hour LC_{50}: 1.6 mg/L (ECOSAR class: Epoxides, mono); 0.78 mg/L (ECOSAR class: Esters phosphinates); 1.1 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 4.The estimated values exceed the water solubility (0.0082 mg/L). The chemical may not be soluble enough to measure the 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 EC_{50}	NES (Estimated)	Professional judgment	Estimations for the oligomers with a high MW; limited bioavailability and low water solubility suggest there will be NES.
	Green algae 96-hour EC_{50}: 9.6 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 1. The estimated value exceeds the water solubility (0.62 mg/L). The chemical may not be soluble enough to measure the 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}: 0.34 mg/L (ECOSAR class: Epoxides,	ECOSAR v1.11	Estimations for confidential representative structure 2. The

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	mono); 0.99 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)		estimated values exceed the water solubility (0.0023 mg/L). The chemical may not be soluble enough to measure the 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}: 0.093 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 3. NES: The log K_{ow} of 6.9 for this chemical exceeds the SAR limitation for the 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 EC_{50}: 0.9 mg/L (ECOSAR class: Epoxides, mono); 2.3 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 4. The estimated values exceed the water solubility (0.0082 mg/L). The chemical may not be soluble enough to measure the predicted effect. Narcosis classes (neutral organics)

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			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 chronic aquatic toxicity values for the confidential representative structures 1 and 4 for fish and daphnia.**		
Fish ChV	NES (Estimated)	Professional judgment	Estimations for the oligomers with a high MW; limited bioavailability and low water solubility suggest there will be NES.
	Freshwater fish ChV: 0.041 mg/L (ECOSAR class: Esters, phosphinate); 1.2 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 1. 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.
	Freshwater fish ChV: 0.003 mg/L (ECOSAR class: Epoxides, mono); 0.008 mg/L (ECOSAR class: Esters phosphinates); 0.069 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 2. The estimated values exceed the water solubility (0.0023 mg/L). The chemical may not be soluble enough to measure the predicted effect. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Freshwater fish ChV: 0.0014 mg/L (ECOSAR class: Epoxides, poly); 0.0016 mg/L (ECOSAR class: Esters phosphinates); 0.004 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 3. The estimated values exceed the water solubility ($7.7x10^{-6}$). The chemical may not be soluble enough to measure the 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.
	Freshwater fish ChV: 0.004 mg/L (ECOSAR class: epoxides, mono); 0.02 mg/L (ECOSAR class: Esters phosphinates); 0.20 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 4. 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	NES (Estimated)	Professional judgment	Estimations for the oligomers with a high MW; limited bioavailability and low water solubility suggest there will be NES.
	Daphnid ChV: 0.042 mg/L (ECOSAR class: Esters,	ECOSAR v1.11	Estimations for confidential representative structure 1.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	phosphinate); 1.03 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)		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 ChV: 0.064 mg/L (ECOSAR class: Epoxides, mono); 0.012 mg/L (ECOSAR class: Esters phosphinates); 0.086 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 2. The estimated values exceed the water solubility (0.0023 mg/L). The chemical may not be soluble enough to measure the 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.
	Daphnid ChV: 0.005 mg/L (ECOSAR class: Epoxides, poly); 0.003 mg/L (ECOSAR class: Esters phosphinates); 0.007 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 3. The estimated values exceed the water solubility ($7.7x10^{-6}$). The chemical may not be soluble enough to measure the predicted effect. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnid ChV: 0.15 mg/L (ECOSAR class: Epoxides, mono); 0.02 mg/L (ECOSAR class: Esters phosphinates): 0.22 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 4. 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	NES (Estimated)	Professional judgment	Estimations for the oligomers with a high MW; limited bioavailability and low water solubility suggest there will be NES.
	Green algae ChV: 3.6 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 1. The estimated values exceed the water solubility (0.62 mg/L). The chemical may not be soluble enough to measure the 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 ChV: 0.69 mg/L (ECOSAR class: Epoxides, mono);	ECOSAR v1.11	Estimations for confidential representative structure 2. The estimated values exceed the water

Dow XZ-92547			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	0.51 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)		solubility (0.0023 mg/L). The chemical may not be soluble enough to measure the 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 ChV: 0.068 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 3. The estimated value exceeds the water solubility ($7.7x10^{-6}$). The chemical may not be soluble enough to measure the 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 ChV: 1.5 mg/L (ECOSAR class: Epoxides, mono); 1.0 mg/L (ECOSAR class: Neutral organic SAR) (Estimated)	ECOSAR v1.11	Estimations for confidential representative structure 4. The estimated values exceed the water solubility (0.0082 mg/L). The chemical may not be soluble enough to measure the predicted effect. Narcosis classes (neutral organics) are provided for comparative

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				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		**The estimated negligible water solubility and estimated negligible vapor pressure indicate that this polymer, including the low MW and high MW components, is anticipated to partition predominantly to soil. The estimated Henry's Law Constant of $<10^{-8}$ atm-m^3/mole indicates that it is not expected to volatilize from water to the atmosphere. Although estimates for one confidential representative structure results in a moderate absorption coefficient of 1,596, the estimated K_{oc} of >30,000 for the high MW components and 3 other confidential representative substances indicate that the majority of this polymeric mixture is not anticipated to migrate from soil into groundwater and also has the potential to adsorb to sediment.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ Bond SAR Method (Estimated)	EPI v4.11; Professional judgment	Estimated value based on four confidential representative structures with MW <1,000. Cutoff value for nonvolatile compounds.
		$<10^{-8}$ (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the MW >1,000 oligomers. High MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization.
	Sediment/Soil Adsorption/Desorption - K_{oc}	1,595 (Estimated)	EPI v4.11; Professional judgment	Estimate based on confidential representative structure 1.
		>30,000 (Estimated)	EPI v4.11; EPA, 1999	Estimated values for confidential representative structures 2, 3 and 4. Cutoff value for nonmobile compounds according to HPV assessment guidance.
		>30,000 (Estimated)	Boethling and Nabholz, 1997; Professional judgment	Estimated for the oligomers with MW >1,000; cutoff value used for large, high MW polymers. High

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				MW polymers are expected to adsorb strongly to soil and sediment.
	Level III Fugacity Model	Air = 0% Water = 12% Soil = 88% Sediment = 1% (Estimated)	EPI v4.11	Estimates based on confidential representative structure 1. No data located for the high MW component of the polymers.
Persistence		**VERY HIGH: The persistence designation for this polymer is based on its higher MW components (MW >1,000). The higher MW components are expected to have Very High persistence because of their low water solubility and poor bioavailability, indicating that neither biodegradation nor hydrolysis are expected to be important environmental fate processes. The lower MW oligomers (MW <1,000) of this polymer have higher estimated water solubility and increased bioavailability to microorganisms and therefore would be expected to have lower persistence. This polymer does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths. Evaluation of these degradation values suggest a half-life of >180 days.**		
Water	**Aerobic Biodegradation**	Days-weeks (Primary Survey Model) Weeks-months (Ultimate Survey Model) (Estimated)	EPI v4.11	Estimates based on confidential representative structure 1.
		Recalcitrant for MW >1,000 components (Estimated)	Professional judgment; Boethling and Nabholz, 1997	High MW polymers are expected to be non-biodegradable.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI v4.11; Professional judgment	Estimated value based on four confidential representative structures with MW <1,000; the high MW polymer components are anticipated to be nonvolatile.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI v4.11; Professional judgment	Estimated value based on four confidential representative structures with MW <1,000; the high MW polymer components are anticipated to be nonvolatile.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Recalcitrant for MW >1,000 components (Estimated)	Professional judgment; Boethling and Nabholz, 1997	High MW polymers are expected to be resistant to removal under anoxic conditions due to their limited bioavailability.

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	<0.19 days (Estimated)	EPI v4.11	Estimated value based on four confidential representative structures with MW <1,000.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	This polymer does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	50%/>1 month (Estimated)	Professional judgment	While this polymer contains a functional group with the potential to hydrolyze, this group does not readily hydrolyze under environmental conditions. The low water solubility of this polymer will further decrease the rate of hydrolysis.
		50%/>1 year (Estimated)	EPI v4.11	Estimated value based on confidential representative structures 2, 3 and 4 with MW <1,000.
Environmental Half-life		75 days in soil (Estimated)	PBT Profiler v1.301; EPI v4.11	Half-life estimated for confidential representative structure 1; in the predominant compartment, soil, as determined by EPI and the PBT Profiler methodology.

Dow XZ-92547				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**HIGH: The bioaccumulation designation is based on the estimated BCF and BAF values >1,000; these values are estimated using confidential representative structures of lower MW components (MW <1,000) of Dow XZ-92547. The higher MW oligomers that may be found in this mixture are expected to have low potential for bioaccumulation based on their large size and low solubility according to polymer assessment literature.**		
	Fish BCF	9,900 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 3 with MW <1,000.
		610 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 4 with MW <1,000.
		820 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 2 with MW <1,000.
		68 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 1 with MW <1,000.
		<100 (Estimated)	Professional judgment	Estimated for the oligomers with a MW >1,000. Cutoff value for large, high MW, insoluble polymers.
	Other BCF			No data located.
	BAF	620 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 4 with MW <1,000.
		2,300 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 3 with MW <1,000.
		600 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 2 with MW <1,000.
		180 (Estimated)	EPI v4.11	Estimates based on confidential representative structure 1 with MW <1,000.

Dow XZ-92547				
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, 2013).		

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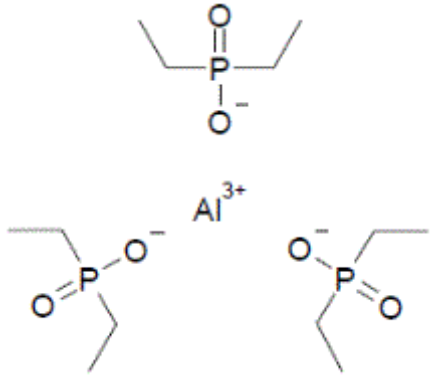
Aluminum Diethylphosphinate

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[§] Based on analogy to experimental data for a structurally similar compound. [R] Recalcitrant: Substance is comprised of metallic species (or metalloids) that will not degrade, but may change oxidation state or undergo complexation processes under environmental conditions. [¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

		Human Health Effects											**Aquatic Toxicity**		**Environmental Fate**	
Chemical	**CASRN**	**Acute Toxicity**	**Carcinogenicity**	**Genotoxicity**	**Reproductive**	**Developmental**	**Neurological**	**Repeated Dose**	**Skin Sensitization**	**Respiratory Sensitization**	**Eye Irritation**	**Dermal Irritation**	**Acute**	**Chronic**	**Persistence**	**Bioaccumulation**
Aluminum Diethylphosphinate[¥]	225789-38-8	**L**	***L***[§]	**L**	**L**	***M***[§]	***M***[§]	***M***[§]	**L**		**L**	**VL**	**M**	**M**	***H***[R]	***L***

Aluminum Diethylphosphinate



CASRN: 225789-38-8

MW: 390.27

MF: 3 $C_4H_{11}PO_2 \cdot Al$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: CCP(=O)(CC)O[Al](OP(=O)(CC)CC)OP(=O)(CC)CC

Synonyms: Exolit OP 930, Aluminium diethylphosphinate, Aluminium tris(diethylphosphinate)

Chemical Considerations: This alternative is an inorganic compound and in the absence of experimental data, professional judgment using chemical class and structural considerations were used to complete this hazard profile.

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Aluminum and diethylphosphinic acid may dissociate (Australia, 2005)

Analog: Confidential aluminum metal salts; aluminum hydroxide; phosphate esters

Endpoint(s) using analog values: Absorption, distribution, metabolism & excretion, carcinogenicity, developmental toxicity, immunotoxicity, neurotoxicity, repeated dose effects

Analog Structure: Not applicable

Structural Alerts: Not applicable

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

Hazard and Risk Assessments: Hazard assessment in Design for the Environment Alternatives Assessment for Flame Retardants in Printed Circuit Boards, Review Draft, November 8, 2008 (EPA, 2008).

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	Decomposes at 315 (Measured)	Submitted confidential study	Adequate.
	Decomposes at 300 (Measured)	Submitted confidential study	Adequate.
	>400 according to EU Method A.1 using differential scanning calorimetry (Measured)	ECHA, 2013; Submitted confidential study	Adequate.
	Decomposes at 330 (Measured)	DeBoysère and Dietz, 2005	Sufficient details were not available to assess the quality of this study.
	Decomposes at > 300 (Measured)	Clariant, 2007	Sufficient details were not available to assess the quality of this study.
	>400 (Measured)	Australia, 2005	Sufficient details were not available to assess the quality of this study. Reported for a commercial formulation.
Boiling Point (°C)	Expected to decompose before boiling (Estimated)	Professional judgment	Based on available data for melting point.
Vapor Pressure (mm Hg)	$<10^{-8}$ (Estimated)	EPA, 1999; Professional judgment	Cutoff value for nonvolatile compounds according to HPV assessment guidance.
Water Solubility (mg/L)	$2.5x10^{3}$ (Measured)	Submitted confidential study	Sufficient details were not available to assess the quality of this study. Aluminum diethylphosphinate has low wettability and very slow dissolution. This gives a kinetically controlled solubility of <1 mg/L by guideline 92/69/EEC A.6. If aluminum diethylphosphinate is formed by precipitation of a soluble salt, the remaining equilibrium solubility of 2.5×10^{3} mg/L is found. This can be assumed to be the true limit of solubility under ideal conditions.
	<1	ECHA, 2013; Submitted	Guideline study; aluminum

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	According to EU Method A.6 (Measured)	confidential study	diethylphosphinate has low wettability and very slow dissolution. If aluminum diethylphosphinate is formed by precipitation of a soluble salt, the remaining equilibrium solubility of 2.5×10^3 mg/L is found, which can be assumed to be the true limit of solubility under ideal conditions.
	<1 According to EU Method A.6 (Measured)	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation.
Log K_{ow}	-0.44 (Estimated)	Beard and Marzi, 2005; Stuer-Lauridsen et al., 2007	Reported in a secondary source with limited study details; it is unclear whether this value reflects the chemical's low water solubility or its lipophobicity.
Flammability (Flash Point)	No self-ignition below 402°C (Measured)	ECHA, 2013; Submitted confidential study	Adequate.
	Not readily combustible according to guideline 96/69/EEC, test A.10. (Measured)	Submitted confidential study	Guideline study.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No data located; based on its use as a flame retardant.
Pyrolysis	Major products are diethylphosphinic acid, ethylphosphonic acid, phosphoric acid, and their respective salts (Measured)	Beard and Marzi, 2005	Study details and test conditions were not available.

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pH	pH of an aqueous suspension was 4.0; aluminum diethylphosphinate completely dissociated within 24 hours at pH 4.5 during Japanese Ministry of International Trade and Industry (MITI) test. (Measured)	Beard and Marzi, 2005; Australia, 2005	Inadequate. Although this compound does not contain acidic protons, the reference indicates that the acidity results from equilibria involving the dissociated species in solution. Study details and test conditions were not available. Available data for commercial formulations suggest that this compound is likely to dissociate under environmental conditions. However, dissociation is expected to vary as a function of pH to a degree that will have a significant influence on its environmental fate. Available data are not adequate to assess its dissociation under typical environmental conditions.
pK_a			No data located.
Particle Size	D10 = mean ca. 0.4 ≤ 2 µm D50 = mean ca. 0.4 ≤ 29 µm According to Laser-Diffraction method. (Estimated)	ECHA, 2013	Nonguideline study reported in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Based on estimates of physical and chemical properties, analogs, and professional judgment, aluminum diethylphosphinate is determined to not be readily absorbed through skin but may be absorbed through the inhalation of dust and oral exposure. Absorption is estimated to be good through the gastrointestinal tract based on physical/chemical properties and analogs; however, only a small amount of administered dose was reported to be absorbed in the gastrointestinal tract in a submitted confidential rat study. Elimination was reported primarily in the feces in a confidential study, while in contrast, elimination was reported to occur primarily in the urine within 12 hours of oral administration in another study.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Absorption as neat solid expected to be negligible through skin. Absorption good through lungs. Absorption good through gastrointestinal tract. (Estimated)	Professional judgment	Estimates based on physical/chemical properties and confidential analogs.
		Following oral administration, excretion was almost quantitative via the urine within 12 hours.	Stuer-Lauridsen et al., 2007	Study details reported in a secondary source
		Male rats (2/dose group) administered (unradiolabeled) test substance via single oral gavage at 180 and 1,000 mg/kg-day. Only a small amount of the administered dose was absorbed by the gastro-intestinal tract. The major route of elimination was in the feces (unabsorbed fraction) and a small amount of free test substance was detected in the urine. After 36 hours, no test substance was detected.	Submitted confidential study	Study details from an abstract reported in a confidential submission; study conducted according to OECD 417; small number of animals tested.
	Other			No data located.
Acute Mammalian Toxicity		**LOW: Experimental studies indicate that oral and dermal routes to rats do not produce mortality at oral and dermal doses up to 2,000 mg/kg. No lethality data was located for inhalation exposure.**		

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Lethality	**Oral**	Rat oral LD_{50} >2,000 mg/kg	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation. Test substance was Exolit OP 930. Conducted according to OECD TG 401.
	Dermal	Rat dermal LD_{50} >2,000 mg/kg	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation. Test substance was Exolit OP 930. Conducted according to OECD TG 402.
	Inhalation			No data located.
Carcinogenicity		**LOW: Aluminum diethylphosphinate is estimated to be of low hazard for carcinogenicity based on comparison to analogous metal salts and professional judgment.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)	Not expected to be carcinogenic. (Estimated)	Professional judgment	Estimated based on analogy to confidential metal salts.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**LOW: Experimental studies indicate that aluminum diethylphosphinate does not cause gene mutations in bacteria or chromosomal aberrations in mammalian cells.**		
	Gene Mutation *in vitro*	Negative, *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 with and without metabolic activation	Australia, 2005; Stuer-Lauridsen et al., 2007; Submitted confidential study	Reported in a secondary source for a commercial formulation. Conducted according to OECD TG 471.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative, chromosomal aberrations in Chinese hamster lung cells with and without metabolic activation	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation. Conducted according to OECD TG 473.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vivo*	Negative, mammalian erythrocyte micronucleus test in NMRI mice; oral (unspecified)	Submitted confidential study	Study reported in a submitted confidential study; Study conducted according to OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test).
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: Changes (characterized as minor) in the number of days of pre-coital interval and a reduction in copulation plugs were reported in a submitted confidential study at 1,000 mg/kg-day. The study-reported NOAEL is on the margin of the Low to Very Low hazard designation; therefore a Low hazard designation was assigned. Aluminum diethylphosphinate is also estimated to be of low hazard for reproductive effects based on professional judgment and comparison to analogous metal salts.**		
	Reproduction/Developmental Toxicity Screen	Expected to have low hazard potential for reproductive effects. (Estimated)	Professional judgment	Estimated based on analogy to confidential metal salts.
		Rats (Sprague Dawley); oral administration of 250 and 1,000 mg/kg bw-day; 15 days prior to mating and throughout gestation and lactation up to post-partum Day 3. Parental effects: No clinical signs of toxicity or change in food consumption. Slight reduction in body weight and body weight gain (both sexes, 1,000 mg/kg-day); Reduced terminal body weight and absolute and relative kidney weights (males, 1,000 mg/kg-day). No adverse effect on oestrus cycle, implantation, gestation length, corpora lutea or sex ratios. No effect on sperm (motility, morphology, concentration). Increase in the number of days of pre-coital interval and a reduction in copulation plugs (1,000 mg/kg-day);	Submitted confidential study	Study reported in a submitted confidential study; Study conducted according to OECD Guideline 421 (Reproductive/Developmental Toxicity Screening Test).

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		these changes were reported as "minor" No treatment-related macroscopic anomalies in pups dying or sacrificed at term. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established		
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
	Other			No data located.
Developmental Effects		**MODERATE: There were no developmental effects reported in a reproduction/developmental toxicity screen in rats at doses up to 1,000 mg/kg-day. There is moderate hazard for aluminum diethylphosphinate given exposure may result in neurodevelopmental effects based on the presence of a phosphinate; there were no experimental studies specifically designed to evaluate the neurodevelopmental endpoint located. The potential for neurodevelopmental effects cannot be ruled out.**		
	Reproduction/ Developmental Toxicity Screen	Expected to have a moderate hazard potential for developmental and neurodevelopmental effects resulting from the presence of a phosphinate. (Estimated)	Professional judgment	Estimated based on analogy to phosphate esters and associated cholinesterase inhibition.
		Rats (Sprague Dawley); oral administration of 250 and 1,000 mg/kg bw-day; 15 days prior to mating and throughout gestation and lactation up to post-partum Day 3. Parental: No clinical signs of toxicity or change in food consumption. Slight reduction in body weight and body	Submitted confidential study	Study details reported in a confidential submission; Study conducted according to OECD Guideline 421 (Reproductive/Developmental Toxicity Screening Test).

Aluminum Diethylphosphinate CASRN 225789-38-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		weight gain; reduced terminal body weight and absolute and relative kidney weights (males, 1,000 mg/kg-day). No adverse effect on estrus cycle, implantation, gestation length, corpora lutea or sex ratios. No effect on sperm (motility, morphology, concentration). Increase in the number of days of pre-coital interval and a reduction in copulation plugs (1,000 mg/kg-day). No treatment-related macroscopic anomalies in pups dying or sacrificed at term. NOAEL = 1,000 mg/kg-day		
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity			No data located.
	Other			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Aluminum diethylphosphinate is expected to be of Moderate hazard for based on analogy to aluminum hydroxide and professional judgment. Exposure to the analog resulted in impaired learning in a labyrinth maze test in a 90-day oral study in rats at 35 mg Al/kg/day as aluminum hydroxide with citric acid. Impaired learning in a labyrinth maze test was also reported in rats orally exposed to 300 mg Al/kg/day (only dose tested) as the analog aluminum hydroxide (without citric acid). There is uncertainty in the threshold of response; the possibility that effects occur at doses <100 mg/kg/day (In the Moderate – High hazard designation range) cannot be ruled out.**		
	Neurotoxicity Screening Battery (Adult)	Expected to have a moderate hazard potential for neurotoxic effects resulting from the presence of bioavailable metal species. (Estimated)	Professional judgment	Estimated based on professional judgment and analogy to aluminum hydroxide.
		28-day, Rat, oral gavage, 0, 62.5, 250 or 1,000 mg/kg bw-day. No treatment-related changes in behavior or appearance, no changes in body weight, food consumption, blood chemistry or organ weight. No alterations in gross or microscopic tissue examination. Rat NOAEL >1,000 mg/kg (highest dose tested).	Beard and Marzi, 2005; Stuer-Lauridsen et al., 2007	Reported in a secondary source; study details and test conditions were not available.
		90-day Rat, oral gavage, impaired learning in a labyrinth maze test. NOAEL: Not established LOAEL: 35 mg Al/kg-day as aluminum hydroxide with citric acid (only dose tested) (Estimated by analogy)	Bilkei-Gorzo, 1993 (as cited in ATSDR, 2008)	Reported in a secondary source; dose reported as 35 mg/kg-day as aluminum hydroxide with citric acid; citric acid was added to increase absorption; it is not proven that negative effects only related to aluminum hydroxide and not based on citric acid; also, the background aluminum content of the diet fed to rats was not reported; only one dose tested.
		90-day Rat, oral gavage, impaired learning in a labyrinth maze test. NOAEL: Not established	Bilkei-Gorzo, 1993	The background aluminum content of the diet fed to rats was not reported; only one dose tested

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		LOAEL: 300 mg Al/kg-day as aluminum hydroxide (only dose tested) (Estimated by analogy)		(aluminum hydroxide without citric acid); study description lacks sufficient details on individual results.
	Other	Oral exposure to aluminum is usually not harmful. Some studies show that people exposed to high levels of aluminum may develop Alzheimer's disease, but other studies have not found this to be true. It is not known for certain that aluminum causes Alzheimer's disease.	ATSDR, 2008	Summary statement from a secondary source.
Repeated Dose Effects		**MODERATE: Estimated to be of moderate hazard for immunotoxicity, due to the presence of a bioavailable metal species, based on comparison to analogous metal salts and professional judgment. Experimental studies indicate that oral exposure to rats produces no adverse effects at levels up to 1,000 mg/kg-day.**		
		28-day, Rat, oral gavage, 0, 62.5, 250 or 1,000 mg/kg bw-day. No treatment-related changes in behavior or appearance, no changes in body weight, food consumption, blood chemistry or organ weight. No alterations in gross or microscopic tissue examination. 28-day NOAEL >1,000 mg/kg-day, rats.	Australia, 2005; Stuer-Lauridsen et al., 2007; Submitted confidential study	Reported in a secondary source for a commercial formulation. Test substance was Exolit OP 930.
		Expected to have a moderate hazard potential for immunotoxicity effects resulting from the presence of bioavailable metal species. (Estimated)	Professional judgment	Estimated based on analogy to confidential metal salts.
Skin Sensitization		**LOW: Negative for skin sensitization in guinea pigs.**		
	Skin Sensitization	Non-sensitizing, guinea pigs.	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation. Conducted according to OECD TG 406.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Aluminum diethylphosphinate is slightly to non-irritating in rabbit eyes.**		
	Eye Irritation	Slightly irritating, rabbits.	Australia, 2005	Reported in a secondary source for a commercial formulation. Conducted according to OECD TG 405.
		Not irritating, rabbits.	Submitted confidential study	Study reported in a submitted confidential study.
Dermal Irritation		**VERY LOW: Aluminum diethylphosphinate is not irritating to rabbit skin.**		
	Dermal Irritation	Non-irritating, rabbit.	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation. Conducted according to OECD 404.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**Aluminum diethylphosphinate is estimated to be of moderate hazard for immunotoxicity, due to the presence of a bioavailable metal species, based on comparison to analogous metal salts and professional judgment.**		
	Immune System Effects	Expected to have a moderate hazard potential for immunotoxicity effects resulting from the presence of bioavailable metal species. (Estimated)	Professional judgment	Estimated based on analogy to confidential metal salts.
ECOTOXICITY				
ECOSAR Class		Not applicable		
Acute Aquatic Toxicity		**MODERATE: The measured green algae EC_{50} is between 50 and > 180 mg/L. For fish and *Daphnia*, LC_{50} values could not be determined because there were no effects at the highest concentrations tested.**		
Fish LC_{50}		*Danio rerio* (Zebra fish) 96-hour LC_{50} >11 mg/L (Experimental)	Australia, 2005	Reported in a secondary source for a commercial formulation.
		Danio rerio (Zebra fish) 96-hour LC_{50} >9.2 mg/L	Submitted confidential study	Study reported in a submitted confidential study.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		
	Danio rerio (Zebra fish) 96-hour LC_{50} >100 mg/L (Experimental)	Submitted confidential study	Study reported in a submitted confidential study; Study conducted according to EU Method C.1 (Acute Toxicity for Fish).
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50} >33.7 mg/L. (Experimental)	Australia, 2005	Reported in a secondary source for a commercial formulation.
	Daphnia magna 48-hour LC_{50} >33 mg/L. (Experimental)	Submitted confidential study	Study reported in a submitted confidential study.
	Daphnia magna 48-hour EC_{50} >100 mg/L 48-hour NOEC = 100 mg/L. (Experimental)	Submitted confidential study	Study reported in a submitted confidential study; Study conducted according to OECD Guideline 202 (Daphnia sp. Acute Immobilization Test).
Green Algae EC_{50}	*Scenedesmus subspicatus* 72-hour E_bC_{50} of 60 mg/L; *Scenedesmus subspicatus* 72-hour E_rC_{50} of 76 mg/L. (Experimental)	Australia, 2005	Reported in a secondary source for a commercial formulation.
	72-hour EC_{50} = 50 mg/L. (Experimental)	Submitted confidential study	Study reported in a submitted confidential study.
	Scenedesmus subspicatus 72-hour EC_{50} >180 mg/L. (Experimental)	Submitted confidential study	Study details reported in a confidential submission; Study conducted according to EU Method c.3 (Algal Inhibition Test).
Chronic Aquatic Toxicity	**MODERATE: An experimental value for green algae is 1.8 mg/L, while measured toxicity values for fish and *Daphnia* are >10 mg/L.**		
Fish ChV	ChV = 48 mg/L. (Estimated) (Estimated)	Submitted confidential study	Study reported in a submitted confidential study.
	Danio rerio (Zebra fish) 28-day NOEC = 100 mg/L; LOEC >100 mg/L. (Experimental)	Submitted confidential study	Study reported in a submitted confidential study; Study conducted according to OECD Guideline 215 (Fish, Juvenile Growth Test).

