

SCREENING-LEVEL HAZARD CHARACTERIZATION Dithiophosphate Alkyl Esters Category

Sponsored Chemicals

Subcategory 1

Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters
CASRN 84605-28-7

Phosphorodithioic acid, mixed O,O-bis(isobutyl and pentyl) esters
CASRN 68516-01-8

Phosphorodithioic acid, mixed O,O-bis(secbutyl and 1,3-dimethylbutyl) esters
CASRN 68784-30-5

Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isopropyl) esters
CASRN 68909-92-2

Phosphorodithioic acid, 2-ethylhexyl 2-methylpropyl ester
CASRN 68389-47-9

2-Pentanol, 4-methyl-hydrogen phosphorodithioate
CASRN 6028-47-3

Subcategory 2

Phosphorodithioic acid mixed O,O-bis(secbutyl and isooctyl) mixed esters
CASRN 113706-14-2

Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isobutyl) esters
CASRN 68784-32-7

Subcategory 3

Phosphorodithioic acid, O,O-dioctyl ester, branched
CASRN 68649-43-4

Phosphorodithioic acid, O,O-bis(2-ethylhexyl) esters
CASRN 5810-88-8

Phosphorodithioic acid, O,O-diisooctyl ester
CASRN 26999-29-1

The High Production Volume (HPV) Challenge Program¹ was conceived as a voluntary initiative aimed at developing and making publicly available screening-level health and

¹ U.S. EPA. High Production Volume (HPV) Challenge Program; <http://www.epa.gov/chemrtk/index.htm>.

environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year. In the Challenge Program, producers and importers of HPV chemicals voluntarily sponsored chemicals; sponsorship entailed the identification and initial assessment of the adequacy of existing toxicity data/information, conducting new testing if adequate data did not exist, and making both new and existing data and information available to the public. Each complete data submission contains data on 18 internationally agreed to “SIDS” (Screening Information Data Set^{1,2}) endpoints that are screening-level indicators of potential hazards (toxicity) for humans or the environment.

The Environmental Protection Agency’s Office of Pollution Prevention and Toxics (OPPT) is evaluating the data submitted in the HPV Challenge Program on approximately 1400 sponsored chemicals by developing hazard characterizations (HCs). These HCs consist of an evaluation of the quality and completeness of the data set provided in the Challenge Program submissions. They are not intended to be definitive statements regarding the possibility of unreasonable risk of injury to health or the environment.

The evaluation is performed according to established EPA guidance^{2,3} and is based primarily on hazard data provided by sponsors; however, in preparing the hazard characterization, EPA considered its own comments and public comments on the original submission as well as the sponsor’s responses to comments and revisions made to the submission. In order to determine whether any new hazard information was developed since the time of the HPV submission, a search of the following databases was made from one year prior to the date of the HPV Challenge submission to the present: (ChemID to locate available data sources including Medline/PubMed, Toxline, HSDB, IRIS, NTP, ATSDR, IARC, EXTTOXNET, EPA SRS, etc.), STN/CAS online databases (Registry file for locators, ChemAbs for toxicology data, RTECS, Merck, etc.) and Science Direct. OPPT’s focus on these specific sources is based on their being of high quality, highly relevant to hazard characterization, and publicly available.

OPPT does not develop HCs for those HPV chemicals which have already been assessed internationally through the HPV program of the Organization for Economic Cooperation and Development (OECD) and for which Screening Initial Data Set (SIDS) Initial Assessment Reports (SIAR) and SIDS Initial Assessment Profiles (SIAP) are available. These documents are presented in an international forum that involves review and endorsement by governmental authorities around the world. OPPT is an active participant in these meetings and accepts these documents as reliable screening-level hazard assessments.

These hazard characterizations are technical documents intended to inform subsequent decisions and actions by OPPT. Accordingly, the documents are not written with the goal of informing the general public. However, they do provide a vehicle for public access to a concise assessment of the raw technical data on HPV chemicals and information previously not readily available to the public.

² U.S. EPA. HPV Challenge Program – Information Sources; <http://www.epa.gov/chemrtk/pubs/general/guidocs.htm>.

³ U.S. EPA. Risk Assessment Guidelines; <http://cfpub.epa.gov/ncea/raf/rafguid.cfm>.