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid ChV		*Daphnia magna* 21-day EC_{50} = 22.3 mg/L for immobility *Daphnia magna* 21-day EC_{50} = 46.2 mg/L for reproduction *Daphnia magna* 21-day LOEC = 32 mg/L for immobility and reproduction *Daphnia magna* 21-day NOEC = 10 mg/L for immobility and reproduction (Experimental)	Australia, 2005; Submitted confidential study	Reported in a secondary source for a commercial formulation.
Green Algae ChV		Green algae ChV = 1.8 mg/L. (Experimental) (Experimental)	Submitted confidential study	Study reported in a submitted confidential study.
ENVIRONMENTAL FATE				
Transport		**Although the behavior of metal salts under environmental conditions is dependent on the characteristics of the local environment (predominately pH), transport of both the metal species and the organic anion is anticipated to be dominated by leaching through soil, runoff to aqueous environments, adsorption and/or precipitation of the metal ion onto soil or sediment, and wet and dry deposition of dust particulates in air to land or surface water. Volatilization of this ionic compound from either wet or dry surfaces is not expected to be an important fate process. Nevertheless, the environmental fate of this organic salt will be dependent on its pH-dependent dissociation, and adequate data are not available.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	Approximately 0.38 according to OECD Guideline 121 (Measured)	ECHA, 2013; Submitted confidential study	Guideline study.
	Level III Fugacity Model			This substance is not amenable to the model.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: For the organic counter-ion, estimates indicate that the half-life for ultimate aerobic biodegradation in water is less than 60 days, which converts to moderate potential for persistence. However, the metal ion is recalcitrant to biodegradation or other typical environmental removal processes.**		
Water	**Aerobic Biodegradation**	Passes Ready Test: No Test method: OECD TG 301F: Manometric Respirometry Test (Measured)	ECHA, 2013; Submitted confidential study	Guideline study.
		Not readily biodegradable (Measured)	Australia, 2005	Reported in a secondary source for a commercial formulation
		Not readily biodegradable (Measured)	Stuer-Lauridsen et al., 2007	Sufficient details were not available to assess the quality of this study.
		Organic counter-ion: Days-weeks (primary survey model) Weeks (ultimate survey model) (Estimated)	EPI v4.10	
		Metal ion: Recalcitrant (Estimated)	Professional judgment	Metal ions will not degrade in the environment.
		Study results: Not indicated Test method: 302C: Inherent - Modified MITI Test (II) Not inherently biodegradable (Measured)	ECHA, 2013; Submitted confidential study	Guideline study.
		Not inherently biodegradable (Measured)	Stuer-Lauridsen et al., 2007	Sufficient details were not available to assess the quality of this study.
	Volatilization Half-life for Model River	>1 year Not a significant fate process (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year Not a significant fate process (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	No degradation according to ISO/DIS 14853	Stuer-Lauridsen et al., 2007	Guideline study reported in a secondary source.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	Not a significant fate process (Estimated)	Professional judgment	This chemical is expected to exist entirely in particulate form in air.
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	Metal salts form a variety of hydroxylation products as a function of pH. Hydrolysis of the organic counter-ion is not expected to be a significant fate process (Estimated)	Professional judgment; Wolfe and Jeffers, 2000	The organic counter ion does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
Environmental Half-life		**Organic counter-ion:** <60 days **Metal ion:** Recalcitrant (Estimated)	EPI v4.10; Professional judgment	Based on estimated biodegradation half-lives for the organic counter-ion and metal ions will not degrade in the environment.
Bioaccumulation		**LOW: Aluminum diethylphosphinate is not expected to have potential for bioaccumulation.**		
	Fish BCF	<100 (Estimated)	Professional judgment	Available data suggests this chemical will dissociate under environmental conditions. The estimated log K_{OW} and limited lipophilicity are indicative of a lower potential for bioconcentration.
	Other BCF			No data located.
	BAF			No data located.
	Metabolism in Fish			No data located.

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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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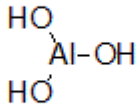
Aluminum Hydroxide

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[§] Based on analogy to experimental data for a structurally similar compound. [R] Recalcitrant: Substance is comprised of metallic species (or metalloids) that will not degrade, but may change oxidation state or undergo complexation processes under environmental conditions. [¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

		Human Health Effects											Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Aluminum Hydroxide[¥]	21645-51-2	L	*L*[§]	L	*L*[§]	L	M	*M*[§]	L		VL	VL	L	L	*H*[R]	*L*

Aluminum hydroxide



CASRN: 21645-51-2

MW: 78.01

MF: AlH_3O_3

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: O[Al](O)O

Synonyms: Aluminum hydroxide ($Al(OH)_3$), Gibbsite, Bayersite, Nordstrandite, Aluminum trihydrate

Chemical Considerations: This alternative is an inorganic compound and in the absence of experimental data, professional judgment using chemical class and structural considerations were used to complete this hazard profile.

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: None

Analog: Unspecified analogous aluminum compounds were discussed in the structural based professional judgment rationale

Endpoint(s) using analog values: Carcinogenicity, reproductive effects, immunotoxicity

Analog Structure: Not applicable

Structural Alerts: Aluminum compounds (EPA, 2010).

Risk Phrases: Not classified by Annex I Directive 67/548/European Economic Community & IUCLID (Pakalin et al., 2007).

Hazard and Risk Assessments: Risk assessment completed for aluminum hydroxide by the National Research Council Subcommittee on Flame-Retardant Chemicals (NRC, 2000). Hazard assessment completed for Design for the Environment Alternatives Assessment for Flame Retardants in Printed Circuit Boards, Review Draft, November 8, 2008. (EPA, 2008; NRC, 2000).

Aluminum Hydroxide CASRN 21645-51-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	Decomposes at approximately 200 (Measured)	European Commission, 2000	Adequate.
	Decomposes at approximately 150-220 to Al_2O_3 and H_2O (Measured)	European Commission, 2000	Adequate.
	Decomposes (loses water) at 300 (Measured)	Lewis, 2000	Adequate.
Boiling Point (°C)	The substance is expected to decompose before boiling. (Estimated)	Professional judgment	Based on the values included in the melting point section of this assessment.
Vapor Pressure (mm Hg)	$<10^{-8}$ (Estimated)	EPA, 1999; Professional judgment	Cutoff value for compounds that are anticipated to be nonvolatile accorded to HPV assessment guidance
Water Solubility (mg/L)	≤ 0.09 at 20°C, pH 6-7 Organisation for Economic Cooperation and Development (OECD) Guideline 105 Purity calculated based on aluminum oxide (Measured)	ECHA, 2013	Guideline study reporting non-specific value that is in agreement with other experimental values indicating poor solubility.
	0.0117 to 0.0947 at pH 7.5-8.1 and 21-24°C Reported as 11.7 to 94.7 µg/L $Al(OH)_3$ and 4.06 to 32.75 µg/L Al 100 mg of $Al(OH)_3$ was dissolved in 100 mL distilled water or test media prepared according to OECD 201, 202 or 211, filtered, and then analyzed using Graphite Furnace Atomic Absorption Spectrometry (GF AAS) and Inductively coupled plasma atomic emission spectroscopy (ICP-AES) (Measured)	Submitted confidential study	Reported in a nonguideline study done to prepare for toxicity testing.
	1.5 at 20°C at pH 7 (Measured)	European Commission, 2000	Measured values were not consistently reported, but are sufficient for subsequent components of the hazard assessment.
	$1.5x10^{-2}$ at 20°C at pH 8-9 (Measured)	European Commission, 2000	Measured values were not consistently reported, but are sufficient for subsequent components of the hazard assessment.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Insoluble in water (Estimated)	Lide, 2006	Measured values were not consistently reported, but are sufficient for subsequent components of the hazard assessment.
	Practically insoluble in water (Estimated)	Lewis, 2000; O'Neil et al., 2001	Measured values were not consistently reported, but are sufficient for subsequent components of the hazard assessment.
Log K_{ow}			No data located. This inorganic compound is not amenable to available estimation methods.
Flammability (Flash Point)	Not flammable (Measured)	ECHA, 2013	Reported in a secondary source and based on its use as a flame retardant.
Explosivity	Not explosive (Estimated)	European Commission, 2000	Adequate.
Pyrolysis	Not flammable (Estimated)	European Commission, 2000	Adequate.
pH	pH of a saturated solution in water was 6 to 7 (Measured)	ECHA, 2013	Determined in a water solubility study.
pK_a	Not applicable (Estimated)	Professional judgment	Determination of dissociation constant is not possible due to the insolubility of the test substance.
Particle Size	<100 µm; 88% for the fine unground hydrate and 52-61% for the coarse unground hydrate < 2 µm; 1.3-2% for the fine unground hydrate and 1% for the coarse unground hydrate According to OECD Guideline 110 (Particle Size Distribution / Fibre Length and Diameter Distributions) (Measured)	ECHA, 2013	Guideline study reported in a secondary source.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Toxicokinetic data suggest that aluminum hydroxide is not readily absorbed in humans following oral exposure. Excretion occurs primarily through feces, and less so in urine. Animal studies indicated that aluminum accumulated in intestinal cells but was not found in other tissues.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	^{26}Al labeled aluminum hydroxide (in water suspension) was administered to rats by oral gavage. The mean fractional uptake (absorption) into the bloodstream of ^{26}Al from aluminum hydroxide was 0.025±0.041%. Compared to the uptake into the bloodstream of rats injected with 0.19 ng ^{26}Al labeled aluminum citrate in solution, aluminum hydroxide as an insoluble compound is less bioavailable than soluble compounds (mean fractional uptake of ^{26}Aluminum citrate: 0.079 ±0.0057%; ^{26}Aluminum hydroxide: 0.025±0.041%).	ECHA, 2013	Reported in a secondary source. Adequate, performed in accordance with OECD guidelines and Good Laboratory Practices (GLP); Aluminum hydroxide, was suspended in water with added 1% carboxymethylcellulose (to maintain a suspension).
		After rats were exposed to aluminum hydroxide in drinking water for 10 weeks, aluminum accumulated in intestinal cells but not in other tissues.	HSDB, 2013	Reported in a secondary source, study details and test conditions were not provided.
		In metabolic studies in humans, 12% of an oral load of aluminum hydroxide was retained, but absorption was not calculated.	HSDB, 2013	Reported in a secondary source, study details and test conditions were not provided.
		The absorbed fraction of aluminum hydroxide in two human males dosed orally was 0.01%.	HSDB, 2013	Reported in a secondary source, study details and test conditions were not provided.
		Adult humans with renal failure who ingested 1.5-3.0 g aluminum hydroxide per day for 20-32 days absorbed between 100 and 568 mg aluminum per day (7-19% of the dose).	HSDB, 2013	Reported in a secondary source, study details and test conditions were not provided.
		Adult humans taking aluminum antacids had a 3-fold increase of aluminum levels in the	ATSDR, 2008	Reported in a secondary source, study details were not provided.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		urine; minimal aluminum was absorbed and was mostly excreted in the feces.		
	Other	Certain complexing agents such as citric acid and lactic acid can increase the bioavailability/absorption of aluminum hydroxide.	Gomez et al., 1991; Bilkei-Gorzo, 1993; Colamina et al., 1994; Professional judgment.	Based on studies using citric acid and lactic acid in conjunction with aluminum hydroxide and professional judgment.
Acute Mammalian Toxicity		**LOW: Aluminum hydroxide has low acute toxicity based on oral LD_{50} > 2,000 mg/kg in rats.**		
Acute Lethality	**Oral**	Rat oral LD_{50} >5,000 mg/kg	European Commission, 2000	Reported in a secondary source, study details and test conditions were not provided.
		Rat oral LD_{50} >2,000 mg/kg	ECHA, 2013	Reported in a secondary source. Performed in accordance with OECD guidelines and GLP.
	Dermal			No data located.
	Inhalation			No data located.
Carcinogenicity		**LOW: Aluminum hydroxide is estimated to be of low hazard for carcinogenicity based on professional judgment and comparison to analogous aluminum compounds.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)	Low potential for carcinogenicity (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
	Combined Chronic Toxicity/Carcinogenicity			No data located.
	Other			No data located.
Genotoxicity		**LOW: Aluminum hydroxide did not cause mutations in mammalian cells *in vitro* and did not result in an increased incidence of micronuclei in rats *in vivo*.**		
	Gene Mutation *in vitro*	Negative in mouse lymphoma cells with and without metabolic activation	ECHA, 2013	Adequate, performed in accordance with OECD guidelines and GLP.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vivo*	Negative for induction of micronuclei in polychromatic erythrocytes of bone marrow in Sprague-Dawley rats	ECHA, 2013	Adequate, performed in accordance with OECD guidelines and GLP.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: Aluminum hydroxide is estimated to be of low hazard for reproductive effects based on professional judgment and comparison to analogous aluminum compounds.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	Low potential for reproductive effects (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
	Other			No data located.
Developmental Effects		**LOW: Aluminum hydroxide does not show developmental toxicity when administered orally to rats or mice at dose levels up to 266 mg/kg-day. There were no data located regarding developmental neurotoxicity.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	Rat (Sprague-Dawley), oral (gavage), 384 mg/kg/day $Al(OH)_3$ alone or 384 mg/kg/day $Al(OH)_3$ concurrent with 62 mg/kg/day citric acid on GD 6-15. No significant differences between controls and Al-treated rats on pre- or postimplantation loss, number of live fetuses per litter, or sex ratio. Reduced fetal body weight and increased incidence of skeletal variations in groups receiving $Al(OH)_3$ and citric acid.	Gomez et al., 1991	Study details reported in a primary source. Citric acid was added to increase absorption; it is not proven that effects are solely related to aluminum hydroxide and not based on citric acid.
		Swiss mice, oral (gavage), 166 mg/kg $Al(OH)_3$ alone or 166 mg/kg $Al(OH)_3$ concurrent with 570 mg/kg lactic acid on GD 6-15. Maternal toxicity was evident in groups treated with $Al(OH)_3$ and lactic acid. There were no embryotoxic effects in any group. There was a non-statistically significant increased incidence of skeletal variations in groups receiving $Al(OH)_3$ and lactic acid.	Colomina et al., 1992	Study details reported in a primary source Lactic acid was added to increase absorption; it is not proven that effects are solely related to aluminum hydroxide and not based on lactic acid.
		Rat (Sprague-Dawley), oral (gavage), 0 or 384 mg/kg-day on GD 6-15 There were no significant changes in pre- or post-implantation losses, number of live fetuses per litter, sex ratio, fetal body weight, incidence of malformations, or skeletal variations. NOAEL: 384 mg/kg-day (only dose tested) LOAEL: Not established	Gomez et al., 1991	Study details reported in a primary source; only one dose tested.
		Mouse, oral, no developmental effects. NOAEL: 266 mg/kg-day (highest dose tested)	Domingo et al., 1989	Adequate.
		Mouse, oral, no developmental effects. NOAEL: 268 mg/kg-day (highest dose tested)	Gomez et al., 1989	Abstract only.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Mouse, oral, no developmental effects. NOAEL: 300 mg/kg-day (only dose tested)	Colamina et al., 1994	Abstract only.
		Rat, oral (gavage), 192, 384, 768 mg/kg-day on GD 6-15 There were no significant changes in the number of litters, corpora lutea, total implants, pre- or post-implantation losses, and live fetuses per litter. There were also no significant differences in the sex ratio, fetal body weight, or fetal malformations. NOAEL: 768 mg/kg-day (highest dose tested) LOAEL: Not established	Gomez et al., 1990	Study details reported in a primary source.
		Rat, oral, no developmental effects. NOAEL: 384 mg/kg-day (only dose tested)	Llobet et al., 1990	Abstract only.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	Low potential for developmental neurotoxicity (Estimated)	Professional judgment	Estimated based on analogy to structurally similar compounds.
	Other			No data located.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Aluminum hydroxide is expected to be of moderate hazard for neurotoxicity. Impaired learning in a labyrinth maze test was reported in a 90-day oral study in rats at 300 mg Al/kg/day as aluminum hydroxide (only dose tested; a NOAEL was not identified). Impaired learning in a labyrinth maze test was also reported in rats orally exposed to 100 mg Al/kg/day as aluminum hydroxide in combination with 30 mg/kg-day citric acid (only dose tested; a NOAEL was not identified). There is uncertainty in the threshold of response for this effect for exposure to aluminum hydroxide alone and in combination with citric acid. The possibility that effects occur at doses <100 mg/kg/day (in the Moderate - High hazard designation range) cannot be ruled out; therefore a Moderate hazard designation was assigned.**		
	Neurotoxicity Screening Battery (Adult)	30-day Rat, oral diet, no significant effects noted. NOAEL: 1,252 mg Al/kg-day (highest dose tested)	Thorne et al., 1986; Thorne et al., 1987; ATSDR, 2008	Reported in a secondary source.
		90-day Rat, oral gavage, impaired learning in a labyrinth maze test NOAEL: not established LOAEL: 300 mg/kg-bw (only dose tested)	Bilkei-Gorzo, 1993	The background aluminum content of the diet fed to rats was not reported; only one dose tested; study description lacks sufficient details on individual results. Exposure to 100 mg /kg-day as aluminum hydroxide combined with 30 mg/kg-day citric acid (only dose tested) was also investigated for which impaired learning was observed; citric acid was added to increase absorption; it is not proven that negative effects only related to aluminum hydroxide and not based on citric acid.
		Low potential for repeated dose effects but moderate potential for immunotoxicity. (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
	Other	Oral exposure to aluminum is usually not harmful. Some studies show that people exposed to high levels of aluminum may develop Alzheimer's disease, but other studies have not found this to be true. It is not known for certain that aluminum causes Alzheimer's disease.	ATSDR, 2008	Summary statement from a secondary source.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**MODERATE: Aluminum hydroxide is estimated to have potential for immunotoxicity based on professional judgment and comparison to analogous aluminum compounds. Aluminum hydroxide is of low hazard for other repeated dose effects based on an experimental study indicating no adverse effects in rats following oral doses up to 14,470 ppm (302 mg/kg-day). In addition, a low potential for repeated dose effect is estimated based on professional judgment and comparison to analogous aluminum compounds.**		
		Low potential for repeated dose effects but moderate potential for immunotoxicity (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
		28-day Rat (male), oral diet, no systemic effects noted. NOAEL: 14,470 ppm/diet (302 mg aluminum/kg-day; highest dose tested).	Hicks et al., 1987	Study details from primary source.
	Immune System Effects	6-Week human, oral. LOAEL: 25 mg Al/kg-day (Reduction in primed cytotoxic T-cells, only dose tested).	ATSDR, 2008	Study details reported in a secondary source.
		Moderate potential for immunotoxicity. (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
Skin Sensitization		**LOW: Aluminum hydroxide is not a skin sensitizer.**		
	Skin Sensitization	Low potential for skin sensitization. (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
		Not sensitizing to guinea pigs in an *in vivo* maximization test	ECHA, 2013	Reported in a secondary source; conducted in accordance with OECD guidelines and GLP.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**VERY LOW: Aluminum hydroxide is not irritating to rabbit eyes.**		
	Eye Irritation	Not irritating, rabbits.	ECHA, 2013	Reported in a secondary source; Conducted in accordance with OECD guidelines and GLP.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Dermal Irritation		**VERY LOW: Aluminum hydroxide is not irritating to skin.**		
	Dermal Irritation	Not irritating, rabbits.	ECHA, 2013	Reported in a secondary source. Conducted in accordance with OECD guidelines and GLP.
		Not irritating, rabbits, mice and pigs	ECHA, 2013	Reported in a secondary source; nonguideline studies.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**Aluminum hydroxide is estimated to have potential for immunotoxicity based on professional judgment and comparison to analogous aluminum compounds.**		
	Immune System Effects	Moderate potential for immunotoxicity. (Estimated)	Professional judgment	Estimated based on professional judgment and comparison to analogous aluminum compounds.
		6-Week human, oral. LOAEL: 25 mg Al/kg-day (Reduction in primed cytotoxic T-cells, only dose tested).	ATSDR, 2008	Reported in a secondary source.
ECOTOXICITY				
ECOSAR Class		Not applicable		
Acute Aquatic Toxicity		**LOW: Effect values from experimental studies for fish, daphnia and algae indicate no effects at the saturation limit (NES).**		
Fish LC_{50}		*Salmo trutta* 96-hour NOEC >100 mg/L (Experimental)	European Commission, 2000	Reported in a secondary source. The effect concentration is greater than the measured water solubility.
Daphnid LC_{50}		*Daphnia magna* 48-hour EC_{50} = NES static test conditions. (Experimental)	Tóthová and Šimo, 2013a	Study details reported in an unpublished study; conducted according to OECD 202; no effects at test substance saturation limit (> 0.079 mg/L).
		Daphnia magna 48-hour NOEC >100 mg/L (Experimental)	European Commission, 2000	Reported in a secondary source. Study details and test conditions were not available and the effect concentration is greater than the measured water solubility.
		Daphnia magna 48-hour NOEC > 0.135	ECHA, 2013	Study conducted with aluminum powder.

Aluminum Hydroxide CASRN 21645-51-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	mg/L (Experimental)		
	Daphnia magna 48-hr EC_{50} = 0.8240 mg/L (Experimental)	TSCATS, 1996	Study incorrectly cited in source; results are for a different test substance, vanadium hydroxide oxide.
Green Algae EC_{50}	*Desmodesmus subspicatus* 72-hour EC_{50} = NES (Experimental)	Tóthová and Šimo, 2013c	Study details reported in an unpublished study; conducted according to OECD 201; no effects at test substance saturation limit (> 0.078 mg/L).
	Selenastrum capricornutum 96-hour EC_{50} = 0.6560 mg/L (Experimental)	TSCATS, 1996	Study incorrectly cited in source; results are for a different test substance, vanadium hydroxide oxide.
	Pseudokirchneriella subcapitata 96-hour EC_{50} = 0.46 mg/L (Experimental)	ECHA, 2013	Reported in a secondary source. EC_{50} range: 0.57 mg/L at pH of 7.6 and 0.46 mg/L at pH of 8.2. The water solubility of aluminum hydroxide under basic pH conditions is not available; experimental details are not sufficient to address the confidence limits of these data points.
Chronic Aquatic Toxicity	**LOW: Experimental data for daphnia and algae indicate NES. Although there were no experimental data for fish located, the available chronic toxicity data for daphnia and algae suggests low chronic toxicity for fish.**		
Fish ChV	*Pimephales promelas* 42-day NOEC = 0.102 mg/L, LOEC = 0.209 mg/L (Experimental)	TSCATS, 1996	Study incorrectly cited in source; results are for a different test substance, vanadium hydroxide oxide.
Daphnid ChV	Daphnia magna 21-day ChV = NES semi-static test conditions (Experimental)	Tóthová and Šimo, 2013b	Study details reported in an unpublished study; conducted according to OECD 211; no effects at test substance saturation limit (> 0.076 mg/L).
	Daphnia magna 21-day NOEC = 0.091 mg/L, LOEC = 0.197 mg/L (Experimental)	TSCATS, 1996	Study incorrectly cited in source; results are for a different test substance, vanadium hydroxide oxide.
Green Algae ChV	*Selenastrum capricornutum* 72-hour NOEC >100 mg/L (Experimental)	European Commission, 2000	Reported in a secondary source. The effect concentration is greater than the measured water solubility.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
ENVIRONMENTAL FATE				
Transport		**Although the behavior of aluminum salts under environmental conditions is dependent on the characteristics of the local environment (predominately pH), transport of the aluminum (III) species is anticipated to be dominated by leaching through soil; runoff to aqueous environments; adsorption and/or precipitation of the metal ion onto soil or sediment; and wet and dry deposition dust particulates in air to land or surface water. Volatilization of this ionic compound from either wet or dry surfaces is not expected to be an important fate process. Under acidic pHs typically encountered in the environment, it may form insoluble polymeric aluminum hydroxide colloids while under basic conditions; anionic aluminum hydroxide is expected to predominate. Other factors influencing its behavior include the presence of dissolved organic matter, the extent of absorption on suspended particles, and the presence of other aluminum species.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 (Estimated)	EPA, 2004; Professional judgment	Cutoff value for nonmobile compounds.
	Level III Fugacity Model			No data located.
Persistence		**HIGH: As an inorganic material, aluminum hydroxide is not expected to biodegrade or oxidize under typical environmental conditions. Aluminum hydroxide does not absorb light at environmentally relevant wavelengths and is not expected to photolyze. No degradation processes for aluminum hydroxide under typical environmental conditions were identified.**		
Water	**Aerobic Biodegradation**	Recalcitrant (Estimated)	Professional judgment	Substance is or contains inorganic elements, such as metal ions or oxides, that are expected to be found in the environment >180 days after release.
	Volatilization Half-life for Model River	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**	Recalcitrant (Estimated)	Professional judgment	Substance contains inorganic elements.
	Anaerobic Biodegradation	Recalcitrant	Professional judgment	Substance contains inorganic elements.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.

Aluminum Hydroxide CASRN 21645-51-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Air	**Atmospheric Half-life**	>1 year (Estimated)	Professional judgment	Substance contains inorganic elements.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment	Aluminum hydroxide does not absorb UV light at environmentally relevant wavelengths and is not expected to undergo photolysis.
	Hydrolysis			Dissociation of aluminum hydroxide in environmental waters is dependent both on the pH and the local concentration of other aluminum species; dissociation will not occur unless in highly acidic waters, e.g., pH 3.
Environmental Half-life				No data located. Inorganic compounds are outside the estimation domain (EPI).
Bioaccumulation		**LOW: Aluminum hydroxide is not expected to bioaccumulate.**		
	Fish BCF	<100 (Estimated)	Professional judgment	Aluminum hydroxide is an inorganic compound and is not anticipated to bioaccumulate or bioconcentrate. This inorganic compound is not amenable to available quantitative structure activity relationship (QSAR) models.
	Other BCF			No data located.
	BAF	<100 (Estimated)	Professional judgment	Aluminum hydroxide is an inorganic compound and is not anticipated to bioaccumulate or bioconcentrate. This inorganic compound is not amenable to available QSAR models.
	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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Colomina MT, Gomez M, Domingo JL, et al. (1992) Concurrent ingestion of lactate and aluminum can result in developmental toxicity in mice. 77(1):95-106.

Colomina MT, Gomez M, Domingo JL, et al. (1994) Lack of maternal and developmental toxicity in mice given high doses of aluminum hydroxide and ascorbic acid during gestation. Pharmacol Toxicol 74:236-239.

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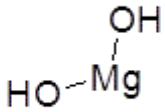
Magnesium Hydroxide

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[R] Recalcitrant: Substance is comprised of metallic species (or metalloids) that will not degrade, but may change oxidation state or undergo complexation processes under environmental conditions. [¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical	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
Magnesium Hydroxide[¥]	1309-42-8	L	L	L	L	L	*L*	L	L		M	L	*L*	*L*	*H*[R]	*L*

Magnesium Hydroxide



CASRN: 1309-42-8

MW: 58.32

MF: MgH_2O_2

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: O[Mg]O

Synonyms: Magnesium hydroxide ($Mg(OH)_2$); Brucite, Milk of Magnesia; Alcanex NHC 25, Asahi Glass 200-06, Baschem 12, Combustrol 500, Duhor, Duhor N, Ebson RF, FloMag H, FloMag HUS, Hydro-mag MA, Hydrofy G 1.5, Hydrofy G 2.5, Hydrofy N, Kisuma 4AF, Kisuma 5, Kisuma 5A, Kisuma 5B, Kisuma 5B-N, Kisuma 5BG, Kisuma 5E, Kisuma 78, Kisuma S 4, Kyowamag F, Lycal 96 HSE, Mag Chem MH 10, Magnesia hydrate, MagneClear 58, Magnesia magma, Magnesiamaito, Magnesium dihydroxide, Magnesium hydroxide gel, Magnesium(II) hydroxide, Magnifin H 10, Magox, Marinco H, Marinco H 1241, Martinal VPF 8812, Milmag, Mint-O-Mag, Nemalite, Oxaine M, Phillips Magnesia Tablets, Phillips Milk of Magnesia Liquid, Reachim, Star 200, Versamag

Chemical Considerations: This alternative is an inorganic compound. In the absence of experimental data, professional judgment using chemical class and structural considerations were used to complete this hazard profile.

Polymeric: No
Oligomeric: Not applicable

Metabolites, Degradates and Transformation Products: Not applicable

Analog: No analogs; Mg^{2+} ions are expected to form when $Mg(OH)_2$ and other magnesium containing compounds dissociate in aqueous conditions. Studies included in this assessment include other sources of Mg^{2+} like $MgCl_2$.

Endpoint(s) using analog values: Not applicable

Analog Structure: Not applicable

Structural Alerts: None

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

Hazard and Risk Assessments: Risk assessment completed for magnesium hydroxide by the National Academy of Sciences in 2000 (NAS, 2000).

Magnesium Hydroxide CASRN 1309-42-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	Decomposes at 350 (Measured)	Hodgman, 1959; Lewis, 1997; Lewis, 2000	MgO and H_2O are decomposition products.
	Decomposes at 380 (Measured)	IUCLID, 2000	MgO and H_2O are decomposition products.
	350 (Measured)	Lide, 2000; Aldrich Chemical Company, 2006	MgO and H_2O are decomposition products.
Boiling Point (°C)	Will decompose before boiling (Measured)	IUCLID, 2000	Decomposition occurs upon melting as described in additional sources above.
Vapor Pressure (mm Hg)	$<10^{-8}$ (Estimated)	EPA, 1999; Professional judgment	Cutoff value for nonvolatile compounds according to HPV assessment guidance. This inorganic compound is not amenable to available estimation methods.
Water Solubility (mg/L)	1.78 at 20°C, pH 8.3 According to Organisation for Economic Cooperation and Development (OECD 105) Column elution method. (Measured)	ECHA, 2013	Guideline study; results are in agreement with other experimental values.
	9 at 18°C (Measured)	Hodgman, 1959; IUCLID, 2000	Measured values, which span a relatively narrow range, are consistently reported in numerous sources.
	1 at 20°C (Measured)	IUCLID, 2000	Measured values, which span a relatively narrow range, are consistently reported in numerous sources.
	6 at 20°C (Measured)	IUCLID, 2000	Measured values, which span a relatively narrow range, are consistently reported in numerous sources.
	<8 at 20°C (Measured)	IUCLID, 2000	Measured values, which span a relatively narrow range, are consistently reported in numerous

Magnesium Hydroxide CASRN 1309-42-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
			sources.
	40 at 100°C (Measured)	Hodgman, 1959	Value obtained at an elevated temperature.
Log K_{ow}			No data located; inorganic compounds are outside the estimation domain of EPI.
Flammability (Flash Point)	Not flammable (Measured)	IUCLID, 2000	Reported in a secondary source and based on its use as a flame retardant.
Explosivity	Not explosive (Estimated)	IUCLID, 2000	Adequate.
Pyrolysis	Not applicable (Estimated)	Professional judgment	Inorganic compounds do not undergo pyrolysis.
pH	pH of a saturated solution in water was 8.3 (Measured)	ECHA, 2013	Reported in a secondary source, determined from a water solubility study.
	9.5-10.5 (Measured)	O'Neil et al., 2011	Reported in a secondary source, limited study details provided.
pK_a			No data located.
Particle Size	D10 = mean 2.013 µm D50 = mean 13.915 µm D90 = mean 154.107 µm According to OECD Guideline 110 (Particle Size Distribution / Fibre Length and Diameter Distributions). (Estimated)	ECHA, 2013	Guideline study reported in a secondary source.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Some magnesium hydroxide is absorbed following ingestion and is excreted primarily in urine.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	The magnesium ion is poorly absorbed; when taken orally, only 5-15% of the magnesium from a dose of magnesium hydroxide is absorbed and this magnesium is readily excreted in the urine, if kidney function is normal.	IUCLID, 2000	Reported in a secondary source, limited study details provided.
	Other			No data located.
Acute Mammalian Toxicity		**LOW: Acute lethality values suggest that magnesium hydroxide is of low concern for acute toxicity for oral exposure. There were no data located regarding acute dermal exposure.**		
Acute Lethality	**Oral**	Rat oral LD_{50} = 8,500 mg/kg	Lewis, 2000	Reported in a secondary source, limited study details provided.
		Mouse oral LD_{50} = 8,500 mg/kg.	Lewis, 2000	Reported in a secondary source, limited study details provided.
		Human infant oral TD_{Lo} (behavioral) = 2,747 mg/kg.	Lewis, 2000	Reported in a secondary source, limited study details provided.
		Probable human oral lethal dose = 5-15 g/kg.	HSDB, 2003	Reported in a secondary source, limited study details provided.
	Dermal			No data located.
	Inhalation	Rat inhalation 4-hour LC_{50} >2.1 mg/L (whole-body inhalation to aerosol)	ECHA, 2013	Reported in a secondary source. There was no mortality at the highest dose tested (2.1 mg/L); conducted according to OECD 403.
Carcinogenicity		**LOW: Experimental studies indicate low concern for carcinogenicity based on results from studies on magnesium hydroxide and the related magnesium chloride.**		
	OncoLogic Results			Structure could not be evaluated by OncoLogic.
	Carcinogenicity (Rat and Mouse)	5-week, repeated-dose/carcinogenicity study, oral (diet), rat; Decreased number of carcinogen-induced DNA synthesis in	BIBRA, 1993	Reported in a secondary source, limited study details provided; study duration insufficient as a cancer

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		the large bowel epithelial cells. NOAEL: 2,000 ppm (approximately 100 mg/kg-day, highest dose tested)		study.
	Combined Chronic Toxicity/Carcinogenicity	96-week chronic toxicity/carcinogenicity study on $MgCl_2$, oral, mouse; no significant differences in tumor incidence between treated and control animals except for dose-related decrease in the incidence of hepatocellular carcinomas in males.	Kurata et al., 1989	Sufficient study details reported in a primary source; test substance: magnesium chloride.
		227-day, chronic toxicity/ carcinogenicity study, oral (diet), rat; decreased number of colon tumors in rats pretreated with a known colon carcinogen. NOAEL: 50 mg/kg-day (highest dose tested).	BIBRA, 1993	Reported in a secondary source, limited study details provided; study duration insufficient as a cancer study.
		16-week carcinogenicity study, oral (diet), rat; inhibitory effects on colon carcinogenesis, carcinogen-induced expression of c-myc proto-oncogene and cell proliferation. NOAEL: 0.2% in diet (highest concentration tested)	Wang et al., 1993	Sufficient study details reported in a primary source; study duration insufficient as a cancer study.
		Inhalation exposure of male rats to short (4.9 x 0.31 mm) or long (12 x 0.44 mm) $MgSO_4/5Mg(OH)_2 \cdot 3H_2O$ filaments for 6 hour/day, 5 day/week for up to 1 year did not increase the incidence of any tumor types in animals sacrificed 1 day or 1 year after cessation of exposure.	NAS, 2000	Reported in a secondary source, limited study details provided; study duration insufficient as a cancer study.
	Other			No data located.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**LOW: Experimental studies indicate that magnesium hydroxide is not mutagenic to bacteria or mammalian cells *in vitro* and does not cause chromosomal aberrations in human lymphocytes *in vitro*.**		
	Gene Mutation *in vitro*	Negative, Ames Assay in *Salmonella* and *Escherichia coli*.	BIBRA, 1993	Reported in a secondary source, limited study details provided. Only 3 strains of *Salmonella* were tested; current regulatory guidelines suggest that at least 4 strains be used in Ames tests.
		Negative; mouse lymphoma assay, L5178Y cells; with and without metabolic activation.	ECHA, 2013	Reported in a secondary source.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative; did not induce chromosomal aberrations in human lymphocytes; with and without metabolic activation.	ECHA, 2013	Reported in a secondary source.
	Chromosomal Aberrations *in vivo*			No data located.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: There were no reproductive effects observed in rats in a repeated dose toxicity study with the reproduction/developmental toxicity screen at doses of magnesium hydroxide as high as 1,000 mg/kg-day.**		
	Reproduction/Developmental Toxicity Screen			No data located.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Repeated dose toxicity study with the reproduction/developmental toxicity screen; rat, oral (gavage), 0, 110, 330, 1,000 mg/kg-day magnesium hydroxide. Males exposed for 29 days: 2 weeks prior to mating, during mating and up to termination; females exposed for 41-45 days: 2 weeks premating, during mating, post coitum, and 4 days of lactation. There were no reproductive effects observed in any dose group. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	ECHA, 2013	Reported in a secondary source. Study conducted according to OECD 422.
	Reproduction and Fertility Effects			No data located.
	Other			No data located.
Developmental Effects		**LOW: Magnesium hydroxide is expected to be of low concern for developmental effects based on a nonstandard experimental study indicating magnesium chloride produces no adverse effects on developmental outcomes at levels up to 96 mg/kg/day of Mg^{2+} ion and an experimental study from a secondary source showing no effect on human newborns.**		
	Reproduction/ Developmental Toxicity Screen			No data located.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Repeated dose toxicity study with the reproduction/developmental toxicity screen; rat, oral (gavage), 0, 110, 330, 1,000 mg/kg-day. Males exposed for 29 days: 2 weeks prior to mating, during mating and up to termination; females exposed for 41-45 days: 2 weeks premating, during mating, post coitum, and 4 days of lactation. There were no developmental effects observed in any dose group. NOAEL:1,000 mg/kg-day (highest dose tested) LOAEL: Not established	ECHA, 2013	Reported in a secondary source. Study conducted according to OECD 422.
		Repeated-dose/developmental study (fetal exposure at unspecified dose levels during 3rd trimester), 27 hypertensive women treated with magnesium hydroxide, no effect on newborns except slightly increased body weight and hypermagnesiumemia. Cord serum Mg levels reported to be 70-100% of maternal levels after treatment (potentially causing neurological depression in neonate, characterized by respiratory depression, muscle weakness, decreased reflexes). Prolonged magnesium treatment during pregnancy may be associated with maternal and fetal hypocalcemia and adverse effects on fetal bone mineralization.	HSDB, 2003	Reported in a secondary source, limited study details provided. Maternal treatment doses not specified.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	10-day (GD 6-15) reproductive/developmental study on $MgCl_2$, oral, rat; no treatment-related effects. NOAEL: 96 mg/kg-day for Mg^{2+} ion (highest dose tested) LOAEL: Not established	NAS, 2000	Reported in a secondary source, limited study details provided.
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity			No data located.
	Other			No data located.
Neurotoxicity		**LOW: Magnesium hydroxide is expected to be of low hazard for neurotoxicity based on expert judgment.**		
	Neurotoxicity Screening Battery (Adult)	Low potential for neurotoxicity. (Estimated)	Expert judgment	Estimated based on expert judgment.
	Other			No data located.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects		**LOW: Experimental studies indicate magnesium ions produce no adverse systemic effects in rats or mice at levels ≥ 1,000 mg/kg-day of magnesium hydroxide.**		
		96-week repeated-dose study for $MgCl_2$, oral (0, 0.5, 2% in the diet), mouse; decreased body weight gain, increased food/water consumption and increased relative brain, heart and kidney weights in high dose (2%) females, no effects in males. Female: NOAEL: 87 mg/kg-day for Mg^{2+} ion LOAEL: 470 mg/kg-day for Mg^{2+} ion Male: NOAEL: 336 mg/kg-day for Mg^{2+} ion (highest dose tested) LOAEL: Not established	Kurata et al., 1989	Adequate, primary source.
		90-day repeated-dose study for $MgCl_2$, oral, mouse (M: 73, 146, 322, 650, 1,368 mg/kg-day for Mg^{2+} ion; F: 92, 190, 391, 817, 1,660 mg/kg-day for Mg^{2+} ion); decreased body weight gain in males and females at highest dose tested (1,660 mg/kg-day); renal tubular vacuolation in males administered 650 mg/kg-day for Mg^{2+} ion. Female: NOAEL: 817 mg/kg-day for Mg^{2+} ion LOAEL: 1,660 mg/kg-day for Mg^{2+} ion Male: NOAEL: 322 mg/kg-day for Mg^{2+} ion LOAEL: 650 mg/kg-day for Mg^{2+} ion	NAS, 2000	Reported in a secondary source, no study details provided.
		90-day repeated-dose study in B6C3F1 mice; $MgCl_2$ administered orally at doses	NAS, 2000	Reported in a secondary source, no study details provided.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		of 0.3, 0.6, 1.25 and 2.5% in the diet. Effects included decreased body weight gain and renal tubular vacuolation in males in the high-dose group (840 mg/kg-day). Female: NOAEL: 587 mg/kg-day for Mg^{2+} ion Male: NOAEL: 420 mg/kg-day for Mg^{2+} ion LOAEL: 840 mg/kg-day for Mg^{2+} ion		
		32-week repeated-dose study, diet, rat; no effects on body weight or liver weight. NOAEL: 1,000 ppm (approximately 50 mg/kg-day, highest dose tested) LOAEL: Not established	BIBRA, 1993	Reported in a secondary source, no study details provided.
		Repeated dose toxicity study with the reproduction/developmental toxicity screen; rat, oral (gavage), 0, 110, 330, 1,000 mg/kg-day $MgOH_2$. Males exposed for 29 days: 2 weeks prior to mating, during mating and up to termination; females exposed for 41-45 days: 2 weeks premating, during mating, post coitum, and 4 days of lactation. There were no toxicologically relevant changes in any of the parental parameters examined. NOAEL: 1,000 mg/kg-day (highest dose tested) LOAEL: Not established	ECHA, 2013	Reported in a secondary source. Study conducted according to OECD 422.
		4-week repeated-dose study, oral, human; caused diarrhea, abdominal discomfort,	BIBRA, 1993	Reported in a secondary source, no study details provided.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		and increased serum magnesium levels. NOAEL: Not established LOAEL: 400 mg/kg-day (only dose reported)		
		Inhalation exposure of male rats to short (4.9 x 0.31 mm) or long (12 x 0.44 mm) $MgSO_4/5Mg(OH)_23H_2O$ filaments for 6 hour/day, 5 day/week for up to 1 year (concentration not specified) exhibited a slight increase in the incidence of pulmonary lesions 1 year after cessation of exposure. Histopathological examination revealed a slight increase in segmental calcification of the pulmonary artery and thickening of the lung pleura in rats exposed to both short and long filaments for 4 weeks or 1 year. There were no effects on survival or body, lung, liver, kidney and spleen weights of animals sacrificed 1 day or 1 year following a 1-year exposure period.	NAS, 2000	Reported in a secondary source, no study details provided.
		Human systemic effects: chlorine level changes, coma, somnolence in a neonate.	Lewis, 2000	A case study of intoxication after oral exposure to magnesium in a neonate. Reported in a secondary source; no study details provided.
		Repeated oral exposure in humans may cause rectal stones composed of magnesium carbonate and magnesium hydroxide (rare occurrence).	IUCLID, 2000	Reported in a secondary source, no study details provided.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: A mouse local lymph node assay (LLNA) reported some sensitization following exposure to $Mg(OH)_2$ (purity not reported), while negative results for sensitization were reported in guinea pigs in a maximization test. Magnesium hydroxide is not expected to cause skin sensitization based on professional judgment. Based on the weight-of-evidence (WOE), a hazard designation of Low is appropriate.**		
	Skin Sensitization	Not sensitizing in a modified Magnusson and Kligman maximization test in Guinea pigs; phase 1 induction: administered intra-dermally at a concentration of 5% v/v in 0.5% methyl cellulose; phase 2 induction: topically administered at a concentration of 25% in petrolatum; challenged: topical application of 25% in petrolatum; no reaction was observed in any treated animal in the challenge phase.	Submitted confidential study	Test substance identified as $Mg(OH)_2$; purity not reported; negative and positive controls were used.
		Sensitizing in a mouse local lymph node assay (LLNA); application of 10, 25 or 50% w/w $MgOH_2$ in propylene glycol to the ears. Very slight erythema in all animals treated with 50% $MgOH_2$, staining on the ears at 10, 25 and 50%. SI (stimulation index) at 10, 25 and 50% was 2.0, 3.6 and 5.9, respectively. Dose response and EC3 value >/= 3.	ECHA, 2013	Well documented secondary source; GLP study conducted according to guidelines. $MgOH_2$, purity not stated
		Does not cause skin sensitization. (Estimated)	Professional judgment	Estimated by professional judgment.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: Based on irritation and damage to the corneal epithelium in rabbits that cleared within 2-3 days.**		
	Eye Irritation	Moderately irritating to rabbit eyes.	IUCLID, 2000	Reported in a secondary source, limited study details provided.
		Administration of milk of magnesia twice a day for 3-4 days caused damage to corneal epithelium of rabbit eyes;	HSDB, 2003	Reported in a secondary source, limited study details provided. Milk of magnesia is a mixture containing

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		however, effects disappeared within 2-3 days.		magnesium hydroxide and inactive ingredients.
Dermal Irritation		**LOW: An experimental study indicates that magnesium hydroxide is not an irritant to rabbit skin.**		
	Dermal Irritation	Moderate potential for dermal irritation based on experimental aqueous pH values. (Estimated)	Expert judgment	Estimated based on expert judgment.
		Not corrosive in an *in vitro* human skin corrosion test.	ECHA, 2013	Reported in a secondary source. Study conducted according to OECD guideline 431.
		Not irritating in an *in vitro* skin irritation test.	ECHA, 2013	Reported in a secondary source. *In vitro* skin irritation: reconstructed human epidermis model test.
		Not irritating, rabbits.	Submitted confidential study	Reported in a submitted confidential study.
Endocrine Activity		**No data located.**		
				No data located.
Immunotoxicity		**Magnesium hydroxide is expected to have low potential for immunotoxicity based on expert judgment.**		
	Immune System Effects	Low potential for immunotoxicity. (Estimated)	Expert judgment	Estimated based on expert judgment.
ECOTOXICITY				
ECOSAR Class		Not applicable		
Acute Aquatic Toxicity		**LOW: Estimated LC_{50} values for all of the standard toxicity test organisms are greater than 100 mg/L. Experimental LC_{50} values are much greater than the anticipated water solubility, suggesting no effects at saturation (NES).**		
Fish LC_{50}		96-hour LC_{50} = $MgCl_2$: 2,120 mg/L $MgSO_4$: 2,820 mg/L (Estimated)	Mount et al., 1997	Estimated based on analogy to $MgCl_2$ and $MgSO_4$; expected to display NES because this amount of test substance is not anticipated to dissolve in water at a concentration at which adverse effects may be expressed.

Magnesium Hydroxide CASRN 1309-42-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Pimephalis promelas 96-hour LC_{50} = 511 mg/L; static conditions. (Experimental)	ECHA, 2013	Reported in a secondary source. Test material diluted to 61% in aqueous suspension.
	Onchorinchus mykiss 96-hour LC_{50} = 775.8 mg/L; static conditions. (Experimental)	ECHA, 2013	Reported in a secondary source. Test material diluted to 61% in aqueous suspension.
Daphnid LC_{50}	*Daphnia magna* 48-hour LC_{50} = $MgCl_2$: 1,330 mg/L $MgSO_4$: 1,820 mg/L (Estimated)	Biesinger and Christensen, 1972; Mount et al., 1997	Estimated based on analogy to $MgCl_2$ and $MgSO_4$; expected to display NES because this amount of test substance is not anticipated to dissolve in water at a concentration at which adverse effects may be expressed.
	Daphnia magna 48-hour LC_{50} = 284.76 mg/L; static conditions. (Experimental)	ECHA, 2013	Reported in a secondary source. Test material diluted to 61% in aqueous suspension.
	Gammarus lacustris LC_{50} = 64.7 mg/L. (Experimental)	O'Connell et al., 2004	Reported in a secondary source, study details and test conditions were not provided. Not a standard test species.
Green Algae EC_{50}	*Scenedesmus subspicatus* and *Selenastrum capricornutum* 72-hour EC_{50} >100 mg/L (for growth and biomass). (Experimental)	ECHA, 2013	Reported in a secondary source.
Chronic Aquatic Toxicity	**LOW: Estimated chronic values (ChV) are all >10 mg/L and exceed the anticipated water solubility, suggesting NES.**		
Fish ChV	Fish ChV: 50-80 mg/L (Experimental)	ECHA, 2013	An acute to chronic ratio of 10 was applied to experimental acute data for *Pimephalis promelas* and *Onchorinchus mykiss*. Reported in a secondary source. Test material diluted to 61% in aqueous suspension.
	Freshwater fish ChV = 403 mg/L.	Professional judgment	Estimated using an acute to chronic

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(Estimated)		ratio of 3:3; expected to display NES because this amount of test substance is not anticipated to dissolve in water at a concentration at which adverse effects may be expressed.
Daphnid ChV		Daphnia ChV = 82 mg/L (Estimated)	Suter, 1996	Estimated based on analogy to the measured ChV for Mg^{2+} ion; based on tests that were not standard but were judged to be of good quality; expected to display NES because this amount of test substance is not anticipated to dissolve in water at a concentration at which adverse effects may be expressed.
Green Algae ChV		Green algae NOEC: 980 mg/L LOEC: 1,230 mg/L (Estimated)	ECOTOX, 2012	Estimated based on analogy to $MgSO_4$; expected to display NES because this amount of test substance is not anticipated to dissolve in water at a concentration at which adverse effects may be expressed.
ENVIRONMENTAL FATE				
Transport		**The low water solubility, the estimated vapor pressure of <1x10^{-8} mm Hg, estimated K_{OC} of >30,000 and estimated Henry's Law constant of <1x10^{-8} atm-m^3/mole indicate that magnesium hydroxide will be relatively immobile in the environment. Magnesium hydroxide is a mineral occurring naturally in the environment.**		
	Henry's Law Constant (atm-m^3/mole)	<10^{-8} (Estimated)	Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	>30,000 (Estimated)	EPA, 2004; Professional judgment	Cutoff value for nonmobile compounds.
	Level III Fugacity Model			Not all input parameters for this model were available to run the estimation software (EPI).

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: As an inorganic compound, magnesium hydroxide is not expected to biodegrade, oxidize in air, or undergo hydrolysis under environmental conditions. Magnesium hydroxide does not absorb light at environmentally relevant wavelengths and is not expected to photolyze. Magnesium hydroxide is recalcitrant and it is expected to be found in the environment >180 days after release. As a naturally occurring compound, it may participate in natural cycles and form complexes in environmental waters.**		
Water	**Aerobic Biodegradation**	Recalcitrant (Estimated)	Professional judgment	Substance is or contains inorganic elements, such as metal ions or oxides, that are expected to be found in the environment >180 days after release.
	Volatilization Half-life for Model River	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**	Recalcitrant (Estimated)	Professional judgment	This inorganic compound is not amenable to available estimation methods.
	Anaerobic Biodegradation	Recalcitrant (Estimated)	Professional judgment	This inorganic compound is not amenable to available estimation methods.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	>1 year (Estimated)	Professional judgment	Substance does not contain functional groups amenable to atmospheric degradation processes.
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Professional judgment	Magnesium hydroxide does not absorb UV light at environmentally relevant wavelengths and is not expected to undergo photolysis.
	Hydrolysis	Not a significant fate process (Estimated)	Professional judgment	Substance does not contain functional groups amenable to hydrolysis.

Magnesium Hydroxide CASRN 1309-42-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Environmental Half-life				Not all input parameters for this model were available to run the estimation software (EPI).
Bioaccumulation		**LOW: Magnesium hydroxide is not expected to bioaccumulate based on professional judgment.**		
	Fish BCF	<100 (Estimated)	Professional judgment	This inorganic compound is not amenable to available estimation methods.
	Other BCF			No data located.
	BAF	<100 (Estimated)	Professional judgment	This inorganic compound is not amenable to available estimation methods.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Magnesium hydroxide is a mineral that occurs naturally in the environment (HSDB, 2003).		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2013).		

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Melamine Polyphosphate

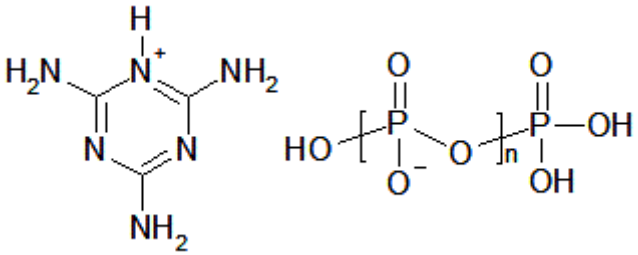
VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[¥] Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical	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
Melamine Polyphosphate[1¥]	15541-60-3	L	*M*	*M*	*H*	*M*	*M*	*M*	*L*		L	VL	L	L	*H*	*L*

[1]Hazard designations are based upon the component of the salt with the highest hazard designation, including the corresponding free acid or base.

Melamine Polyphosphate



CASRN: 15541-60-3

MW: >1,000

MF: $C_3H_6N_6 \cdot (H_3PO_4)_n$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: n(c(nc(n1)N)N)c1N(H)(H)OP(=O)(O)OP(=O)(O)O (n =1) SMILES for the representative structure was created using the methodology described in the EPI help file.

Synonyms: Diphosphoric acid, compound with 1,3,5-triazine-2,4,6-triamine; Polyphosphoric acids, compounds with melamine.

The CASRN for the compound melamine pyrophosphate is 15541-60-3. The CASRN 218768-84-4 is associated with the product Melapur 200, not the chemical melamine polyphosphate.

Chemical Considerations: This alternative contains a polymeric moiety. Although the chain length of the polyphosphoric acid is not specified, the smaller, water-soluble polyphosphate ions were used in assessment (generally as the diphosphate ion, n=1). Melamine polyphosphate will freely dissociate under environmental conditions based on professional judgment. Measured values from studies on the dissociated components were used to supplement data gaps as appropriate and EPI v 4.10 was used to estimate physical/chemical and environmental fate values in the absence of experimental data. Measured values from experimental studies were incorporated into the estimations.

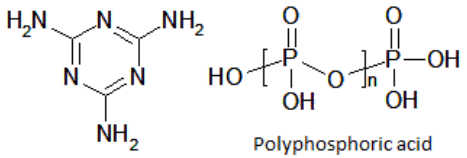
Polymeric: Yes
Oligomeric: Melamine polyphosphate is a complex mixture consisting of melamine and polyphosphate chains of varying length.

Metabolites, Degradates and Transformation Products: Melamine (CASRN 108-78-1)

Analog: Confidential structurally similar polymers; Polyphosphoric acid (CASRN 8017-16-1) and melamine (CASRN 108-78-1) are the dissociated components of this salt

Endpoint(s) using analog values: Reproductive effects, neurotoxicity, immunotoxicity

Analog Structure:



Melamine
(CASRN 108-78-1)

Polyphosphoric acid
(CASRN 8017-16-1)

Structural Alerts: Aromatic amine, genetic toxicity (EPA, 2012).
Risk Phrases: Not classified by Annex I Directive 67/548/European Economic Community (EEC) & IUCLID (Pakalin et al., 2007).
Hazard and Risk Assessments: Australian Safety and Compensation Council National Industrial Chemicals Notification and Assessment Scheme (NICNAS), October 30, 2006 (Australia, 2006).

Melamine Polyphosphate CASRN 15541-60-3			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	>400 (Measured)	Submitted confidential study	Adequate; value for the melamine polyphosphate salt.
	>400 (Measured)	Australia, 2006	Adequate; value for the melamine polyphosphate salt.
Boiling Point (°C)	>300 (Estimated)	EPI v4.10; Professional judgment	As an organic salt, it is expected to decompose before boiling.
	225 Decomposes Reported for activated melamine pyrophosphate (CASRN 15541-60-3) (Measured)	New Line Safety, 2011	No study details reported in an MSDS.
Vapor Pressure (mm Hg)	$<10^{-8}$ (Estimated)	EPI v4.10; Boethling and Nabholz, 1997	Cutoff value for nonvolatile compounds.
Water Solubility (mg/L)	20,000 (Measured)	Submitted confidential study	Adequate; value for the melamine polyphosphate salt.
	20,000 (Measured)	Australia, 2006	Adequate.
Log K_{ow}	<-2 (Estimated)	EPI v4.10	Cutoff value for highly water soluble substances.
Flammability (Flash Point)	Not highly flammable (Measured)	Submitted confidential study	Reported in a secondary source and based on its use as a flame retardant.
Explosivity	Not a potential explosive (Measured)	Australia, 2006	Adequate.
	Not a potential explosive (Measured)	Submitted confidential study	Adequate.
Pyrolysis	May produce carbon monoxide, ammonia, oxides of nitrogen, and oxides of phosphorus by thermal decomposition. Reported for activated melamine pyrophosphate (CASRN 15541-60-3). (Estimated)	New Line Safety, 2011	No study details reported in an MSDS.
pH	7 Reported for activated melamine pyrophosphate (CASRN 15541-60-3) (Measured)	New Line Safety, 2011	No study details reported in an MSDS.

Melamine Polyphosphate CASRN 15541-60-3			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
pK_a	**Pyrophosphoric Acid:** pK_{a1} = 0.85 pK_{a2} = 1.96 pK_{a3} = 6.78 pK_{a4} = 10.39 (Estimated)	ECHA, 2014	Reported for pyrophosphoric acid (CASRN 2466-09-3); study reported in a secondary source.
	Melamine: pK_{b1}= 7.3; pK_{b2}= 11.4 according to OECD 112 (Measured)	ECHA, 2013	Guideline study reported for melamine in a secondary source.
	Melamine: pK_{b1} = 9 There are several amino groups that result in basic properties. pK_{b1} = 9 pK_{b2} = 14 K_{b1}= $1.1x10^{-9}$ K_{b2} = $1.0x10^{-14}$ at 25°C (Measured)	Baynes et al., 2008	Reported from a nonguideline study for melamine.
	Melamine: pK_{b1} = 9 pK_{b2} = 14 K_{b1}= $1.1x10^{-9}$ K_{b2} = $1.0x10^{-14}$ at 25°C (Measured)	Crews et al., 2006	For melamine; study details were not available.
	Melamine: Considered a weak base Neutral at pH values of 6 to 13; Cation formation at the triazine ring nitrogen at pH values of 1 to 4 (Measured)	OECD SIDS, 1998	Supporting information provided in a secondary source for melamine.
	Melamine: 5 (Measured)	HSDB, 2008; Weber, 1970	Reported in a secondary source for melamine, value is assumed to be the pK_b.
Particle Size			No data located.
HUMAN HEALTH EFFECTS			

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Toxicokinetics		**No toxicokinetic data were located for melamine polyphosphate or polyphosphoric acid; limited data for melamine indicate that melamine was rapidly absorbed, distributed to body fluids, cleared from plasma and excreted mainly via urine in monkeys. In rats, melamine was distributed to the stomach, small intestine, cecum, and large intestine, and found in blood and urine. Following a single oral exposure to pregnant rats, melamine was detected in the maternal serum, breast milk, whole foetus, amniotic fluid, neonatal serum and neonatal kidney. There is evidence that Melamine passed through the placenta, reached the fetus and accumulated in the lactating mammary gland. Excretion occurred through the placenta of the fetus and the kidneys of neonates and was later excreted into amniotic fluid. Melamine was transferred quickly to fetal circulation in studies where placentas from mothers following caesarean section or normal delivery were perfused with melamine. Melamine was readily cleared by the kidney in pigs administered melamine intravenously; distribution may be limited to the extracellular fluid compartment. There was no concern for binding in tissues. The half-life was reported as 4.04 hours. In monkeys, the half-life in plasma was ~4.41 hours. Other data for the melamine indicate an elimination phase half-life of 2.7 hours from plasma and 3 hours for urine.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	**Melamine:** Distributed to stomach, small intestine, cecum, and large intestine, and found in blood, and urine of rats.	ECHA, 2011b	Study details reported in a secondary source.
		Melamine: The elimination phase half-life calculated from plasma data was 2.7 hours, and the urinary half-life was 3.0 hours. The renal clearance was determined to be 2.5 mL/minute. (Measured)	Mast et al., 1983	For melamine; adequate, nonguideline study.
		Melamine polyphosphate: Low for all routes (Estimated)	Professional judgment	Estimates based on physical/chemical properties.
		Rhesus monkeys were orally administered melamine at a single dose of 1.4 mg/kg bw. Melamine was rapidly absorbed, distributed to body fluids, rapidly cleared from plasma and excreted mainly via urine. The half-life in plasma was ~4.41 hours. There was no correlation (concentration-time curve in plasma and urine) between melamine and	Liu et al., 2010	Adequate, primary source

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		cyanuric acid, suggesting that melamine may not be metabolized to cyanuric acid *in vivo*.		
		Pregnant Sprague-Dawley rats were administered a single oral dose of melamine (~6-7 mg in <2 ml water) on gestation day 17. Melamine was also administered to neonates at postnatal day 14 (~0.3-0.6 mg in <0.2 ml in water). Melamine was detected in the maternal serum, breast milk, whole foetus, amniotic fluid, neonatal serum and neonatal kidney. This is evidence that Melamine passed through the placenta, reached the fetus and accumulated in the lactating mammary gland. Excretion occurred through the placenta of the fetus and the kidneys of neonates and was later excreted into amniotic fluid.	Chu et al., 2010	Adequate primary source
	Other	Pigs (5 weanling) were administered Melamine intravenously at a dose of 6.13 mg/kg. Melamine is readily cleared by the kidney; distribution may be limited to the extracellular fluid compartment. No concern for binding in tissues. Half-life: 4.04 hours; clearance: 0.11 L/h/kg; volume distribution: 0.61 L/kg.	Baynes et al., 2008	Adequate primary source
		Placentas from mothers following caesarean section or normal delivery were perfused with 0 mM or 1 mM melamine, or 10 mM melamine with 10 nM cyanuric acid (CYA). Melamine (34-45%) was transferred quickly to fetal circulation (0.12-1.34% within 5 minutes, 34% within 4 hours); addition of CYA had no	Partanen et al., 2012	Adequate, primary study

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		effect. Functionality of the placental tissue was not affected. Viability of BeWo cells was decreased. It is concluded that melamine may be fetotoxic.		
Acute Mammalian Toxicity		**LOW: Melamine polyphosphate is expected to be of low hazard for acute toxicity based on experimental evidence for melamine polyphosphate, phosphoric acids and melamine with LD50s > 1,000 mg/kg following oral and dermal exposure. One inhalation study reported an LC_{50} of 3.25 mg/L; however, the reported study details were too limited to consider for the hazard designation.**		
Acute Lethality	**Oral**	**Melamine polyphosphate:** Rat (Gavage) LD_{50} >2,000 mg/kg	Ciba, 2005 (as cited in Australia, 2006)	Sufficient study details reported.
		Melamine polyphosphate: Rat LD_{50} >2,000 mg/kg	NOTOX BV, 1998 (as cited in Australia, 2006)	Limited study details reported.
		Melamine polyphosphate: Rat (Gavage) LD_{50} >2,000 mg/kg	Submitted confidential study	Study details reported in a confidential study.
		Melamine polyphosphate: Rat LD_{50} >2,000 mg/kg	Submitted confidential study	Limited study details reported in a confidential study.
		Polyphosphoric acid: LD_{50} = 4,000 mg/kg (species unknown)	ARZNAD, 1957	Limited study details reported. The test substance was identified as polyphosphates, and was described as containing 1/3 Kurrol's potassium salt and 2/3 pyrophosphate.
		Melamine: Rat LD_{50} = 3,161 mg/kg (male), 3,828 mg/kg (females)	NTP, 1983b; Melnick et al., 1984	Sufficient study details reported.
		Melamine: Mouse LD_{50} = 3,296 mg/kg (male), 7,014 mg/kg (female)	NTP, 1983b; Melnick et al., 1984	Sufficient study details reported.
		Melamine: Mouse LD_{50} = 4,550 mg/kg	American Cyanamid Company, 1955; May, 1979; Trochimowicz et al., 2001	Limited study details reported.
		Melamine: Rat LD_{50} = 3,160 mg/kg (male) and 3,850 mg/kg (female)	Trochimowicz et al., 2001	Limited study details reported.
		Melamine: Rat LD_{50} >6,400 mg/kg	BASF, 1969 (as cited in OECD SIDS, 1999; IUCLID, 2000a)	Limited study details reported.

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: LD_{50} ≈ 4,800 mg/kg	Hoechst, 1963 (as cited in IUCLID, 2000a)	Limited study details reported.
	Dermal	**Melamine:** Rabbit LD_{50} >1,000 mg/L	Unknown, 1990	Limited study details reported.
	Inhalation	**Melamine:** Rat LC_{50} = 3.25 mg/L	Ubaidullajev, 1993 (as cited in IUCLID, 2000a)	Limited study details reported in a secondary source.
Carcinogenicity		**MODERATE: Estimated based on the dissolution product melamine. There is experimental evidence that oral melamine exposure to high doses of melamine causes carcinogenicity in animals. However, there is no evidence for carcinogenicity to humans. In addition, Oncologic estimated a marginal concern that is consistent with a Moderate hazard designation using DfE criteria. Tumor formation in animals appeared to be due to mechanical irritation by bladder calculi/stones. IARC classifies melamine as Group 3: *not classifiable as to its carcinogenicity to humans*.**		
	OncoLogic Results	**Melamine:** Marginal (Estimated)	OncoLogic, 2008	
	Carcinogenicity (Rat and Mouse)	**Melamine:** Group 3: melamine is not classifiable as to its carcinogenicity to humans; there is inadequate evidence in humans for the carcinogenicity of melamine, and there is sufficient evidence in experimental animals for the carcinogenicity of melamine under conditions in which it produces bladder calculi.	IARC, 1999	IARC classification statement.
		Melamine: Significant formation of transitional cell carcinomas in the urinary bladder of male rats and significant chronic inflammation in the kidney of dosed female rats were observed. Carcinoma formation was significantly correlated with the incidence of bladder stones. A transitional-cell papilloma was observed in the urinary bladder of a single high dose male rat, and compound related lesions were observed in the urinary tract of dosed animals.	NTP, 1983b; Huff, 1984; Melnick et al., 1984	Sufficient study details reported.
		Melamine: Increased incidence of acute and chronic inflammation and epithelial	NTP, 1983b; Huff, 1984; Melnick et al., 1984	Sufficient study details reported.

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		hyperplasia of the urinary bladder was observed in male mice. Bladder stones and compound-related lesions were observed in the urinary tract of test animals. Melamine was not considered carcinogenic.		
		Melamine: Melamine-induced proliferative lesions of the rat urinary tract were directly due to the irritant stimulation of calculi, and not to molecular interactions between melamine or its metabolites with the bladder epithelium.	Okumura et al., 1992	Sufficient study details reported.
		Melamine: Water intake, used as an index of urinary output, was increased by NaCl treatment. Calculus formation resulting from melamine administration was suppressed dose-dependently by the simultaneous NaCl treatment. The main constituents of calculi were melamine and uric acid (total contents 61.1- 81.2%). The results indicate that melamine-induced proliferative lesions of the urinary tract of rats were directly due to the irritation stimulation of calculi, and not molecular interactions between melamine itself or its metabolites with the bladder epithelium.	Ogasawara et al., 1995	Sufficient study details reported.
		Melamine: As an initiator, melamine caused no significant increase in papillomas per mouse when compared to controls.	Perrella and Boutwell, 1983	Nonguideline study.
		Melamine: Diffuse papillary hyperplasia of the bladder epithelium and bladder calculi were observed in all melamine treated rats. Elevated	Matsui-Yuasi et al., 1992	Nonguideline study.

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		spermidine/spermine N1-acetyltransferase activity following melamine treatment was considered to be an indicator of cell proliferation.		
		Melamine: Decreased antitumor activity was correlated with increasing demethylation; melamine was considered inactive as an antitumor drug.	Rutty and Connors, 1977	Limited study details reported.
		Melamine: In an *in vitro* cytotoxicity study in cultured ADJ/PC6 plasmacytoma ascites tumor cells, the ID50 was 470 µg/mL after 72 hours of treatment.	Rutty and Abel, 1980	Limited study details reported.
	Combined Chronic Toxicity/Carcinogenicity	**Melamine:** No effects were observed in rats fed 1,000 ppm of melamine. 4 of the 10 rats fed 10,000 ppm melamine had bladder stones associated with the development of benign papillomas.	Anonymous, 1958 (as cited in Wolkowski Tyl and Reel, 1992)	Limited study details reported.
		Melamine: Increased incidence of urinary bladder stones (6/20 rats) was noted in the 10,000 ppm dose group, and was associated with an increase in benign papillomata. The NOAEL was determined to be 1,000 ppm (67 mg/kg-day).	American Cyanamid Company, 1955	Limited study details reported.
	Other			No data located.
Genotoxicity		**MODERATE: Melamine polyphosphate is estimated to be a moderate hazard for genotoxicity based on a weight of evidence from multiple studies for melamine. For melamine, positive results were observed for *in vivo* chromosome aberration and sister chromatid exchange assays conducted by National Toxicology Program (NTP) in 1988 and 1989. Available in vitro genotoxicity testing was conducted with metabolic activation systems from the liver. NTP suggests this may not account for potential activation from bladder epithelial cells, which is the target organ. Proposed genotoxicity testing using a metabolic activation system from bladder epithelial cells (NTP, 1983) was never conducted (Personal Communication, 2007; 2008).**		
	Gene Mutation *in vitro*	**Melamine:** Bacterial forward mutation assay: Negative with and without liver activation	Haworth et al., 1983; NTP, 1983a	Sufficient study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: Bacterial forward mutation assay: Negative	Seiler, 1973	Limited study details reported.
		Melamine: Bacterial reverse mutation assay: Negative with and without liver activation	Lusby et al., 1979	Limited study details reported.
		Melamine: Bacterial reverse mutation assay: Negative with and without unspecified metabolic activation	Mast et al., 1982b	Limited study details reported.
		Melamine: *In vitro* mouse lymphoma test: Negative with and without liver activation	NTP, 1983a; McGregor et al., 1988	Sufficient study details reported.
		Melamine: Chinese hamster ovary (CHO) cells/hypoxanthine-guanine phosphoribosyl-transferase forward mutation assay: Negative with and without liver activation.	Mast et al., 1982b	Limited study details reported.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	**Melamine:** *In vitro* chromosomal aberrations test: Negative in CHO with and without liver activation.	NTP, 1983a; Galloway et al., 1987	Sufficient study details reported.
		Melamine: *In vitro* sister chromatid exchange assay: Negative in CHO with and without liver activation.	NTP, 1983a; Galloway et al., 1987	Sufficient study details reported
		Melamine: *In vitro* sister chromatid exchange assay: Negative in CHO with and without liver activation.	Mast et al., 1982b	Limited study details reported.
	Chromosomal Aberrations *in vivo*	**Melamine:** *In vivo* mouse micronucleus test: The initial test gave a positive trend (P = 0.003) for chromosomal damage; however, both peripheral blood smears and the repeat bone marrow test were negative. The overall conclusion was that melamine does not induce chromosomal damage.	NTP, 1983b; Shelby et al., 1993	Sufficient study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: *In vivo* mouse micronucleus test: Negative	Mast et al., 1982c	Limited study details reported.
		Melamine: *In vivo* chromosome aberrations test in mice: Positive	NTP, 1983a	Sufficient study details reported.
		Melamine: *In vivo* sister chromatid exchange assay in mice: Positive	NTP, 1983a	Sufficient study details reported.
	DNA Damage and Repair	**Melamine:** *In vivo* and *in vitro* unscheduled DNA synthesis (UDS) test: None of the tested chemicals, including melamine, were genotoxic hepatocarcinogens in the *in vivo* assay, and melamine was negative for UDS in the *in vitro* assay.	Mirsalis et al., 1983	Limited study details reported.
		Melamine: SOS/*umu* test: Negative for its ability to result in DNA damage and induce the expression of the *umu* operon.	Reifferscheid and Heil, 1996	Nonguideline study.
		Melamine: DNA synthesis-inhibition test in Hela S3 cells: Inhibits DNA synthesis by 50% at greater than 300 µM.	Heil and Reifferscheid, 1992	Limited study details reported.
	Other	**Melamine:** Sex-linked recessive lethal/reciprocal translocation: Results were considered equivocal based on 0.18% and 0.36% total lethal following oral and injection exposure, respectively, compared to control total lethal of 0.07% for oral and 0.09% for injection.	NTP, 1983a	Sufficient study details reported.
		Melamine: *Drosophila* Muller-5 test: Negative for mutagenicity	Rohrborn, 1959	Limited study details reported.
		Melamine: *Drosophila melanogaster* Sex-linked recessive lethal: No mutagenic effects were observed	Luers and Rohrborn, 1963	Limited study details reported.
		Melamine: *In vitro* flow cytometric DNA repair assay: Negative for genotoxic effects	Seldon et al., 1994	Nonguideline study.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: Microscreen assay: Positive for genetic toxicity in *E. coli* WP2 cells	Rossman et al., 1991	Nonguideline study.
		Melamine: Growth and genotoxic effects to bacteria (*Salmonella typhimurium*) and yeast (*Saccharomyces cerevisiae*): Non-mutagenic in *S. typhimurium* with or without S-9 mix. The growth of eight out of nine strains tested was delayed by 10 mM melamine during 24 hour cultivation. *S. cerevisiae* strain was tested, and did not recover its growth following 48 hour cultivation.	Ishiwata et al., 1991	Limited study details reported.
		Proposed genotoxicity testing using a metabolic activation system from bladder epithelial cells (NTP, 1983) was never conducted.	Lehner and Vokes, 2008; Shigeru, 2007	Supporting information.
Reproductive Effects		**HIGH: Estimated based on experimental data for melamine. A NOAEL of 10 mg/kg-day (LOAEL of 50 mg/kg-day) for increased apoptotic index of spermatogenic cells was reported in male mice orally administered melamine for 5 days. In addition, altered epididymal sperm morphology and damage of testicular DNA were reported at a dietary dose of 412 mg/kg-day (lowest dose tested). No experimental data were located for melamine polyphosphate.**		
	Reproduction/Developmental Toxicity Screen	Rat, oral; potential for reproductive toxicity (Estimated by analogy)	Professional judgment	Estimated based on analogy to confidential analog; LOAEL not identified; study details not provided.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	**Melamine:** In a 5-day study, male mice (8/group) were orally administered melamine only at doses of 0, 2, 10 and 50 mg/kg-day or melamine in combination with cyanuric acid at doses of 0, 1, 5 and 25 mg/kg-day. Sperm abnormalities were evaluated in a	Yin et al., 2013	Adequate, primary study

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		separate select group of mice (8/group), which were fed melamine only at doses of 0, 412, 824, and 1,648 mg/kg-day, or melamine in combination with cyanuric acid at doses of 0, 206, 412, or 824 mg/kg-day. No deaths in mice fed 2, 10 and 50 mg/kg-day melamine or 1 and 5 mg/kg-day melamine and cyanuric acid; 3 deaths in co-administration group fed 25 mg/kg/day. Grossly enlarged, pale yellow kidneys in all mice that survived. Increase in apoptotic index of spermatogenic cells in mice fed 50 mg/kg-day melamine-only; more severe apoptosis in co-administered mice at 5 and 25 mg/kg-day. NOAEL: 10 mg/kg-day LOAEL: 50 mg/kg-day (increased apoptotic index of spermatogenic cells) Sperm abnormality group: no deaths in mice administered melamine-only; all co-administered mice died before day 6 and exhibited anorexia, decreased activity and hunched posture. Altered epididymal sperm morphology (particularly the head abnormality) and damage of testicular DNA in all melamine-only treatment groups. NOAEL: Not established LOAEL: 412 mg/kg-day (altered epididymal sperm morphology; damage of testicular DNA)		

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: There were no treatment-related macroscopic or microscopic effects on mammary glands, ovaries, prostate, seminal vesicles, testes and uterus in rats and mice up to dietary concentrations of 18,000 ppm in a 13-week study.	Melnick et al., 1984 (as cited in OECD SIDS, 1999)	Limited study details reported in a secondary source.
		Melamine: Reproductive dysfunction was observed at 0.5 mg/m^3 and included effects on spermatogenesis (genetic material, sperm morphology, motility, and count), effects on the embryo/fetus (fetal death), pre-implantation mortality (reduction in the number of implants per female), and total number of implants per corpora lutea.	Ubaidullajev, 1993	Study details, if present, were not translated into English.
	Other			No data located.
Developmental Effects		**MODERATE: Estimated based on a structural alert for aromatic amines. Limited experimental data for melamine indicated no developmental effects in rats exposed during gestation to doses up to 1,060 mg/kg-day. This experimental data is insufficient to determine a hazard designation for this endpoint. There was no data located for the developmental neurotoxicity endpoint for this substance or its analogs.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Prenatal Development	**Melamine:** Signs of maternal toxicity at 136 mg/kg b.w. included decreased body weight and feed consumption, hematuria (23/25 rats), indrawn flanks (7/25 rats), and piloerection (1/25 rats). No adverse effects on gestational parameters and no signs of developmental toxicity were noted. NOAEL ≥ 1,060 mg/kg-day (highest concentration tested); LOAEL: Not established	Hellwig et al., 1996 (as cited in OECD SIDS, 1999)	Sufficient study details reported.
	Postnatal Development	**Melamine:** Only minor effects on the fetuses or litters, including a non-significant increase in resorptions in the group treated on the 4th and 5th days of gestation, were observed.	Thiersch, 1957	Sufficient study details were not available.
	Prenatal and Postnatal Development			No data located.
	Developmental Neurotoxicity	There was no data located for the developmental neurotoxicity endpoint.		No data located.
	Other	Potential for developmental toxicity based on a structural alert for aromatic amines. (Estimated)	Professional judgment	Estimated based on a structural alert for aromatic amines and professional judgment.
Neurotoxicity		**MODERATE: Estimated based on experimental data for melamine. Several neurological effects were reported for different endpoints in 28-day studies evaluating mode of action in the brain. Impaired memory abilities and cognition deficits were mediated by alterations of the pathways affecting the hippocampus at a dose of 300 mg/kg-day (only dose tested). Design for the Environment (DfE) Alternatives Assessment criteria values are tripled for chemicals evaluated in 28-day studies; the LOAEL of 300 mg/kg-day falls on the threshold between Moderate and LOW hazard criteria. A NOAEL was not established and it is assumed that effects would occur at a dose within the Moderate-High hazard criteria range; due to this uncertainty, a Moderate hazard designation was assigned.**		
	Neurotoxicity Screening Battery			
		Melamine: In a 28-day study, male	An et al. 2011	Sufficient study details reported in

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	(Adult)	Wistar rats (control group n = 8, treatment group n = 10) were orally administered melamine only at doses of 0, or 300 mg/kg-day. A significant deficit of learning and memory in a Morris water maze test was reported in the treated group. In addition significantly lower field excitatory postsynaptic potential (fEPSPs) slopes were determined in a long term potentiation (LTP) test from Schaffer collaterals to CA1 region in the hippocampus in the treated group compared to the control group. Authors concluded that melamine had a toxic effect on hippocampus resulting in deficits of learning and memory in rats associated with impairments of synaptic plasticity. NOAEL: Not established LOAEL: 300 mg/kg-day		primary source; only one dose tested.
		Melamine: In a 28-day study, male Wistar rats (10/group) were orally administered melamine only at doses of 0, or 300 mg/kg-day. A significant deficit of learning and memory in a Morris water maze test was reported in the treated group. In addition significantly lower field excitatory postsynaptic potential (fEPSPs) slopes were determined in a long term potentiation (LTP) test in the treated group compared to the control group. Decreased frequencies of spontaneous EPSCs and minitura EPSCs were observed in a long-time potentiation test,	Yang et al., 2011	Sufficient study details reported in primary source; only one dose tested.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		though there was no change in the amplitude or kinetics of spontaneous or minitura EPSCs suggesting melamine's influence on glutamatergic transmission likely occurred presynaptic. NOAEL: Not established LOAEL: 300 mg/kg-day		
		Melamine: In a 28-day study, male Wistar rats (8/group) were orally administered melamine only at doses of 0, or 300 mg/kg-day. A significant deficit of learning and memory in a Morris water maze test was reported in the treated group. Increased levels of superoxide anion radical, hydroxyl free radical and malonaldehyde were reported. There was also decreased superoxide dismutase and glutathione peroxidase activity in the treated group compared to the control. Hippocampal energy metabolism analysis showed significantly decreased adenosine-triphosphate (ATP) content suggestive of reduced energy synthesis in the hippocampal neurocytes possibly associated with oxidative damage. NOAEL = Not established LOAEL = 300 mg/kg-day	An et al., 2012	Sufficient study details reported in primary source; only one dose tested.
		Melamine: In a 28-day study, male Wistar rats (8/group) were orally administered melamine only at doses of 0, or 300 mg/kg-day.	An et al., 2013	Sufficient study details reported in primary source; only one dose tested.

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		A significant deficit of learning and memory in a Morris water maze test was reported in the treated group. Increased field excitatory postsynaptic potential slopes was reported in the treated group. There was decreased Ach levels and increased AChE activity suggesting damage to the function of cholinergic system. NOAEL = Not established LOAEL = 300 mg/kg-day		
		Melamine: In a 28-day study, male Wistar rats (8/group) were orally administered melamine only at doses of 0, or 300 mg/kg-day. Impaired memory abilities were reported in treated rats in the Morris water maze tests compared to the control group. Cognition deficits consistent with reduced long-term potentiation in the CA1 area of the hippocampus were induced. Phase locking values showed reduced synchronization between CA3 and CA1 in theta and LG rhythms. Decreased unidirectional indices for theta and LG rhythms were reported in treated rats suggesting that alterations of neural information flow on CA3-CA1 pathway in the hippocampus mediated cognitive impairment in treated rats. NOAEL = Not established LOAEL = 300 mg/kg-day	Xu et al., 2013	Sufficient study details reported in primary source; only one dose tested.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	Potential for neurotoxicity is expected to be low. (Estimated)	Professional judgment	Estimated based on analogy and professional judgment.
Repeated Dose Effects		**MODERATE: Melamine polyphosphate is expected to be a moderate hazard for repeated dose effects based on the data for melamine. Stones and diffuse epithelial hyperplasia in the urinary bladders were observed in male rats at doses as low as 700 ppm (72 mg/kg-day; lowest dose tested). Exposure to melamine has been associated with toxicity in humans.**		
		Polyphosphoric Acid: Rat Repeated-Dose Toxicity Study: An oral repeated-dose toxicity test in rats resulted in a TD_{Lo} of 450 mg/kg. The test substance was identified as polyphosphates, and was described as containing 1/3 Kurrol's potassium salt and 2/3 pyrophosphate. Toxic effects included changes in liver weight, changes in tubules (including acute renal failure, acute tubular necrosis), and weight loss or decreased weight gain.	ARZNAD, 1957	Sufficient study details were not available.
		Melamine: Rat 28-day dietary toxicity study: Clinical signs included a dose-related increase in pilo-erection, lethargy, bloody urine spots in the cage and on the pelage of animals, and chromodacryorrhea. The incidence of urinary bladder calculi and urinary bladder hyperplasia in treated animals was dose-dependent, with a significant relationship between the calculi and hyperplasia. Calculi composition indicated the presence of an organic matrix containing melamine, phosphorus, sulfur, potassium, and chloride. Crystals of dimelamine monophosphate were identified in the urine.	RTI, 1983	Sufficient study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL: estimated to be 2,000 ppm (240 mg/kg/day), excluding the observed increase in water consumption and the incidence of crystalluria. LOAEL: 4,000 ppm (475 mg/kg/day) based on the formation of calculi.		
		Melamine: Rabbit and dog 28-day dietary toxicity study: No significant rise in the body temperature of rabbits was noted. Gross histological examination of the heart, lung, liver, spleen, thyroid, pancreas, intestines, kidneys and bladder did not show pathological changes. A zone of fat was found in the inner part of the renal cortex in two dogs, but also in the kidneys of 3 control dogs.	Lipschitz and Stokey, 1945	Sufficient study details were not available.
		Melamine: Rat 28-day dietary toxicity study: Incidence and size of bladder stones were directly related to the amount of substance administered. The larger stones were found to be unchanged melamine in a matrix of protein, uric acid and phosphate. Lowest effective dose: 1,500 ppm (~125 mg/kg-day) in males	American Cyanamid Company, 1984	Sufficient study details were not available.
		Melamine: Rat 90-day dietary toxicity study: one male rat receiving 18,000 ppm and two males receiving 6,000 ppm died. Mean body weight gain and feed consumption were reduced. Stones and diffuse epithelial hyperplasia in the urinary bladders were observed in male rats of all treatment groups. Focal epithelial hyperplasia was observed in	NTP, 1983b; Melnick et al., 1984; ECHA, 2011a	Sufficient study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		only 1 male. A second and third 13-week repeated dose toxicity study was conducted in rats at a dose range of 750 to 18,000 ppm; bladder stones were observed at all dose levels. LOAEL: 700 ppm (72 mg/kg/day)		
		Melamine: Mouse 90-day Dietary Toxicity Study: A single female mouse died after receiving 9,000 ppm. Mean body weight gain relative to controls was depressed. The incidence of mice with bladder stones was dose-related and was greater in males than in females. Sixty percent of mice having bladder ulcers also had urinary bladder stones. Bladder ulcers were multifocal or associated with inflammation (cystitis). Epithelial hyperplasia and bladder stones were observed together in 2 mice. Also, epithelial cell atypia was seen. NOAEL: 6,000 ppm (600 mg/kg-day) LOAEL: 9,000 ppm (900 mg/kg-day)	NTP, 1983b; Melnick et al., 1984	Sufficient study details reported.
		Melamine: Increased incidence of acute and chronic inflammation and epithelial hyperplasia of the urinary bladder was observed in mice following oral (feed) exposure for up to 103 weeks. There was also increased incidence of bladder stones in male mice. LOAEL: 2,250 ppm (~380 mg/kg bw-day; lowest dose tested)	NTP, 1983b; ECHA, 2011b	Repeated dose effects described in a carcinogenicity bioassay study.
		Melamine: Dog 1-year dietary toxicity study: crystalluria started 60 to 90 days into treatment, and persisted during the study period. No other effects attributable to melamine were observed.	American Cyanamid Company, 1955	Sufficient study details were not available.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: Rat 30-month dietary toxicity study: neither accumulation of calculi nor any treatment-related urinary bladder lesions were found.	Mast et al., 1982a (as cited in Wolkowski Tyl and Reel, 1992)	Sufficient study details were not available.
		Melamine: Rat 24- to 30-month dietary toxicity study: a dose related trend for dilated glands in glandular gastric mucosa and inflammation in non glandular gastric mucosa was observed. Urinary bladder calculi formation was not observed.	American Cyanamid Company, 1983 (as cited in OECD SIDS, 1999)	Sufficient study details were not available.
		Melamine: Children affected by melamine contaminated milk for approximately 3 to 6 months before the onset of kidney stones. The highest content of melamine ranged from 0.090 to 619 mg/kg milk powder. A total of 52,857 children had received treatment for melamine-tainted milk. 99.2% of the children were younger than 3 yr. Some children were asymptomatic; however irritability, dysuria, difficulty in urination, renal colic, hematuria, or stone passage, hypertension, edema, or oliguria were also reported. Mortality occurred in four cases.	Hau et al., 2009	Summary of toxic effects from food contamination.
		Melamine: Renal damage is believed to result from kidney stones formed from melamine and uric acid or from melamine and cyanuric acid. Cyanuric acid can be produced in the gut by microbial transformation of melamine. The bacteria *Klebsiella terrigena* was shown to convert melamine to cyanuric acid and rats colonized by *K. terrigena* showed exacerbated melamine-induced nephrotoxicity.	Zheng et al., 2013	Supporting information about the renal toxicity of melamine.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Melamine polyphosphate is not expected to be a skin sensitizer based on the data for melamine.**		
	Skin Sensitization	**Melamine:** No evidence of primary dermal irritation or sensitization in a human patch test	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Limited study details reported.
		Melamine: Non-sensitizing to guinea pigs	Fasset and Roudabush, 1963 (as cited in OECD SIDS, 1999; Trochimowicz et al., 2001)	Limited study details reported.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Melamine polyphosphate is slightly irritating to eyes.**		
	Eye Irritation	**Melamine polyphosphate:** Slightly irritating	NOTOX BV, 1998 (as cited in Australia, 2006)	Limited study details reported.
		Melamine polyphosphate: Slightly irritating	Submitted confidential study	Limited study details reported.
		Melamine: Non-irritating to rabbit eyes	BASF, 1969 (as cited in OECD SIDS, 1999; IUCLID, 2000a)	Limited study details reported.
		Melamine: Non-irritating to rabbit eyes following 0.5 mL of 10% melamine	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Limited study details reported.
		Melamine: Mild irritant to rabbit eyes following exposure to 30 mg of dry powder	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Limited study details reported.
		Melamine: Slightly irritating to rabbit eyes	Marhold, 1972 (as cited in IUCLID, 2000a; RTECS, 2009)	Limited study details reported.
Dermal Irritation		**VERY LOW: Melamine polyphosphate is not a skin irritant.**		
	Dermal Irritation	**Melamine polyphosphate:** Not irritating	NOTOX BV, 1998 (as cited in Australia, 2006)	Limited study details reported.
		Melamine polyphosphate: Not irritating	Submitted confidential study	Limited study details reported.
		Melamine: Not irritating to rabbit skin	Rijcken, 1995 (as cited in OECD SIDS, 1999)	Organisation for Economic Cooperation and Development (OECD) 404 guideline study.
		Melamine: Not irritating to rabbit skin	BASF, 1969 (as cited in OECD SIDS, 1999; IUCLID, 2000a)	Limited study details reported.

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: Not irritating to rabbit skin	American Cyanamid Company, 1955; Trochimowicz et al., 2001	Limited study details reported.
		Melamine: Not irritating to rabbit skin	Fasset and Roudabush, 1963 (as cited in OECD SIDS, 1999; Trochimowicz et al., 2001)	Limited study details reported.
Endocrine Activity		**There were insufficient data located to describe the effect of melamine polyphosphate on the endocrine system. In one study, melamine did not exhibit estrogenic activity *in vitro* in a yeast two-hybrid assay.**		
		Melamine: Showed no estrogenic activity (no change in B-galactosidase activity) in an *in vitro* yeast two-hybrid assay in *Saccharomyces cerevisiae* Y 190	ECHA, 2011b	Reported in a secondary source. Nonguideline study.
Immunotoxicity		**Potential for immunotoxic effects based on analogy to structurally similar polymers and professional judgment.**		
	Immune System Effects	Potential for immunotoxicity	Professional judgment	Estimated based on confidential analogs and professional judgment.
		Melamine: Did not inhibit the mitogenesis of B- and T- lymphocytes in an *in vitro* mouse lymphocyte mitogenesis test.	ECHA, 2011a	Data from a secondary source.
ECOTOXICITY				
ECOSAR Class		Melamines		
Acute Aquatic Toxicity		**LOW: Melamine polyphosphate is expected to be of low hazard for acute toxicity to aquatic organisms based on experimental data for melamine polyphosphate and experimental data for melamine. For melamine, the weight of evidence suggests that the acute values are >100 mg/L. For melamine polyphosphate, no effects were observed in algae at the highest concentration tested (3.0 mg/L). Melamine polyphosphate is not predicted to cause eutrophication based on laboratory testing.**		
Fish LC_{50}		**Melamine polyphosphate:** Freshwater fish 96-hour LC_{50} = 100 mg/L (Experimental)	Ciba, 2005 (as cited in Australia, 2006)	Reported in a secondary source, study details and test conditions were not reported.
		Melamine: *Leuciscus idus melanotus* 48-hour LC_{50} >500 mg/L (Experimental)	OECD SIDS, 1999	Study details reported in secondary source.
		Melamine: *Oryzias latipes* 48-hour LC_{50}	OECD SIDS, 1999	Study details reported in secondary

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	= 1,000 mg/L (Experimental)		source.
	Melamine: *Poecilia reticulata* 96-hour LC_{50} >3,000 mg/L (Experimental)	OECD SIDS, 1999	Study details reported in secondary source.
	Melamine: *Poecilia reticulata* 4,400 mg/L dose lethal to <10% (Experimental)	OECD SIDS, 1999	Study details reported in secondary source.
	Melamine: Fish 96-hour LC_{50} = >100 mg/L (Estimated) ECOSAR: Anilines (amino-meta)	ECOSAR v1.11	ECOSAR provided results for the Anilines (amino-meta) class; however, professional judgment indicates that this compound does not lie within the domain of the ECOSAR model.
	Melamine: Fish 96-hour LC_{50} = >100 mg/L (Estimated) ECOSAR: Melamines	ECOSAR v1.11	
Daphnid LC_{50}	**Melamine polyphosphate:** *Daphnia magna* 48-hour EC_{50} >100 mg/L (Experimental)	Ciba, 2005 (as cited in Australia, 2006)	Reported in a secondary source, study details and test conditions were not reported.
	Melamine: *Daphnia magna* 48-hour LC_{50} >2,000 mg/L (Experimental)	OECD SIDS, 1999	Study details reported in secondary source.
	Melamine: Daphnid 48-hour LC_{50} = 6.23 mg/L (Estimated) ECOSAR: Anilines (amino-meta)	ECOSAR v1.11	ECOSAR provided results for the Anilines (amino-meta) class; however, professional judgment indicates that this compound does not lie within the domain of the ECOSAR model.
	Melamine: Daphnid 48-hour LC_{50} = >100 mg/L ECOSAR: Melamines (Estimated)	ECOSAR v1.11	

Melamine Polyphosphate CASRN 15541-60-3			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae EC_{50}	**Melamine polyphosphate:** In a 96-hour control growth test (*Selenastrum capricornutum*), melamine polyphosphate causes increased algal growth, but growth is 95% less than growth in standard medium with adequate phosphorous. This indicates that melamine polyphosphate is not a good source of phosphorous for algal growth and does not cause eutrophication. (Experimental)	Submitted confidential study	Sufficient study details reported in a confidential study.
	Melamine: *Scenedesmus pannonicus* 4-day EC_{50} = 940 mg/L; 4-day NOEC = 320 mg/L (Experimental)	OECD SIDS, 1999	Reported in a secondary source, study details and test conditions were not provided.
	Melamine: Green algae 96-hour EC_{50} = 2.79 mg/L (Estimated) ECOSAR: Anilines (amino-meta)	ECOSAR v1.11	ECOSAR provided results for the Anilines (amino-meta) class; however, professional judgment indicates that this compound does not lie within the domain of the ECOSAR model.
	Melamine: Green algae 96-hour EC_{50} = >100 mg/L (Estimated) ECOSAR: Melamines	ECOSAR v1.11	
Chronic Aquatic Toxicity	**LOW: Melamine polyphosphate is expected to be of low hazard for chronic toxicity to aquatic organisms based on experimental data for melamine. For melamine, the weight of evidence suggests that the chronic values are >10 mg/L. For melamine polyphosphate, no effects were observed in algae at the highest concentration tested (3.0 mg/L).**		
Fish ChV	**Melamine:** *Jordanella floridae* 35-day NOEC ≥ 1,000 mg/L (Experimental)	OECD SIDS, 1999	Reported in a secondary source, study details and test conditions were not provided.
	Melamine: *Salmo gairdneri* NOEC (macroscopic) = 500 mg/L; NOEC (microscopic) <125 mg/L	OECD SIDS, 1999	Reported in a secondary source, study details and test conditions were not provided.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	(Experimental)		
	Melamine: Fish ChV = >100 mg/L (Estimated) ECOSAR: Anilines (amino-meta)	ECOSAR v1.11	ECOSAR provided results for the Anilines (amino-meta) class; however, professional judgment indicates that this compound does not lie within the domain of the ECOSAR model.
	Melamine: Fish ChV = >100 mg/L (Estimated) ECOSAR: Melamines	ECOSAR v1.11	
Daphnid ChV	**Melamine:** *Daphnia magna* 21-day LC_{50} = 32-56 mg/L, 21-day LC_{100} = 56 mg/L, 21-day NOEC = 18 mg/L (Experimental)	OECD SIDS, 1999	Reported in a secondary source, study details and test conditions were not provided.
	Melamine: Daphnid ChV = 0.078 mg/L (Estimated) ECOSAR: Anilines (amino-meta)	ECOSAR v1.11	ECOSAR provided results for the Anilines (amino-meta) class; however, professional judgment indicates that this compound does not lie within the domain of the ECOSAR model.
	Melamine: Daphnid ChV = 14.85 mg/L (Estimated) ECOSAR: Melamines	ECOSAR v1.11	
Green Algae ChV	**Melamine polyphosphate:** *Selenastrum capricornutum* 96-hour EC_{50} >3.0 mg/L; 96-hour NOEC = 3.0 mg/L (Experimental)	Submitted confidential study	No effects observed at highest concentration tested.
	Melamine polyphosphate: *Selenastrum capricornutum* 96-hour EC_{50} >3.0 mg/L; 96-hour NOEC = 3.0 mg/L (Experimental)	Australia, 2006	Reported in a secondary source, study details and test conditions were not provided; no effects observed at highest concentration tested.

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Melamine: Green algae ChV = 0.70 mg/L (Estimated) ECOSAR: Anilines (amino-meta)	ECOSAR v1.11	ECOSAR provided results for the Anilines (amino-meta) class; however, professional judgment indicates that this compound does not lie within the domain of the ECOSAR model.
		Melamine: Green algae ChV = 81.26 mg/L (Estimated) ECOSAR: Melamines	ECOSAR v1.11	
ENVIRONMENTAL FATE				
Transport		**Melamine polyphosphate has a high measured water solubility of 20 g/L and its Henry's Law constant and vapor pressure are below cutoff values. It is expected to partition predominately to water and soil. It may migrate from soil into groundwater. As a salt, volatilization from either wet or dry surfaces is not expected to be an important fate process.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	EPI v4.10; Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption - K_{oc}	**Melamine polyphosphate:** 13 (Estimated)	EPI v4.10	
	Level III Fugacity Model	Air = 0% Water = 37% Soil = 63% Sediment = 0% (Estimated) for Melamine Polyphosphate	EPI v4.10	

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**HIGH: Melamine polyphosphate is expected to show high persistence in the environment based on the data for melamine. Melamine polyphosphate is expected to be fully dissociated under environmental conditions. The weight of evidence suggests that melamine will biodegrade at rates consistent with a High hazard designation. Although pure culture studies showed evidence of biodegradation by enzymatic hydrolytic deamination in less than 10 days, an original MITI test detected less than 30% degradation after 14 days and two separate guideline OECD 302B studies observed no degradation after 28 days and 16% degradation after 20 days. This results in an expected environmental persistence half-life between 60 and 180 days. Degradation of melamine or its cation by hydrolysis or direct photolysis is not expected to be significant as the functional groups present on this molecule do not tend to undergo these reactions under environmental conditions. Polyphosphoric acid is expected to have low persistence in the environment. The weight of evidence suggests that polyphosphoric acid will hydrolyze under environmental conditions. The phosphates formed are expected to participate in natural cycles and be readily assimilated.**		
Water	**Aerobic Biodegradation**	**Melamine polyphosphate:** Weeks (Primary survey model) Months (Ultimate survey model) (Estimated)	EPI v4.10	
		Melamine: 16% removal after 20 days with activated sludge, 14% removal after 10 days with adapted sludge (Measured)	OECD SIDS, 1999	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Melamine: 0% removal after 28 days with activated sludge (Measured)	OECD SIDS, 1999	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Melamine: 0% removal after 14 days with activated sludge (Measured)	OECD SIDS, 1999	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Melamine: <30% removal after 14 days with activated sludge (Measured)	OECD SIDS, 1999	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Melamine: <1% removal after 5 days with an adapted inoculum (Measured)	IUCLID, 2000a	These values are for the dissociated component, melamine. Reported in a secondary source, study details and

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				test conditions were not provided.
		Melamine: 0% removal after 14 days with activated sludge (Measured)	IUCLID, 2000a	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Melamine: <30% removal after 14 days with activated sludge (Measured)	IUCLID, 2000a	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Melamine: <20% removal after 20 days, 14% removal after 10 days with adapted inoculum (Measured)	IUCLID, 2000a	These values are for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
		Study results: 100%/<10 days Test method: Pure culture study **Melamine:** Bacterium, *Nocardioides sp.* Strain ATD6 rapidly degraded melamine and accumulated cyanuric acid and ammonium ion, via the intermediates ammeline and ammelide. (Measured)	Takagi et al., 2012	Melamine degradation was found to occur in species specific biodegradation studies.
	Volatilization Half-life for Model River	>1 year for **Melamine polyphosphate** (Estimated)	EPI v4.10	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year for **Melamine polyphosphate** (Estimated)	EPI v4.10	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**	Study results: 0%/28 days Test method: 302B: Inherent - Zahn-Wellens/EMPA Test **Melamine:** Not readily biodegradable: 0% biodegradation detected after 2 weeks with 100 ppm in 30 ppm activated sludge (OECD TG 301C) (Measured); 0% degradation after 28 days with 100 mg DOC/L in activated sludge (Zahn-Wellens test, OECD 302B) (Measured)	MITI, 1998; OECD SIDS, 1999	Adequate values from guideline studies for the dissociated component, melamine.

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Study results: 100%/4 days Test method: Pure culture study **Melamine:** Bacterium, *A. citrulli* strain B-12227 rapidly degraded melamine and accumulated cyanuric acid, ammeline and ammelide, via the intermediates ammeline and ammelide. (Measured)	Shiomi and Ako, 2012	Melamine degradation was found to occur in species specific biodegradation studies.
		Melamine: A set of soil bacteria has been identified whose members rapidly metabolize melamine as their source of nitrogen to support growth; these bacteria contain an enzyme which hydrolytically deaminates melamine. (Measured)	Cook and Hutter, 1981; Cook and Hutter, 1984	Melamine degradation was found to occur in species specific biodegradation studies.
	Anaerobic Biodegradation	Study results: <8.9%/28 days Test method: Other **Melamine:** 0-8.9% nitrification was observed after 28 days incubation with bacteria in Webster silty clay loam under anaerobic conditions. (Measured)	IUCLID, 2000a	This value is for the dissociated component, melamine. Reported in a secondary source, study details and test conditions were not provided.
	Soil Biodegradation with Product Identification	**Melamine:** Nitrification of melamine occurs in soil at a low rate (0.7% organic N found as NO_3-N in week 10, and 0 % in week 28). (Measured)	ECHA, 2011b; ECHA, 2011a	Non guideline studies for the dissociated component, melamine.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	**Melamine polyphosphate:** 21 days (Estimated)	EPI v4.10	
Reactivity	**Photolysis**	**Melamine polyphosphate:** Not a significant fate process (Estimated)	Professional judgment; Mill, 2000	The substance does not contain functional groups that would be expected to absorb light at environmentally significant wavelengths.
	Hydrolysis	**Polyphosphoric acid:** The half-life for the hydrolysis to phosphoric acid is several days at 25°C (Measured)	Gard, 2005	This value is for the dissociated component, polyphosphoric acid. These studies indicate polyphosphoric acid would undergo

Melamine Polyphosphate CASRN 15541-60-3				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				hydrolysis under environmental conditions to phosphate ions. Reported in a secondary source, study details and test conditions were not provided.
		Polyphosphoric acid: Hydrolysis occurs in 2 months at 20°C (Measured)	IUCLID, 2000b	This value is for the dissociated component, polyphosphoric acid. Reported in a secondary source, study details and test conditions were not provided available.
Environmental Half-life		**Melamine polyphosphate:** 120 days (Estimated)	PBT Profiler v1.301	Half-life estimated for the predominant compartment, as determined by EPI and the PBT Profiler methodology.
Bioaccumulation		**LOW: Based on the relatively high water solubility of melamine polyphosphate (20 g/L) and an estimated BCF of 3.2. In addition, the experimental bioconcentration values for the melamine component are low, BCF <3.8, and BAF <1.**		
	Fish BCF	**Melamine polyphosphate:** 3.2 (Estimated)	EPI v4.10	
		Melamine: <0.38 in carp (*Cyprinus carpio*) after 6 weeks at 2.0 ppm concentration; <3.8 in carp (*Cyprinus carpio*) after 6 weeks at 0.2 ppm concentration (OECD 302B) (Measured)	MITI, 1998	Adequate values from guideline studies for the dissociated component, melamine.
	Other BCF			No data located.
	BAF	**Melamine polyphosphate:** 0.9 (Estimated)	EPI v4.10	
		Melamine: 0.9 (Estimated)	EPI v4.10	
	Metabolism in Fish	**Melamine:** Uptake, bioaccumulation and elimination study with ^{14}C-melamine in fathead minnow and rainbow trout: BCFs <1 (Measured)	ECHA, 2011b; ECHA, 2011a	Non guideline studies that support the low potential for bioaccumulation of this substance.
ENVIRONMENTAL MONITORING AND BIOMONITORING				

Melamine Polyphosphate CASRN 15541-60-3			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
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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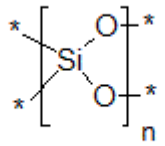
Silicon Dioxide (amorphous)

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 predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

[§] Based on analogy to experimental data for a structurally similar compound. [R] Recalcitrant: Substance is comprised of metallic species (or metalloids) that will not degrade, but may change oxidation state or undergo complexation processes under environmental conditions. [¤]Concern linked to direct lung effects associated with the inhalation of poorly soluble particles less than 10 microns in diameter. [^] Depending on the grade or purity of amorphous silicon dioxide commercial products, the crystalline form of silicon dioxide may be present. The hazard designations for crystalline silicon dioxide differ from those of amorphous silicon dioxide, as follows: VERY HIGH (experimental) for carcinogenicity; HIGH (experimental) genotoxicity; MODERATE (experimental) for acute toxicity and eye irritation.

		Human Health Effects										Aquatic Toxicity		Environmental Fate	
Chemical	CASRN	Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Silicon Dioxide (amorphous)	7631-86-9	L[^]	L[^]	L[^]	L	L	*L*[§]	H[¤]	L		L[^]	VL	L	*L*	*H*[R]	*L*

Silicon Dioxide (amorphous)



* indicates repeating units with indeterminate structure

CASRN: 7631-86-9

MW: 60.09 (for SiO_2)

MF: $(SiO_2)_n$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: Not applicable

Synonyms: Silica (CASRN 7631-86-9)
Silicon dioxide, amorphous: Silica, amorphous fumed, crystalline-free (CASRN 112945-52-5); Pyrogenic (fumed) amorphous silica (CASRN 112945-52-5); Silica, vitreous (CASRN 60676-86-0); Amorphous silica gel, crystalline-free (CASRN 112926-00-8); Silica gel, precipitated, crystalline-free (CASRN 112926-00-8); Silica, amorphous, diatomaceous earth (CASRN 61790-53-2); Silica, amorphous, flux-calcined diatomaceous earth (CASRN 68855-54-9)
Silicon dioxide, crystalline: Silica, crystalline, cristobalite (CASRN 14464-46-1), Silica, crystalline, tripoli (CASRN 1317-95-9); Silica, crystalline, tridymite (CASRN 15468-32-3); Quartz (CASRN 14808-60-7); Sand

Trade names:
Silicon dioxide, amorphous: Aerosil, Art Sorb, Baykisol, Bindzil, Biogenic silica, Britesorb, Cab-O-Sil, Celatom, Celite, Clarcel, Colloidasilica, Decalite, Diamantgel, Diatomaceous earth (flux-calcined), Diatomaceous earth (uncalcined), Diatomite, Fina/Optima, FK, Fused silica, Gasil, HDK, Hi-Sil, Hispacil, KC-Trockenperlen, Ketjensil, Kieselguhr, Lucilite, Ludox, Nalcoag, Neosyl, Nipsil, Nyacol, Opal, Precipitated silica, Quartz glass, Reolosil, Seahostar, Sident, Silcron, Silica fibres (biogenic), Silica-Perlen, Silica-Pulver, Sipernat, Skamol, Snowtex, Spherosil, Suprasil, Sylobloc, Syloid, Sylopute, Syton, TAFQ, Tixosil, Tripolite, Trisyl, Ultrasil
Silicon dioxide, crystalline: Agate, Chalcedony, Chert, Clathrasil, Coesite, alpha, beta Cristobalite, CSQZ, DQ 12, Flint, Jasper, Keatite, Min-U-Sil, Moganite, Novaculite, Porosil, alpha-Quartz, alpha, beta Quartz, Quartzite, Sandstone, Sil-Co-Sil, Silica sand, Silica W, Snowit, Stishovite, Sykron F300, Sykron F600, alpha, beta1, beta2 Tridymite, Zeosil

Chemical Considerations: Silicon dioxide (also known as silica) is an inorganic compound that exists in several physical forms. This report assesses silicon dioxide for flame retardant applications, in which amorphous silicon dioxide is more commonly used. Commercial products may contain crystalline silicon dioxide, depending on the purity and grade.

Silicon dioxide, amorphous consists of randomly arranged rings of silicon dioxide that form a complex structure of roughly spherical particles. Silicon dioxide, crystalline; however is a general term that refers to the many distinct crystal structures or polymorphs of silicon dioxide. Crystalline silicon dioxide includes naturally occurring quartz (CASRN 14808-60-7), cristobalite (CASRN 14464-46-1), and tridymite (CASRN 15468-32-3).

The structural form of silicon dioxide is evaluated in this assessment as it influences the hazards posed to human health. It may be difficult for supply chains to know the difference between the structural forms. Therefore, the hazard designations in this report are based on the amorphous form and a summary of the hazards associated with the crystalline form is provided in the hazard summary table as a footnote (^) for reference, in case the crystalline form is present in the commercial formulation. Concerns based on the nanoscale material were not included in this assessment; however, the potential health concerns from the inhalation of finely divided particulates that are generally less than 10 microns in diameter were considered for human health endpoints.

Although not all literature entries identified which form of silicon dioxide was being discussed, this information was provided whenever available. In the absence of experimental data, structural considerations associated with this mineral were used to complete this hazard profile (IARC, 1997; HSDB, 2009; Waddell, 2013).	
Polymeric: No **Oligomeric:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified.	
Analog: Confidential analogs; a general silicon dioxide CASRN is used to represent all forms of silicon dioxide (CASRN 7631-86-9). Other CASRN for specific silicon dioxide forms are listed in the synonyms section and noted in the data quality column for relevant entries. **Endpoint(s) using analog values:** Neurotoxicity	**Analog Structure:** Not applicable
Structural Alerts: Respirable, poorly soluble particulates - Human health, limited to effects on the lung as a result of inhaling the particles (EPA, 2010).	
Risk Phrases: Not classified by Annex VI Regulation (EC) No 1272/2008 (ESIS, 2012).	
Hazard and Risk Assessments: An Organisation for Economic Co-operation and Development (OECD) Screening Information Dataset Initial Assessment Profile (SIAP) for silicon dioxide was completed in 2004. Silicon dioxide is included in the International Agency for Research on Cancer (IARC) monographs on the evaluation of carcinogenic risks to humans - summaries and evaluations. (IARC, 1997; OECD SIDS, 2004a).	

Silicon dioxide (amorphous) CASRN 7631-86-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	1,710 (Measured)	Lewis, 1999; EC, 2000a	Reported in multiple sources. Test substance form not specified.
	Crystalline silicon dioxide: 1,400-2,000 (Measured)	EC, 2000b	A range of values reported in a secondary source. Study details and test methods were not provided.
Boiling Point (°C)	2,230 (Measured)	Lewis, 1999; EC, 2000a; EC, 2000b	Reported in multiple sources. Test substance form not specified.
Vapor Pressure (mm Hg)	**Amorphous and crystalline silicon dioxide:** $<1x10^{-8}$ (Estimated)	Professional judgment	This substance is a high-boiling solid, so the vapor pressure is estimated to be negligible.
	9.98 at 1,732°C Reported as 13.3 hPa at 1,732°C. (Measured)	EC, 2000a	Reported in secondary source at an elevated temperature. Study details not provided. Test substance form not specified.
Water Solubility (mg/L)	**Amorphous silicon dioxide:** 120 (Measured)	Alexander et al., 1954	Study details and test methods were not provided.
	Amorphous silicon dioxide: 70 mg/L (Measured)	KEMI, 2006	Study details and test methods were not provided.
	Amorphous and crystalline silicon dioxide: Insoluble (Estimated)	Lide, 2000	Adequate, non-quantitative value provided.
	Amorphous and crystalline silicon dioxide: Insoluble for fumed, amorphous and crystalline silica (Estimated)	Lewis, 1999	Adequate, non-quantitative value provided.
	Crystalline silicon dioxide: 6.4-18 The water solubility of SiO_2 minerals is a function of temperature, pH, particle size, and the presence of a disrupted surface layer. The slow rate of dissolution is due to the high activation energy required to hydrolyze the Si-O-Si bond. (Measured)	OECD SIDS, 2011	Reported in a secondary source.
	Reported as ~0.15 wt% SiO_2 at 673 K and 100 MPa for pure water (Measured)	Flörke et al., 2000	Study details and test methods were not provided. Test substance form not specified.

Silicon dioxide (amorphous) CASRN 7631-86-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Practically insoluble (Estimated)	Merck, 1996	Adequate, non-quantitative value provided. Test substance form not specified.
Log K_{ow}			No data located.
Flammability (Flash Point)	**Amorphous silicon dioxide:** Used as a fire-extinguishing agent, not combustible, stable (Measured)	Daubert and Danner, 1989 (as cited in ECHA, 2013)	Reported in a secondary source for Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5) and Silica gel, precipitated, crystalline-free (CASRN 112926-00-8).
Explosivity	**Amorphous and crystalline silicon dioxide:** Silicon dioxide is a fully oxidized inorganic material and is not expected to be explosive. (Estimated)	Professional judgment	No experimental data located; based on its chemical structure and use as a flame retardant.
Pyrolysis	**Amorphous and crystalline silicon dioxide:** Not applicable (Estimated)	Professional judgment	Inorganic compounds do not undergo pyrolysis.
pH	3.5-9 for 5% aqueous suspension of wet process silica. (Measured)	EC, 2000a	Adequate values reported in a secondary source. The values of 20 different types of wet process silica, identified only by trade names, fall within this range.
	3.6-4.5 for 4% aqueous suspension of fumed silica. (Measured)	EC, 2000a	Adequate value reported in a secondary source for fumed silica.
pK_a			No data located.

Silicon dioxide (amorphous) CASRN 7631-86-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Particle Size	**Amorphous silicon dioxide:** D10 = <103 µm D50 = <211 µm D99 = <610 µm According to ISO 13320-1 (Part 1): Particle size analysis - Laser diffraction methods; OECD guideline 110: Particle size distribution / fibre length and diameter distributions and EN 481 (1993): Workplaces atmospheres; size fraction definitions for measurement of airborne particles. (Measured)	ECHA, 2013	Adequate guideline study reported for the commercial product Zeosil 45, Silica gel, precipitated, crystalline-free; (CASRN 112926-00-8).
	Amorphous silicon dioxide: D10 = <230 µm D50 = <615 µm D99 = <1,668 µm According to ISO 13320-1 (Part 1): Particle size analysis - Laser diffraction methods; OECD guideline 110: Particle size distribution / fibre length and diameter distributions and EN 481 (1993): Workplaces atmospheres; size fraction definitions for measurement of airborne particles. (Measured)	ECHA, 2013	Adequate guideline study reported for the commercial product Cab-O-Sil M5: CAS-Name: Silica, amorphous, fumed, crystalline-free; (CASRN 112945-52-5), purity ca. 100 %.
	Amorphous silicon dioxide: 13-27 µm mean distribution according to ISO 13320-1 (Part 1): Particle size analysis - Laser diffraction methods. (Measured)	ECHA, 2013	Reported for HDK T30: >99.8 % SiO_2 with limited study details.
	Amorphous silicon dioxide: D10 = <375 µm D50 = <680 µm D99 = <1,210 µm According to ISO 13320-1 (Part 1): Particle size analysis - Laser diffraction methods; OECD guideline 110: Particle	ECHA, 2013	Adequate guideline study reported for Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).

Silicon dioxide (amorphous) CASRN 7631-86-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	size distribution / fibre length and diameter distributions and EN 481 (1993): Workplaces atmospheres; size fraction definitions for measurement of airborne particles. (Measured)		
	Amorphous silicon dioxide: D13 = 200 µm D45.8 = 315 µm D90.6 = 2,000 µm According to ISO 13320-1 (Part 1): Particle size analysis - Laser diffraction methods; OECD guideline 110: Particle size distribution / fibre length and diameter distributions and EN 481 (1993): Workplaces atmospheres; size fraction definitions for measurement of airborne particles. (Measured)	ECHA, 2013	Adequate guideline study reported for the commercial product HDK T30: >99.8 % SiO_2, Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
	Amorphous silicon dioxide: D10 = <214 µm D50 = <480 µm D99 = <1,414 µm According to ISO 13320-1 (Part 1): Particle size analysis - Laser diffraction methods; OECD guideline 110: Particle size distribution / fibre length and diameter distributions and EN 481 (1993): Workplaces atmospheres; size fraction definitions for measurement of airborne particles. (Measured)	ECHA, 2013	Reported for Syloid 74, CAS-Name: Silica gel, crystalline-free; (CASRN 112926-00-8), purity ca. 100 %.
	Amorphous silicon dioxide: D14.04 = <0.64 µm D100 = <10.23 µm Using Anderson 7-stage cascade impactor (Measured)	ECHA, 2013	Non guideline study reported for HDK T30: >99.8 % SiO_2; Silica, amorphous, fumed, crystalline-free; (CASRN 112945-52-5).
	Amorphous silicon dioxide: Typical size ranges of:	ECHA, 2013	Reported for Silica, amorphous, fumed, crystalline-free (CASRN

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		0.1 - 1 µm for aggregates; 1 - 250 µm for Agglomerates (Measured)		112945-52-5).
		Amorphous silicon dioxide: Typical size ranges of: 0.1 - 1 µm for aggregates; 1 - 250 µm for Agglomerates 1 - 20 µm for silica gel aggregates (Measured)	ECHA, 2013	Reported for Silica gel and amorphous silica, precipitated, crystalline-free (CASRN 112926-00-8) with limited study details.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**Amorphous silicon dioxide (CASRNs 7631-86-9, 112945-52-5, 112926-00-8) is rapidly eliminated from the lung tissue. Disposition in the mediastinal lymph nodes is substantial during and after prolonged inhalation exposures in experimental animals; however the involvement of lymphatic elimination is not as relevant following short exposure periods. Intestinal absorption of amorphous silicon dioxide is limited in animals and humans, and there is evidence of ready renal elimination of the bioavailable fractions of silica. In contrast, crystalline silicon dioxide forms tend to accumulate and persist in the lung and lymph nodes.**		
Dermal Absorption *in vitro*				
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	**Amorphous silicon dioxide:** After prolonged exposure of rats to high concentrations of amorphous silica (40-50 mg/m^3), overall elimination was high and was not found to accumulate in the lung: only 5-6% of respirable material was found after 120 exposure days. On the other hand, following prolonged exposure, there was substantial transfer to mediastinal lymph nodes with about 31% of total deposit = 1.5- 2% of the respirable material. The involvement of lymphatic elimination after short exposures is not as relevant, particularly when there is a lower body burden of amorphous silica.	OECD SIDS, 2004b	Sufficient study details reported in a secondary source. Aerosil 150, pyrogenic silica (CASRN 112945-52-5).
		Amorphous and crystalline silicon dioxide: Crystalline forms of silicon dioxide have a tendency to accumulate	OECD SIDS, 2004a; OECD SIDS, 2004b	Sufficient study details reported in a secondary source. Data are for synthetic amorphous silica and

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		and persist in the lung and lymph nodes. Intestinal absorption of silicon dioxide is insignificant in animals and humans. There is evidence of renal elimination of the bioavailable fractions		crystalline silica.
		Amorphous silicon dioxide: Female Sprague-Dawley rats exposed via inhalation to HDK V15 dust at a concentration of 50 - 55 mg/m^3 (nominal, respirable about 30 mg/m^3 with aerodynamic diameter of ≤7 µm) for 12 months. No substantial increase in the SiO_2 deposition in the lung and the mediastinal lymph nodes were observed between exposure of 18 weeks and of 12 months. About 90 % of the SiO_2 was cleared from the lungs and 50 - 60% from the mediastinal lymph nodes within 5 months. This corresponds to an approximate half-life of 7 weeks, based on first-order elimination kinetics.	ECHA, 2013	Sufficient study details reported in a secondary source. HDK V15: >99.8 % SiO_2, 150 m^2/g (BET), CAS-Name: Silica, amorphous fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Fischer 344 rats exposed via inhalation to Aerosil 200 dust at a concentration of 50.4 mg/m^3 6 hours/day, 5 days/week for 13 weeks. Lung burdens during treatment were as follows: 755.9 µg at 6.5 weeks and 88.27 µg at 13 weeks of exposure. Lung burdens following treatment were 156.0 µg at 12 weeks and 92.6 µg at 32 weeks post- exposure (during the recovery phase).	ECHA, 2013	Sufficient study details reported in a secondary source. Aerosil 200: CAS-Name: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Wistar rats exposed via inhalation to Aerosil 200 at concentrations of 0, 1.3, 5.9 or 31 mg/m^3 for 90 days. Half-life was rapid from the	ECHA, 2013	Sufficient study details reported in a secondary source. Aerosil 200: Silica, amorphous, fumed, crystalline-free (CASRN 112945-

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		lungs; No bioaccumulation potential based on study results.		52-5).
		Amorphous silicon dioxide: Rats receiving 20 daily oral doses of 100 mg HDK V15 per animal (about 500 mg/kg bw) each; tissue values (SiO_2) apparently were very slightly increased in liver and kidney: in liver 4.2 µg (control value 1.8 µg), in the spleen 5.5 µg (7.2 µg) and in the kidneys 14.2 µg (7.8 µg).	ECHA, 2013	Sufficient study details reported in a secondary source. HDK V15: >99.8 % SiO_2, 150 m^2/g (BET), CAS-Name: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Human subjects (10 males and 2 females per test article) were given Aerosil or FK 700 as 0.5% suspensions in apple juice. Urinary excretion for both test substances was <0.5 % of the dose within 4 days. Overall, increases in excretion of SiO_2 after oral ingestion were not unequivocally detectable.	ECHA, 2013	Sufficient study details reported in a secondary source. Aerosil, CAS-Name: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5); or FK 700, Silica gel, precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Silicon dioxide is slowly absorbed from dusts deposited in lungs, or from material taken orally.	HSDB, 2009	Limited data reported in a secondary source for amorphous silica.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	**Amorphous silicon dioxide:** Amorphous silica (HDK V15), 10 mg subcutaneously injected in 0.3 mL water in female Sprague-Dawley rats, was rapidly removed from the site of injection: mean recovery 24 h post-treatment 6.90 mg, after one month 0.65 mg (approx. 10 % left) and after two months 0.30 mg (less than 5 % left) Similar results were obtained in rats after subcutaneous application of 30, 40, and 50 mg AEROSIL 150 as suspension in water or in 0.5% Tween or as dry powder (operative, subcutaneous): after 6 weeks 95 - 97 % of the substance was eliminated.	OECD SIDS, 2004b	Sufficient study details reported in a secondary source. HDK V15: >99.8 % SiO_2, 150 m^2/g (BET), CAS-Name: Silica, amorphous, fumed (CASRN 112945-52-5).
Acute Mammalian Toxicity		**LOW: Amorphous silicon dioxide is not acutely toxic when administered via oral, dermal, or inhalation routes. If the crystalline form of silicon dioxide is present, the hazard designation is Moderate based on an oral LD_{50} of 500 mg/kg and lung effects following short-term inhalation exposure.**		
Acute Lethality	**Oral**	**Amorphous silicon dioxide:** Mouse oral LD_{50} >3,160 mg/kg	ECHA, 2013	Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Rat oral LD_{50} >3,300 - >20,000 mg/kg	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silica, precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Rat oral LD_0 >3,300 - >40,000 mg/kg	EC, 2000a	Sufficient study details reported in a secondary source. Amorphous (CASRN 7631-86-9) or Silica, precipitated, crystalline-free (CASRN 112926-00-8).
		Crystalline silicon dioxide: Rat oral LD_{50} = 500 mg/kg	EC, 2000b	Study details reported in a secondary source; particle size of quartz was 100-200 µm.
	Dermal	**Amorphous silicon dioxide:** Rabbit	EC, 2000a; Waddell, 2013	Sufficient study details reported in a

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		dermal LD_{50} >2,000 - >5,000 mg/kg		secondary source. Silica, precipitated, crystalline-free (CASRN 112926-00-8).
	Inhalation	**Amorphous silicon dioxide:** Rat 4-hour inhalation LC_{50} >58.8 mg/L (nominal, nose only, dust); 4-hour LC_0 >58.8 mg/L (nominal)	ECHA, 2013	Sufficient study details reported in a secondary source. Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5), purity ca. 100 %.
		Amorphous silicon dioxide: Rat 4-hour inhalation LC_0 >0.139 - >0.69 mg/L (nose only, dust); Rat 1-hour inhalation LC_0 >0.139; Rat 7-hour inhalation LC_0 >0.139 - >3.1 mg/L	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silica, precipitated, crystalline-free (CASRN 112926-00-8) or Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Rat 1-hour inhalation LC_{50} >2.2 mg/L	ECHA, 2013	Insufficient study; significant methodological deficiencies. Silica gel, crystalline-free (CASRN 112926-00-8).
		Crystalline silicon dioxide: 3-day inhalation study in rats exposed to 0, 10, or 100 mg/m3 of cristobalite (6 hours/day). Increased granulocytes and other markers of cytotoxicity from the lung lavage fluid were reported in all treated animals. LOAEC: 10 mg/m^3 (0.01 mg/L)	OECD SIDS, 2011	Limited study details reported in a secondary source; test substance identified as cristobalite; an LC_{50} was not calculated for this study, but supports a Moderate hazard designation for the inhalation route.
Carcinogenicity		**LOW: Based on the weight of evidence, amorphous silicon dioxide has a Low potential for carcinogenicity. Amorphous silicon dioxide was not carcinogenic in rats or mice following dietary administration for 103 or 93 weeks, respectively. Amorphous silicon dioxide is not classifiable as to its carcinogenicity to humans. Crystalline silicon dioxide was carcinogenic in several inhalation studies in rats and was shown to have an excess cancer risk following workplace exposure in several epidemiology studies. In addition, estimation software predicts a high-moderate carcinogenic risk for crystalline silicon dioxide. If the crystalline form of silicon dioxide is present, a VERY HIGH hazard designation would be assigned based on the weight of evidence that indicates sufficient evidence of carcinogenicity in humans.**		

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	OncoLogic Results	**Amorphous silicon dioxide:**	OncoLogic, 2008	This compound is not amenable to available estimation methods.
		Crystalline silicon dioxide: High-moderate; there is clear evidence that crystalline silica is a human and animal carcinogen via the inhalation route. (Estimated)	OncoLogic, 2008	Estimated based on silica, crystalline (CASRN 14808-60-7).
	Carcinogenicity (Rat and Mouse)	**Amorphous silicon dioxide:** In a 103 week study, Fischer 344 rats (40/sex/dose) were fed 0, 0.125, 2.5 and 5% Syloid 244 in the diet daily. The mean daily intake was 143.46, 279.55 and 581.18 g/rat in males and 107.25, 205.02 and 435.33 g/rat in females, respectively. The tumor response was not statistically different from controls.	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: In a 93-week study, B6C3F1 mice (40/sex/group) were fed 0, 1.25, 2.5 and 5 % Syloid 244 in the diet daily. The mean cumulative intake after 93 weeks was 38.45, 79.78 and 160 g/mouse in males and 37.02, 72.46 and 157.59 g/mouse in females, respectively. No significant difference in survival rats or behavior was observed. No dose-related alteration in hematologic parameters or organ weights. Malignant lymphoma/leukemia, which occurred in 7/20 females in the 2.5% dose group, was not statistically different than controls. Non-neoplastic lesions were considered to be of no toxicological significance.	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Intrapleural implantation of synthetic amorphous	IARC, 1997	Reported in a secondary source; test substance specified as amorphous

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		silica was negative for tumorigenesis.		silica.
		Amorphous silicon dioxide: Oral administration of food-grade, micronized, amorphous silica to rats and mice was negative for tumorigenesis.	IARC, 1997	Reported in a secondary source; test substance specified as amorphous silica.
		Amorphous silicon dioxide: Slightly increased incidence of intra-abdominal lymphosarcomas was reported after intraperitoneal injection of diatomaceous earth to mice. Subcutaneous and oral administration in mice produced no increase in tumors.	IARC, 1997	Reported in a secondary source; test substance specified as amorphous silica.
		Crystalline silicon dioxide: Several epidemiological investigations have shown an excess cancer risk following workplace inhalational exposure to dust containing respirable crystalline silica. Lung cancer incidence tended to increase with cumulative exposure; increased duration of exposure; peak intensity of exposure; presence of radiographically defined silicosis; and length of follow-up time from date of silicosis diagnosis.	IARC, 1997; OECD SIDS, 2011	Reported in a secondary source; test substance specified as crystalline silica.
		Crystalline silicon dioxide: Study with Balb/x mice (8 hours/day, 5 days/week in three groups of 6 to 16 mice at a concentration of 475 mg/m^3 for 150 days, 1,800 mg/m^3 for 300 days or 1,950 mg/m^3 for 570 days. There was no statistically significant difference in the number of pulmonary adenomas reported in the control or treated groups.	EC, 2000b	Limited study details reported in a secondary source.
		Crystalline silicon dioxide: 2-year study with F344 rats (50/sex), exposed via whole body inhalation for 6 hours/day, 5	EC, 2000b; OECD SIDS, 2011	Limited study details reported in a secondary source.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		days/week at a concentration of 1 mg/m^3. Inhalation exposure caused primary lung tumors (majority were adenocarcinomas) in 18 animals (12 in females, 5 in males). Mean mass of particles in the lungs at the end of the exposure period was 0.91 mg/lung.		
		Crystalline silicon dioxide: Four experiments in rats by inhalation of quartz and four experiments in rats by intratracheal instillation of quartz produced increased incidences of adenocarcinomas and squamous-cell carcinomas of the lungs. Animals that developed tumors also showed fibrosis. For the intratracheal instillation studies, doses ranged from 4 to 57 mg/kg-bw (7, 12 or 20 mg/animal of Min-U-Sil (5) quartz or 20 mg/animal of novaculite quartz). Exposure ranged from single instillation with observation for up to two years, to weekly instillation for 10 weeks. There was an increased incidence of silicotic granulomas after 3 weeks and lung tumors after 11 months following single intratracheal administration of a 95% pure quartz particles (<5 µm).	IARC, 1997; OECD SIDS, 2011	Reported in a secondary source; test substance specified as crystalline silica.
		Crystalline silicon dioxide: Thoracic and abdominal malignant lymphomas, primarily of the histiocytic type (MLHT) were found following intrapleural or intraperitoneal injections of several types of quartz to rats.	IARC, 1997	Reported in a secondary source; test substance specified as crystalline silica.
	Combined Chronic Toxicity/Carcinogenicity			No data located.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	**Amorphous silicon dioxide:** Amorphous silica is not classifiable as to its carcinogenicity to humans (Group 3: This category is used most commonly for agents for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals. Exceptionally, agents for which the evidence of carcinogenicity is inadequate in humans but sufficient in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans. Agents that do not fall into any other group are also placed in this category. An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations).	IARC, 1997	Summarized from a secondary source.
		Crystalline silicon dioxide: Crystalline silica inhaled in the form of quartz or cristobalite from occupational sources is carcinogenic to humans (Group 1: This category is used when there is sufficient evidence of carcinogenicity in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than	IARC, 1997	Summarized from a secondary source.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		sufficient but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity).		
Genotoxicity		**LOW: Based on the weight of evidence, amorphous silicon dioxide was negative both *in vitro* and *in vivo* gene mutation and chromosome aberration assays. If crystalline silicon dioxide is present, the hazard designation is assigned a HIGH based on weight of evidence from multiple studies. Crystalline silicon dioxide induced gene mutations *in vivo* and chromosomal aberrations in several *in vitro* and *in vivo* studies in experimental animals. In addition, crystalline silicon dioxide induced cell transformation in mice and hamsters *in vitro*.**		
	Gene Mutation *in vitro*	**Amorphous silicon dioxide:** Negative in *Escherichia coli* WP2 with and without metabolic activation. Test concentrations: 0.033 - 10 mg/plate, suspended in DMSO.	IARC, 1997; EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silcron G-190 (SCM Glidden): Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Negative in HGPRT assay in Chinese hamster ovary (CHO) cells with and without metabolic activation. Test concentrations: 10, 50, 100, 150, and 250 µg/mL (without S9) and 100, 200, 300, 400, and 500 µg/mL (with S9).	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Cab-O-Sil EH-5: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Negative in *Saccharomyces cerevisiae* strains TA98, TA100, TA1535, TA1537 and TA1538 with and without metabolic activation. Test concentrations: 667, 1,000, 3,333, 6,667, and 10,000 µg/plate	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silcron G-190 (SCM Glidden): Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Negative in *Salmonella typhimurium* and *Escherichia coli* mutagenicity assay.	IARC, 1987	Study details reported in a secondary source; test substance amorphous silica.
		Crystalline silicon dioxide: Direct treatment of rat lung epithelial cells with	IARC, 1987	Study details reported in a secondary source; test substance

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		quartz *in vitro* did not cause HPRT mutation.		crystalline silica.
		Crystalline silicon dioxide: Negative; *Salmonella typhimurium* reverse mutation assay (with or without metabolic activation)	EC, 2000b	Limited study details reported in a secondary source.
	Gene Mutation *in vivo*	**Amorphous silicon dioxide:** Negative; alveolar type-II cells isolated from rats exposed via whole body inhalation to 50-mg/m^3 Aerosil 200 showed no increased mutation frequency. Exposure was for 6 hours/day, 5 days/week for 13 weeks. Crystalline silica was examined simultaneously as a positive control.	ECHA, 2013	Sufficient study details reported in a secondary source. Aerosil 200: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: Negative, gene mutations in host mediated assay; male ICR mice orally gavaged with 1.4, 14, 140, 500 and 5,000 mg/kg suspended in 0.85 % saline and then injected with *Salmonella typhimurium* or *Saccharomyces cerevisiae*.	ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Crystalline silicon dioxide: Epithelial cells from the lungs of rats intratracheally exposed to quartz showed HPRT gene mutations.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
	Chromosomal Aberrations *in vitro*	**Amorphous silicon dioxide:** Negative for chromosomal aberrations in human embryonic lung cells (Wi-38) without metabolic activation. Test concentrations: 0.1, 1.0, and 10 µg/mL.	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Negative for chromosomal aberrations in CHO cells with and without metabolic activation; Test concentrations: 38, 75, 150, 300	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		µg/mL (without S9) and 250, 500, 750, 1,000 µg/mL (with S9).		
		Crystalline silicon dioxide: Tridymite induced sister chromatid exchange in co-cultures of human lymphocytes and monocytes.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
		Crystalline silicon dioxide: Induces micronuclei in Syrian hamster embryo cells, Chinese hamster lung V79 cells, and human embryonic lung Hel 299 cells *in vitro*, but negative for inducing chromosomal aberrations.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
		Crystalline silicon dioxide: Induced micronuclei in Syrian hamster embryo cells	EC, 2000b	Limited study details reported in a secondary source; route and duration of exposure were not specified.
	Chromosomal Aberrations *in vivo*	**Amorphous silicon dioxide:** Negative, chromosomal aberration dominant lethal assay in rats orally gavaged with 1.4, 14.0, 140, 500 and 5,000 mg/kg suspended in 0.85 % saline.	ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Crystalline silicon dioxide: Induced chromosomal aberrations in human peripheral blood lymphocytes following *in vivo* exposure to dust containing crystalline silica.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
		Crystalline silicon dioxide: Positive, induced sister chromatid exchange in human peripheral blood lymphocytes following *in vivo* exposure to dust containing crystalline silica.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
		Crystalline silicon dioxide: Quartz did not induce micronuclei in mice *in vivo*.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Crystalline silicon dioxide: Negative; did not cause sister chromatid exchange or aneuploidy in Syrian hamsters exposed to 2 µg *in vivo*.	EC, 2000b	Limited study details reported in a secondary source; route of administration, exposure duration was not specified.
		Crystalline silicon dioxide: Negative; did not cause sister chromatid exchanges in Chinese hamsters	EC, 2000b	Limited study details reported in a secondary source; route of administration and exposure duration were not specified.
		Crystalline silicon dioxide: DQ 12 quartz did not induce micronuclei in polychromatic erythrocytes of bone marrow of mice at 500 mg/kg bw.	EC, 2000b	Limited study details reported in a secondary source.
		Negative for chromosomal aberrations in two assays following single and subacute oral gavage administration to rats.	IARC, 1997	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report. Test substance unspecified silica.
	DNA Damage and Repair			No data located.
	Other	**Crystalline silicon dioxide:** Five quartz samples induced transformation in BALB/c-3T3 cells *in vitro*.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
		Crystalline silicon dioxide: Two quartz samples induced morphological transformation in Syrian hamster cells *in vitro*.	IARC, 1997	Study details reported in a secondary source; test substance crystalline silica.
		Negative, unscheduled DNA synthesis assay in primary rat hepatocytes.	EC, 2000a	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report. Test substance unspecified silica.
		Negative in two dominant lethal assays in rats following oral gavage administration.	EC, 2000a	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report. Test substance

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				unspecified silica.
Reproductive Effects		**LOW: There was no indication of adverse reproductive effects in an unpublished one-generation oral study in rats administered amorphous silica, fumed. It is estimated that crystalline silicon dioxide, if present, is not likely to produce reproductive effects based on analogy to amorphous silicon dioxide and professional judgment.**		
	Reproduction/Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	**Amorphous silicon dioxide:** In a one-generation oral dietary study, Wistar rats (5 females, 1 male/dose) were fed test substance at doses of 0, 497 mg/kg bw (males) or 509 mg/kg bw (females) in the diet daily. In parents: no clinical signs of toxicity, no mortality, no abnormalities in body-weight gain and feed consumption, no hematological findings. In pups: no behavioral or developmental/structural abnormalities. NOAEL (parental and offspring): 497 mg/kg-day (males); 509 mg/kg bw-day (females) (highest concentrations tested) LOAEL: Not established	EC, 2000a; ECHA, 2013	Significant methodological deficiencies, acceptable as screening. Aerosil, not further specified, hydrophilic: CAS-Name: Silica, amorphous, fumed, crystalline free (CASRN 112945-52-5).
	Other	**Crystalline silicon dioxide:** There is low potential for reproductive effects based on analogy to amorphous silicon dioxide. (Estimated by analogy)	Professional judgment	Estimated based on analogy to amorphous silicon dioxide and professional judgment; no experimental data located.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**LOW: Amorphous silicon dioxide did not produce adverse developmental effects in rats, mice, rabbits or hamsters following oral administration at doses up to 1,600 mg/kg bw-day during gestation. It is estimated that crystalline silicon dioxide, if present, is not likely to produce developmental effects based on analogy to amorphous silicon dioxide and professional judgment. There were no data located for the developmental neurotoxicity endpoint.**		
	Reproduction/ Developmental Toxicity Screen			No data located.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development	**Amorphous silicon dioxide:** Pregnant CD-1 mice (21-26 females/group) were administered Syloid 244 via oral gavage at doses of 0, 13.4, 62.3, 289 and 1,340 mg/kg bw-day from gestation days 6-15. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in controls. NOAEL (maternal and fetal): 1,340 mg/kg-day (highest dose tested) LOAEL: Not established	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Pregnant Wistar rats (20/25 females/group) were administered Syloid 244 via oral gavage at doses of 0, 13.5, 62.7, 292 and 1,350 mg/kg bw-day from gestation days 6-15. No observable effects on maternal or fetal survival or development. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		differ from the number occurring spontaneously controls. NOAEL (maternal and fetal): 1,350 mg/kg-day (highest dose tested) LOAEL: Not established		
		Amorphous silicon dioxide: Pregnant Dutch rabbits (10-14/dose) were administered Syloid 244 via oral gavage at doses of 0, 16.0, 74.3, 345 and 1,600 mg/kg bw-day from gestation days 6-18. No adverse effect on maternal or fetal survival. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in controls. NOAEL (maternal and fetal): 1,600 mg/kg bw-day (highest dose tested) LOAEL: Not established	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Pregnant Syrian hamsters (21-22 females/group) were administered Syloid 244 via oral gavage at doses of 0, 16.0, 74.3, 345 and 1,600 mg/kg bw-day from gestations days 6-10. The number of abnormalities seen in either soft or skeletal tissues of the test groups did not differ from the number occurring spontaneously in controls. NOAEL (maternal and fetal): 1,600 mg/kg-day (highest dose tested) LOAEL: Not established	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica gel, crystalline-free (CASRN 112926-00-8).
	Postnatal Development			No data located.
	Prenatal and Postnatal Development			No data located.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Developmental Neurotoxicity	No data were located for the developmental neurotoxicity endpoint.		No data located.
	Other	**Crystalline silicon dioxide:** There is low potential for developmental effects based on analogy to amorphous silicon dioxide. (Estimated by analogy)	Professional judgment	Estimated based on analogy to amorphous silicon dioxide and professional judgment; no experimental data located.
Neurotoxicity		**LOW: Both amorphous and crystalline silicon are estimated to have low potential for neurotoxic effects based on analogy to a similar compound and professional judgment.**		
	Neurotoxicity Screening Battery (Adult)			No data located.
	Other	Low potential for neurotoxic effects. (Estimated by analogy)	Professional judgment	Estimated for crystalline and amorphous silica based on analogy to a structurally similar chemical compound and professional judgment.
Repeated Dose Effects		**HIGH: Based on the weight of evidence, the hazard designation for both amorphous and crystalline silicon dioxide is High. Extended workplace exposure to amorphous and crystalline silica dust induced silicosis in humans. Effects on the lungs, such as increased weight, focal interstitial fibrosis, pulmonary inflammation and/or granuloma, macrophage accumulation, lesions in the bronchi, and hypertrophy/hyperplasia of the bronchiolar epithelium were observed following inhalation exposures to amorphous and crystalline silica dust or aerosol at concentrations as low as 0.001 mg/L in rats.**		
		Amorphous and crystalline silicon dioxide: Silicosis in humans following extended workplace exposure.	NIOSH, 1978a; NIOSH, 1978b	Test substance amorphous silica and crystalline silica.
		Amorphous silicon dioxide: 27-Month inhalation study, rabbit. Dyspnea, cyanosis, shortness of breath, emphysema, vascular stenosis, alveolar cell infiltration, sclerosis, granulomatous, lesions in the liver, spleen, and kidney. LOAEL: 28 mg/m^3 (0.028 mg/L)	EC, 2000a	Secondary source, test substance amorphous silica, study details, test concentrations, exposure protocol, and test conditions were not provided. The original study was in an unpublished report.
		Amorphous silicon dioxide: 1-Year inhalation study, rabbits. Progressive	EC, 2000a	Secondary source, test substance amorphous silica, study details and

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		functional incapacitation, emphysema, pulmonary vascular obstruction, blood pressure changes, mural cellular infiltration, peribronchiolar cellular catarrh, perivascular cellular nodules, ductal stenosis. LOAEL: <53 mg/m^3 (0.053 mg/L)		test conditions were not provided. The original study was in an unpublished report.
		Amorphous silicon dioxide: 13-Week inhalation study, rats. LOAEC: 1 mg/m^3 (0.001 mg/L), increased lung weight, focal interstitial fibrosis, pulmonary inflammation, and pulmonary granulomas.	Reuzel et al., 1991	Test substance amorphous silica; test concentrations and exposure protocol are unspecified.
		Amorphous silicon dioxide: In a 13-week inhalation study, Wistar rats (70/sex/dose) were exposed whole-body to SiO_2 at concentrations of 0, 1.3, 5.9 or 31 mg/m^3 6 hours/day, 5 days/week. Swollen and spotted lungs and enlarged mediastinal lymph nodes. Increased collagen content in the lungs (5.9 and 31 mg/m^3). Accumulation of alveolar macrophages and granular material, cellular debris, polymorphonuclear leucocytes, increased septal cellularity. Accumulation of macrophages was seen in the mediastinal lymph nodes. Treatment-related microscopic changes in the nasal region. NOAEC: 1.3 mg/m^3 (0.0013 mg/L) LOAEC: 5.9 mg/m^3 (0.0059 mg/L)	ECHA, 2013	Sufficient study details reported in a secondary source. Comparative study including Aerosil 200, Aerosil R 974 (pyrogenic, hydrophobic), Sipernat 22S (precipitated, hydrophilic) as well as quartz (crystalline silica at a concentration of 58 mg/m^3) as a positive control).
		Amorphous silicon dioxide: In a 13-week inhalation study, Wistar rats	ECHA, 2013	Sufficient study details reported in a secondary source. Comparative

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(70/sex/dose) were exposed whole-body to SiO_2 at concentrations of 0 or 35 mg/m^3 6 hours/day, 5 days/ week. Slight mean increase in relative lung weight. Swollen and spotted lungs and enlarged mediastinal lymph nodes. Accumulation of alveolar macrophages, intra-alveolar polymorphonuclear leukocytes, and increased septal cellularity. Treatment-related microscopic changes in the nasal region. Slightly increased collagen content in the lungs at the end of the exposure period. Changes were nearly all reversed during the recovery period. NOAEC: Not established LOAEC: 35 mg/m^3 (0.035 mg/L; only dose tested)		study including Aerosil 200, Aerosil R 974 (pyrogenic, hydrophobic), Sipernat 22S (precipitated, hydrophilic) as well as quartz (crystalline silica at a concentration of 58 mg/m^3) as a positive control.
		Amorphous silicon dioxide: In a 13-week inhalation study, male Fischer 344 rats were exposed whole body to Aerosil 200 dust at a concentration of 0 or 50 mg/m^3 for 6 hours/day, 5 days/week. Quartz (crystalline silica) was used as positive control. Invasion of neutrophils and macrophages into alveoli after both amorphous and crystalline silica exposure; more pronounced with the amorphous type after 6.5 weeks but decreased during post-exposure period. Fibrosis was present in the alveolar septae, but subsided during recovery. NOAEC: Not established LOAEC: 50 mg/m^3 (0.05 mg/L; only concentration tested)	ECHA, 2013	Sufficient study details reported in a secondary source. Aerosil 200: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Amorphous silicon dioxide: In 13 and 18 month inhalation studies, male monkeys (10/group) were exposed whole body to 15 mg/m^3 (total dust, pyrogenic and precipitated; 15.9 mg/m^3 total dust silica gel; 6.9 - 9.9 mg/m^3 (respirable fraction) for 6 hours/day, 5 days/week. Histopathological examination of the lung revealed Incipient fibrosis, inflammatory response: aggregation of great amounts of macrophages, physiological impairment of lung function. NOAEC: Not established LOAEC: ≈ 15 mg/m^3 (0.015 mg/L) (nominal; only dose tested) LOAEC (related to respirable fraction) ≥ 6 ≤ 9 mg/m^3 air (analytical)	ECHA, 2013	Sufficient study details reported in a secondary source. Three silica subclasses: Cab-O-Sil type (pyrogenic), named "fume" silica (Silica F), (CASRN 112945-52-5): commercial quality; Hi-Sil (precipitated): silica P (CASRN 112926-00-8) commercial quality; silica gel: silica G (CASRN 112926-00-8) commercial quality.
		Amorphous silicon dioxide: In a 14-day inhalation study, Wistar rats (40/sex/group) were exposed to Aerosil 200 at concentrations of 0, 17, 44 or 164 mg/m^3 for 6 hours/day, 5 days/week. Respiratory distress, increased lung weight, decreased kidney and liver weights, dose-dependent changes in lung characteristics (pale, spotted, spongy, alveolar interstitial pneumonia, early granulomata). NOAEL: Not established LOAEL: <17 mg/m^3 (<0.017 mg/L, lowest concentration tested)	EC, 2000a; ECHA, 2013	Secondary source, test substance identified as Aerosil 200: >99.8 % (SiO_2): CAS-Name: Silica, amorphous, fumed, crystalline-free; CASRN: 112945-52-5; limited study details and test conditions provided. The original study was in an unpublished report.
		Amorphous silicon dioxide: In a 14-day inhalation study, Wistar rats were exposed whole body to Sipernat 22S at	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. SIPERNAT 22S >98 % (SiO_2): CAS-Name: Silica,

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		concentrations of 46, 180 or 668 mg/m^3. Respiratory distress, increased lung weight, decreased liver weights, dose-dependent changes in lung characteristics (pale, spotted, spongy, alveolar interstitial pneumonia, early granulomata), accumulation of alveolar macrophages and particulate material in lungs. NOAEC: Not established LOAEC: <46 mg/m^3 (<0.046 mg/L, lowest concentration tested)		precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: In a 5-day inhalation study, male Wistar rats (10/dose) were exposed whole body to Syloid 74 at concentrations of 0, 1, 5, and 25 mg/m^3 for 6 hours/day. Quartz (crystalline silica) was examined as a positive control. Significant mean increase in lung weight, very slight hypertrophy of the bronchiolar epithelium, accumulation of alveolar macrophages accompanied by a few granulocytes/neutrophils at high dose. NOAEC: 5.13 mg/m^3 (0.00513 mg/L) LOAEC: 25.1 mg/m^3 (0.0251 mg/L)	ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 74, CAS-Name: Silica gel, crystalline-free (CASRN 112926-00-8), purity ca. 100%.
		Amorphous silicon dioxide: In a 5-day inhalation study, Wistar rats (10/sex/group) were exposed nose-only to Zeosil 45 aerosol at concentrations of 0, 1, 5, 25 mg/m^3 for 6 hours/day. Slight increases in lung weights of the high-dose group, increase in relative weights of tracheobronchial lymph nodes in females. Increased absolute numbers of	ECHA, 2013	Sufficient study details reported in a secondary source. ZEOSIL 45: CAS name, Silica, precipitated, crystalline-free (CASRN 112926-00-8); impurities: Na (1.9 %), S (0.8 %), Al (0.045 %), Fe (0.02 %), Ca 0.06 %.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		neutrophils, hypertrophy and hyperplasia of the bronchiolar epithelium at high dose. NOAEC: 5.39 mg/m^3 (0.00539 mg/L) LOAEC: 25.2 mg/m^3 (0.0252 mg/L)		
		Amorphous silicon dioxide: In a 5-day inhalation study, male Wistar rats (10/group) were exposed nose-only to CAB-O-SIL M5 at concentrations of 0, 1.39, 5.41 and 25 mg/m^3 for 6 hours/day. Significant mean increases in relative and absolute lung weights of the mid- and high-dose groups. Very slight hypertrophy of the bronchiolar epithelium (mid and high dose) and slight hypertrophy (high dose). Accumulation of alveolar macrophages accompanied by a few granulocytes/neutrophils (mid and high dose). Accumulation of macrophages accompanied by infiltration of polymorphonuclear leukocytes (high dose). Very slight macrophage accumulation still present following 3 months of recovery (high dose). NOEC: 1.39 mg/m^3 (0.00139 mg/L) LOAEC: 5.41 mg/m^3 (0.00541 mg/L)	ECHA, 2013	Sufficient study details reported in a secondary source. CAB-O-SIL M5: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5), purity ca. 100%.
		Amorphous silicon dioxide: In a 103 week study, Fischer 344 rats (40/sex/group) were fed Syloid 44 continuously in the diet at concentrations of 1.25, 2.5 and 5%. Interim sacrifice of 10/sex after 6 and 12 months. Reduced liver weight in females after 12 and 24 months is not considered to be treatment-	ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica, precipitated, crystalline-free (CASRN 112926-00-8).

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		related. There were no other treatment-related effects. NOAEL: 5% (~ 2,000 mg/kg bw-day for average of male and female; highest dose tested) LOAEL: Not established		
		Amorphous silicon dioxide: In a 93 week study, B6C3F1 mice (40/sex/dose) were fed Syloid 244 continuously in the diet at concentrations of 0, 1.25, 2.5 or 5%. Interim sacrifice of 10/sex after 6 and 12 months. Transient retardation in body weight gain was not biologically relevant. No other adverse treatment-related effects. NOAEL: 5% (4,500 or 5,800 mg/kg bw-day for average of male/female, respectively; highest dose tested) LOAEL: Not established	ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica, precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: In a 6-month study, Charles River rats (12/sex/group) were fed Syloid 244 in the diet daily at doses of 0, 2,170 and 7,950 mg/kg bw-day (males) or 0, 2,420 and 8,980 mg/kg bw-day (females). There were no treatment-related effects. Isolated pathological findings were not related to test substance. NOAEL: 7,950 mg/kg bw-day (males) or 8,980 mg/kg bw-day (females) (highest doses tested) LOAEL: Not established	ECHA, 2013	Sufficient study details reported in a secondary source. Syloid 244: Silica, precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: In a 13-	ECHA, 2013	Silica, amorphous, fumed,

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		week study, Charles River rats were fed Cab-O-Sil(fluffy) (>99 % SiO_2) continuously in the diet at concentrations of 1, 3, and 5% (mean estimated dose: 700, 2,100, and 3,500 mg/kg bw-day). No clinical signs of toxicity. No gross pathological or histopathological treatment-related changes. NOAEL: 5% (~ 3,500 mg/kg bw-day; highest dose tested) LOAEL: Not established		crystalline-free (CASRN 112945-52-5).
		Amorphous silicon dioxide: In a 13-week dietary study, Wistar rats (10/sex/dose) were fed SiO_2 continuously in the diet at concentrations of approximately 0, 0.05, 2 and 6.7% (mean estimated doses: 300-330, 1,200-1,400, 4,000-4,500 mg/kg-day). Slightly increased mean food intake at high dose, with no corresponding body weight gain. No clinical signs of toxicity or other findings (hematological, blood-chemical and urinary parameters). Gross and microscopic examination did not reveal any treatment-related changes. NOAEL: 6.7% (4,000-45,000 mg/kg bw-day (nominal, highest dose tested) LOAEL: Not established	ECHA, 2013	Sufficient study details reported in a secondary source. Silica, precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: Biogenic silica fibers induced ornithine decarboxylase activity of epidermal cells in mice following topical application.	IARC, 1997	Test substance amorphous silica.
		Crystalline silicon dioxide: 2-Year inhalation (whole body) study, rats	Rice, 2000; OECD SIDS, 2011	Test substance identified as crystalline silica (DQ-12 quartz,

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		(50/sex) exposed to air or 1 mg/m^3 6 hours/day, 5 days/week). Subpleural and peribronchial fibrosis, focal lipoproteinosis cholesterol clefts, enlarged lymph nodes, granulomatous lesions in the walls of large bronchi. LOAEL: 1 mg/m^3 (0.001 mg/L; only dose tested)		containing 74% respirable quartz.
		Crystalline silicon dioxide: Silicotic nodules with reticulin fibrosis was reported by day 220 and dense, rounded collagenous nodules were reported on day 300 in rats following inhalation exposure (18 hours/day, 5 days/week) of 30,000 particles/mL (40% < 0.5 microns) for up to 420 days.	EC, 2000b	Limited study details reported in a secondary source.
		Crystalline silicon dioxide: 6-Month inhalation study, rats. Increased collagen and elastin content in the lungs, induced type II cell hyperplasia in alveolar compartment and intralymphatic microgranulomas around bronchioles. NOAEL: Not established LOAEL: 2 mg/m^3 (0.002 mg/L)	Rice, 2000	Test substance identified as crystalline silica (quartz); test concentrations not specified.
		Crystalline silicon dioxide: 13-week inhalation study in male rats exposed to 0 or 3 mg/m^3 (6 hours/day, 5 days/week). Treated rats presented with pulmonary inflammation and fibrosis. NOAEL: Not established LOAEL: 3 mg/m^3 (0.003 mg/L; only dose tested)	OECD SIDS, 2011	Study details reported in a secondary source; test substance identified at cristobalite.
		Crystalline silicon dioxide: 4-week	OECD SIDS, 2011	Study details reported in a

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		inhalation study in female rats exposed to 0, 0.1, 1, or 10 mg/m^3 (6 hours/day, 5 days/week). Evaluation of bronchoalveolar lavage fluid occurred on weeks 1, 8, and 24 following exposure. Significantly increased levels of granulocytes and increased levels of lactate dehydrogenase and beta-glucuronidase were reported at 24 weeks post exposure at a concentration of 1 mg/m^3. NOAEL: 0.1 mg/m^3 (0.0001 mg/L) LOAEL: 1 mg/m^3 (0.001 mg/L)		secondary source; test substance identified at quartz.
		Crystalline silicon dioxide: 9-day inhalation study in mice Minimal interstitial thickening, accumulation of mononuclear cells, and slight lymphoid hypertrophy in the lungs were reported. NOAEL: Not established LOAEL: 10 mg/m^3 (0.01 mg/L)	OECD SIDS, 2011	Limited study details reported in a secondary source; test concentrations were not specified.
		Crystalline silicon dioxide: 3-day inhalation study in rats exposed to 0, 10, or 100 mg/m^3 of cristobalite (6 hours/day). Increased granulocytes and other markers of cytotoxicity from the lung lavage fluid were reported in all treated animals. NOAEL: Not established LOAEL: 10 mg/m^3 (0.01 mg/L; lowest dose tested)	OECD SIDS, 2011	Limited study details reported in a secondary source; test substance identified as cristobalite.
		14-Day oral dietary study, rats. No clinical signs or other findings.	EC, 2000a	Secondary source, test substance unspecified silica, study details and

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEL: 24,200 mg/kg-day (highest dose tested) LOAEL: Not established		test conditions were not provided. The original study was in an unpublished report.
		6-Month oral dietary study, rats. No clinical signs or other findings. NOAEL: 497 mg/kg-day (highest dose tested) LOAEL: Not established	EC, 2000a	Secondary source, test substance unspecified silica, study details and test conditions were not provided. The original study was in an unpublished report.
		13-Week oral dietary study, rats. No clinical signs or other findings. NOAEL: 8% diet (highest dose tested) LOAEL: Not established	EC, 2000a	Secondary source, test substance unspecified silica, study details and test conditions were not provided. The original study was in an unpublished report.
		Up to 1 year inhalation study, rats. Enlarged and discolored lymph nodes, perivascular and peribronchiolar dust cell granuloma, necrotic cells. NOAEL: Not established LOAEL: <0.045 mg/L (lowest concentration tested)	EC, 2000a	Secondary source, test substance unspecified silica, study details and test conditions were not provided. The original study was in an unpublished report.
		4-Week oral dietary study, dog. No clinical signs or other findings. NOAEL 800 mg/kg-day (highest dose tested) LOAEL: Not established	EC, 2000a	Secondary source, test substance unspecified silica, study details and test conditions were not provided. The original study was in an unpublished report.
		In a 3-week dermal study, SiO_2 was applied to the intact and abraded skin of rabbits (2/sex/group) at doses of 0, 5,000, 10,000 mg/kg bw-day (nominal) for 18 hours/day, 5 days/week. No evidence of systemic toxicity or of gross or	ECHA, 2013	Unassignable. 21-Day dermal exposure study using a prolonged daily exposure regimen (18 h/d, 5 d/wk) instead of 6 h/d. Test substance form not specified.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		microscopic pathology. NOAEL: ≥ 10,000 mg/kg bw-day (highest dose tested) LOAEL: Not established		
	Immune System Effects	**Amorphous silicon dioxide:** In a 12-month study, male Hartley Guinea pigs (20/dose) were exposed whole body to concentrations of 15 mg/m^3 (total dust, pyrogenic and precipitated); 15.9 mg/m^3 (total dust silica gel) and 6.9 - 9.9 mg/m^3 (respirable <4.7 µm) for 5.5 - 6 hours/day, 5 days/week. A few macrophages containing particles of amorphous silica were observed in the lungs and lymph nodes. NOAEC: ≥ 6 ≤ 9 mg/m^3 (≥ 0.006 ≤ 0.009 mg/L) LOAEC: Not established	ECHA, 2013	Sufficient study details reported in a secondary source. Three silica subclasses: Cab-O-Sil type (pyrogenic), named "fume" silica (Silica F), (CASRN 112945-52-5): commercial quality; Hi-Sil (precipitated): silica P (CASRN 112926-00-8) commercial quality; silica gel: silica G (CASRN 112926-00-8) commercial quality.
		Crystalline silicon dioxide: 15- or 27-week inhalation study in mice exposed to 0 or 5 mg/m^3 (6 hours/day, 5 days/week). Increased spleen weight and formation of plaque in the spleen was reported. NOAEL: Not established LOAEL: 5 mg/m^3 (0.005 mg/L; only dose tested)	OECD SIDS, 2011	Study details reported in a secondary source; test substance identified as quartz.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Amorphous silicon dioxide was not a dermal sensitizer in guinea pigs or humans. No experimental data were located for crystalline silicon dioxide. It is estimated that crystalline silicon dioxide, if present, is not likely to be a skin sensitizer based on analogy to amorphous silicon dioxide and professional judgment.**		
	Skin Sensitization	**Amorphous silicon dioxide:** Not sensitizing in a guinea pig maximization test.	EC, 2000a	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report.
		Amorphous silicon dioxide: Not sensitizing, humans (occupational surveys)	ECHA, 2013	Not assignable (no further details). Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5) or Silica gel, precipitated, crystalline-free. (CASRN 112926-00-8).
		Crystalline silicon dioxide: There is low potential for skin sensitization based on analogy to amorphous silicon dioxide. (Estimated by analogy)	Professional judgment	Estimated based on analogy to amorphous silicon dioxide and professional judgment; no experimental data located.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Amorphous silicon dioxide was not irritating to slightly irritating in rabbits and slightly irritating in humans. If present, crystalline silicon dioxide would be assigned a Moderate hazard designation based on a study reporting fibrotic nodules in rabbit eyes.**		
	Eye Irritation	**Amorphous silicon dioxide:** Slightly irritating, rabbits	EC, 2000a	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report.
		Amorphous silicon dioxide: Slightly irritating, humans	EC, 2000a	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report.
		Amorphous silicon dioxide: Not irritating, rabbits (several studies)	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silica, precipitated, crystalline-free

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
				(CASRN 112926-00-8) or Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).
		Crystalline silicon dioxide: Quartz was reported to cause fibrotic nodules in rabbit eyes.	EC, 2000b	Limited study details reported in a secondary source; the severity and duration of the irritation was not specified. Irritation may be a result of mechanical mechanisms and scratching of the eye.
Dermal Irritation		**VERY LOW: Amorphous silicon dioxide was not irritating to the skin of rabbits or humans. No experimental data was located for crystalline silicon dioxide for this endpoint. It is estimated that crystalline silicon dioxide, if present, is not likely to be a skin irritant based on analogy to amorphous silicon dioxide and professional judgment.**		
	Dermal Irritation	**Amorphous silicon dioxide:** Not irritating, rabbits (several studies)	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. Silica, precipitated, crystalline-free (CAS-No. 112926-00-8) or Silica, amorphous, fumed, crystalline-free (CAS-No. 112945-52-5).
		Amorphous silicon dioxide: Not irritating, humans	EC, 2000a	Secondary source, study details and test conditions were not provided. The original study was in an unpublished report.
		Crystalline silicon dioxide: There is low potential for skin irritation based on analogy to amorphous silicon dioxide. (Estimated by analogy)	Professional judgment	Estimated based on analogy to amorphous silicon dioxide and professional judgment; no experimental data located.
Endocrine Activity		**No data located.**		
				No data located.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Subjects that develop silicosis following exposure to crystalline silica have increased numbers of macrophages in the lungs. Effects on the lungs, such as inflammatory response, accumulation of alveolar macrophages, and infiltration of polymorphonuclear leukocytes were observed following inhalation exposures to amorphous and crystalline silica dust or aerosols in experimental animals.**		
	Immune System Effects	**Amorphous silicon dioxide:** In a 5-day inhalation study, male Wistar rats (10/group) were exposed nose-only to CAB-O-SIL M5 at concentrations of 0, 1.39, 5.41 and 25 mg/m^3 for 6 hours/day. Accumulation of alveolar macrophages accompanied by a few granulocytes/neutrophils (mid and high dose). Accumulation of macrophages accompanied by infiltration of polymorphonuclear leukocytes (high dose). Very slight macrophage accumulation still present following 3 months of recovery (high dose). NOAEC: 1.39 mg/m^3 (0.00139 mg/L) LOAEC: 5.41 mg/m^3 (0.00541 mg/L)	ECHA, 2013	Sufficient study details reported in a secondary source. CAB-O-SIL M5: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5), purity ca. 100%.
		Amorphous silicon dioxide: In a 13-week inhalation study, male Fischer 344 rats were exposed whole body to Aerosil 200 dust at a concentration of 0 or 50 mg/m^3 for 6 hours/day, 5 days/week. Quartz (crystalline silica) was used as positive control. Invasion of neutrophils and macrophages into alveoli after both amorphous and crystalline silica exposure; it was more pronounced with the amorphous type after 6.5 weeks but decreased during post-exposure period. Fibrosis was present in the alveolar septae, but subsided during recovery.	ECHA, 2013	Sufficient study details reported in a secondary source. Aerosil 200: Silica, amorphous, fumed, crystalline-free (CASRN 112945-52-5).

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		NOAEC: Not established LOAEC: 50 mg/m^3 (0.05 mg/L; lowest concentration tested)		
		Amorphous silicon dioxide: In a 13-week inhalation study, Wistar rats (70/sex/dose) were exposed whole-body to SiO_2 at concentrations of 0, 1.3, 5.9 or 31 mg/m^3 6 hours/day, 5 days/week. Swollen and spotted lungs and enlarged mediastinal lymph nodes. Accumulation of alveolar macrophages and granular material, cellular debris, polymorphonuclear leucocytes, increased septal cellularity. Accumulation of macrophages was seen in the mediastinal lymph nodes. Treatment-related microscopic changes in the nasal region. NOAEC: 1.3 mg/m^3 (0.0013 mg/L) LOAEC: 5.9 mg/m^3 (0.0059 mg/L)	ECHA, 2013	Sufficient study details reported in a secondary source. Comparative study including Aerosil 200, Aerosil R 974 (pyrogenic, hydrophobic), Sipernat 22S (precipitated, hydrophilic) as well as quartz (crystalline silica at a concentration of 58 mg/m3 was used as a positive control).
		Amorphous silicon dioxide: In a 13-week inhalation study, Wistar rats (70/sex/dose) were exposed whole-body to SiO_2 at concentrations of 0 or 35 mg/m^3 6 hours/day, 5 days/ week. Swollen and spotted lungs and enlarged mediastinal lymph nodes. Accumulation of alveolar macrophages, intra-alveolar polymorphonuclear leukocytes, and increased septal cellularity. NOAEC: Not established LOAEC: 35 mg/m^3 (0.035 mg/L; lowest concentration tested)	ECHA, 2013	Sufficient study details reported in a secondary source. Comparative study including Aerosil 200, Aerosil R 974 (pyrogenic, hydrophobic), Sipernat 22S (precipitated, hydrophilic) as well as quartz (crystalline silica at a concentration of 58 mg/m^3 was used as a positive control).
		Amorphous silicon dioxide: In a 14-Day inhalation study, Wistar rats were	EC, 2000a; ECHA, 2013	Sufficient study details reported in a secondary source. SIPERNAT 22S

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		exposed whole body to Sipernat 22S at concentrations of 46, 180 or 668 mg/m^3. Dose-dependent changes in lung characteristics (pale, spotted, spongy, alveolar interstitial pneumonia, early granulomata), accumulation of alveolar macrophages and particulate material in lungs. NOAEC: Not established LOAEC: <46 mg/m^3 (<0.046 mg/L; lowest concentration tested)		>98 % (SiO_2): CAS-Name: Silica, precipitated, crystalline-free (CASRN 112926-00-8).
		Amorphous silicon dioxide: In a 12-month study, male Hartley Guinea pigs (20/dose) were exposed whole body to concentrations of 15 mg/m^3 (total dust, pyrogenic and precipitated); 15.9 mg/m^3 (total dust silica gel) and 6.9 - 9.9 mg/m^3 (respirable ≤4.7 µm) for 5.5 - 6 hours/day, 5 days/week. A few macrophages containing particles of amorphous silica were observed in the lungs and lymph nodes. NOAEC: ≥ 6 ≤ 9 mg/m^3 (≥ 0.006 ≤ 0.009 mg/L) LOAEC: Not established	ECHA, 2013	Sufficient study details reported in a secondary source. Three silica subclasses: Cab-O-Sil type (pyrogenic), named "fume" silica (Silica F), (CASRN 112945-52-5): commercial quality; Hi-Sil (precipitated): silica P (CASRN 112926-00-8) commercial quality; silica gel: silica G (CASRN 112926-00-8) commercial quality.
		Amorphous silicon dioxide: In 13 and 18 month inhalation studies, male monkeys (10/group) were exposed whole body to 15 mg/m^3 (total dust, pyrogenic and precipitated); 15.9 mg/m^3 (total dust silica gel); and 6.9 - 9.9 mg/m^3 (respirable <4.7 µm) for 6 hours/day, 5 days/week. Inflammatory response: aggregation of great amounts of macrophages,	ECHA, 2013	Sufficient study details reported in a secondary source. Three silica subclasses: Cab-O-Sil type (pyrogenic), named "fume" silica (Silica F), (CASRN 112945-52-5): commercial quality; Hi-Sil (precipitated): silica P (CASRN 112926-00-8) commercial quality; silica gel: silica G (CASRN 112926-

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		physiological impairment of lung function. NOAEC: Not established LOAEC: ca. 15 mg/m^3 (0.015 mg/L) (nominal, lowest concentration tested)		00-8) commercial quality.
		Crystalline silicon dioxide: Human subjects with silicosis have increased macrophages and lymphocytes in the lungs, but minimal increases in neutrophils.	IARC, 1997	Test substance crystalline silica.
		Crystalline silicon dioxide: Exposure of rats to high concentrations of quartz leads to recruitment of neutrophils, marked persistent inflammation, and proliferative responses of the epithelium.	IARC, 1997	Test substance crystalline silica.
		Crystalline silicon dioxide: *In vitro* studies show that crystalline silica can stimulate the release of cytokines and growth factors from macrophages and epithelial cells; some evidence exists that these effects occur *in vivo* (species not specified).	IARC, 1997	Test substance crystalline silica.
		Crystalline silicon dioxide: Crystalline silica results in inflammatory cell recruitment in a dose-dependent manner (species not specified).	IARC, 1997	Test substance crystalline silica.
		Crystalline silicon dioxide: Crystalline silica deposited in the lungs causes macrophage injury and activation (species not stated).	IARC, 1997	Test substance crystalline silica.
		Crystalline silicon dioxide: 15- or 27-week inhalation study in mice exposed to 0 or 5 mg/m^3 (6 hours/day, 5 days/week). Increased spleen weight and formation of	OECD SIDS, 2011	Study details reported in a secondary source; test substance identified as quartz.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		plaque in the spleen was reported. NOAEL: Not established LOAEL: 5 mg/m^3 (0.005 mg/L; only dose tested)		
ECOTOXICITY				
ECOSAR Class		Not applicable		
Acute Aquatic Toxicity		**LOW: Amorphous silicon dioxide experimental LC_{50} and EC_{50} values for fish, daphnia and green algae are all >100 mg/L. The large MW, limited bioavailability and low water solubility suggest there will be no effects at saturation (NES). It is estimated by professional judgment that crystalline forms of silicon dioxide will also have low acute aquatic toxicity based on analogy to amorphous silicon dioxide. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.**		
Fish LC_{50}		**Amorphous silicon dioxide:** Freshwater fish *Brachydanio rerio* 96-hour LC_{50} = 5,000 mg/L (Experimental)	EC, 2000a	Secondary source; test substance form, study details and test conditions were not provided.
		Amorphous silicon dioxide: Freshwater fish *Brachydanio rerio* 96-hour LC_{50} >10,000 mg/L; static test conditions; nominal concentrations: 1,000 and 10,000 mg/L (Experimental)	ECHA, 2013	Sufficient study details reported in a secondary source. GLP guideline study. Data are for amorphous silica.
		Amorphous and crystalline silicon dioxide: Freshwater fish LC_{50} >100 mg/L (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.

Silicon dioxide (amorphous) CASRN 7631-86-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	**Amorphous silicon dioxide:** *Daphnia magna* 24-hour effect level based on mobility EL_{50} >10,000 mg/L (Experimental)	ECHA, 2013	Sufficient study details reported in a secondary source. Guideline study with acceptable restrictions (24 h instead of 48 h). Data are for Silica, amorphous.
	Amorphous silicon dioxide: *Ceriodaphnia dubia* EC_{50} ≈ 7,600 mg/L (Experimental)	EC, 2000a	Secondary source; test substance form, study details and test conditions were not provided. The original study was in an unpublished report.
	Amorphous and crystalline silicon dioxide: *Daphnia magna* LC_{50} >100 mg/L (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.
Green Algae EC_{50}	**Amorphous silicon dioxide:** Green algae *Selenastrum capricornutum* EC_{50} = 440 mg/L (Experimental)	EC, 2000a	Secondary source; test substance form, study details and test conditions were not provided. The original study was in an unpublished report.
	Amorphous and crystalline silicon dioxide: Green algae EC_{50} >100 mg/L (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.

Silicon dioxide (amorphous) CASRN 7631-86-9			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**LOW: No experimental chronic data were located. The large MW, limited bioavailability and low water solubility suggest there will be no effects at saturation (NES). It is estimated by professional judgment that crystalline forms of silicon dioxide will also have low chronic aquatic toxicity based on large MW, limited bioavailability and low water solubility suggesting there will be no effects at saturation (NES). For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.**		
Fish ChV	**Amorphous and crystalline silicon dioxide:** Freshwater fish ChV >10 mg/L (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.
Daphnid ChV	**Amorphous and crystalline silicon dioxide:** Daphnia magna ChV >10 mg/L (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.
Green Algae ChV	**Amorphous and crystalline silicon dioxide:** Green algae ChV >10 mg/L (Estimated)	Professional judgment	The large MW, limited bioavailability and low water solubility suggest there will be NES. For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building some cell walls, skeletal structures or shells.
ENVIRONMENTAL FATE			

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Transport		**Silicon dioxide is a component of sand, soil, and sediment. Silicon dioxide has low water solubility and as a solid, it is expected to have a negligible estimated vapor pressure; these two factors correspond to an expected low Henry's Law constant. Amorphous forms of silicon dioxide will be relatively immobile in the environment with the exception of silicon dioxide dust in the atmosphere. Crystalline forms of silicon dioxide are expected to behave similarly in the environment and be relatively immobile with the exception of dust particulates.**		
	Henry's Law Constant (atm-m^3/mole)	**Amorphous and crystalline silicon dioxide:** $<10^{-8}$ (Estimated)	Professional judgment	Cutoff value for nonvolatile compounds based on professional judgment. This substance contains inorganic compounds that are outside the estimation domain of EPI.
	Sediment/Soil Adsorption/Desorption - K_{oc}	**Amorphous and crystalline silicon dioxide:** Not applicable (Estimated)	Professional judgment	As a component of sand, soil, and sediment, the soil-water partition coefficient is not applicable for silicon dioxide.
	Level III Fugacity Model			No data located.
Persistence		**HIGH: Amorphous silicon dioxide is expected to have high persistence in the environment because silicon dioxide is a recalcitrant, fully oxidized, inorganic substance and therefore will not biodegrade, oxidize in air, or undergo hydrolysis under environmental conditions. Silicon dioxide does not absorb light at environmentally relevant wavelengths and is not expected to photolyze. No degradation processes for silicon dioxide, under typical environmental conditions, were identified. It is also estimated that in the environment crystalline forms of silicon dioxide will behave similarly and have high persistence based on professional judgment.**		
Water	**Aerobic Biodegradation**	**Amorphous and crystalline silicon dioxide:** Recalcitrant (Estimated)	Professional judgment; OECD SIDS, 2004a	
	Volatilization Half-life for Model River	>1 year for both amorphous and crystalline silicon dioxide (Estimated)	Professional judgment	
	Volatilization Half-life for Model Lake	>1 year for both amorphous and crystalline silicon dioxide (Estimated)	Professional judgment	
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	**Amorphous and crystalline silicon dioxide:** Recalcitrant (Estimated)	Professional judgment	

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PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	**Amorphous and crystalline silicon dioxide:** >1 year (Estimated)	Professional judgment	
Reactivity	**Photolysis**	**Amorphous and crystalline silicon dioxide:** Not a significant fate process (Estimated)	Professional judgment	Silicon dioxide does not absorb UV light at environmentally relevant wavelengths and is not expected to undergo photolysis.
	Hydrolysis	**Amorphous and crystalline silicon dioxide:** >1 year (Estimated)	Professional judgment	Silicon dioxide is a fully oxidized, insoluble, inorganic material and is not expected to undergo hydrolysis.
Environmental Half-life				Not all input parameters for this model were available to run the estimation software (EPI). This substance contains inorganic compounds that are outside the estimation domain of EPI.
Bioaccumulation		**LOW: Amorphous silicon dioxide is not expected to bioaccumulate based on professional judgment. Also based on professional judgment crystalline forms of silicon dioxide are not expected to bioaccumulate. Although for some organisms in marine habitats, silica and silicates are used as nutrients. They are used for building some cell walls, skeletal structures or shells.**		
	Fish BCF	**Amorphous and crystalline silicon dioxide:** <100 (Estimated)	Professional judgment	This inorganic compound is not amenable to available estimation methods.
	Other BCF	For some organisms in marine habitats, silica and silicates are used as nutrients; they are used for building skeletal structures or shells. For example, diatoms absorb soluble silica from water and metabolize it for an external skeleton.	EC, 2000b; OECD SIDS, 2004a; HSDB, 2009	Supporting information about the bioaccumulation of this compound in marine environments. Some organisms in marine habitats use silica and silicates as nutrients; they are used for building some cell walls, skeletal structures or shells.

Silicon dioxide (amorphous) CASRN 7631-86-9				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	BAF	**Amorphous and crystalline silicon dioxide:** <100 (Estimated)	Professional judgment	This inorganic compound is not amenable to available estimation methods.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Silicon dioxide is a ubiquitous mineral that occurs naturally in the environment as sand and quartz (HSDB, 2009).		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		No data located.		

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