Chemical Abstract Service Registry Number (CASRN)	See Section 1
Chemical Abstract Index Name	See Section 1
Structural Formula	See Section 1
Summary	
<p>The substances in the dithiophosphate alkyl esters category are amber colored viscous liquids with moderate to high water solubility and low to moderate vapor pressure. The substances in this category are expected to possess low to moderate mobility in soil. Volatilization is expected to be low since these compounds are expected to dissociate in water and exist as anions under environmental conditions and anions do not volatilize. The rate of atmospheric photooxidation is considered rapid. The rate of hydrolysis was shown to be negligible at pH 7 for a single category member; however, structurally similar thiophosphate pesticides are known to undergo hydrolysis under alkaline conditions. The weight of evidence suggests that the members of this category have moderate (P2) to high (P3) persistence. These category members are expected to have low bioaccumulation potential (B1), with the exception of CASRNs 68649-43-4 and 68909-92-2, which may have moderate (B2) bioaccumulation potential.</p> <p>No acute/repeated-dose/reproductive/developmental/genetic toxicity or skin and eye irritation data are available for any category member, with the exception of CASRN 84605-28-7, which did not induce gene mutations or chromosomal aberrations <i>in vitro</i>.</p> <p>Subcategory 1:</p> <p>For the low-range molecular weight subcategory I chemicals, the 96-hour LC₅₀ to fish is 9.2 mg/L and the 48-hour EC₅₀ for aquatic invertebrates ranges from 0.25 – 0.62 mg/L, based on RA data from CASRN 68649-43-4. The estimated 96-hour EC₅₀ for aquatic plants is 10.71 mg/L from the representative chemical CASRN 68909-92-2. The aquatic plant toxicity remains as a data gap.</p> <p>Subcategory 2:</p> <p>For the mid-range molecular weight subcategory 2 chemicals, the 96-hour LC₅₀ to fish is 9.2 mg/L and the 48-hour EC₅₀ for aquatic invertebrates ranges from 0.25 – 0.62 mg/L, based on RA data from CASRN 68649-43-4. The estimated 96-hour EC₅₀ for aquatic plants is 5.74 mg/L from the representative chemical CASRN 68784-32-7. The aquatic plant toxicity remains as a data gap.</p> <p>Subcategory 3:</p> <p>For the high-range molecular weight subcategory 3 chemicals, the measured 96-hour LC₅₀ to fish is 9.2 mg/L and the measured 48-hour EC₅₀ for aquatic invertebrates ranges from 0.25 – 0.62 mg/L, using the data from CASRN 68649-43-4. The estimated 96-hour EC₅₀ for aquatic plants is 0.76 mg/L, and the estimated 21-day chronic toxicity to aquatic invertebrates is 0.0001 mg/L from the representative chemical 68649-43-4. Aquatic plant toxicity and chronic invertebrate</p>	

toxicity endpoints remain as data gaps.

Acute oral, repeated-dose, reproductive, and developmental toxicity studies have been identified as data gaps under the HPV Challenge Program.

The sponsor, American Chemistry Council (ACC) Health, Environmental, and Research Task Group (HERTG), submitted a Test Plan and Robust Summaries to EPA for dithiophosphate alkyl esters on November 12, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on November 27, 2002

(<http://www.epa.gov/oppt/chemrtk/pubs/summaries/dithipae/c14065tc.htm>). EPA comments on the original submission were posted to the website on April 1, 2003. Public comments were also received and posted to the website. The sponsor submitted updated/revised documents on November 10, 2003 and December 22, 2005, which were posted to the ChemRTK website on December 3, 2003 and February 3, 2006 respectively.

Category Justification

The sponsor proposed the dithiophosphate alkyl esters as a category containing nine members based on a common functionality and limited structural variation. All members of the category are highly acidic and are within a narrow molecular weight range (256 – 354 daltons). The category has been divided into molecular weight range subcategories. Estimated physical property values suggest that the dithiophosphate alkyl esters will have low vapor pressure and water solubilities and high octanol/water partition coefficients. EPA agrees that the category is justified. However, EPA also recommends that, for aquatic toxicity endpoints, data are needed for at least three chemicals representing the low-, mid- and high-end ranges of the category and, for human health effects endpoints, data are needed for at least two chemicals representing the molecular weight range of the category. Moreover, genetic toxicity testing should be done with one lower- and one mid- or high-range chemical. Therefore, a read-across approach can be performed only among category members of comparable molecular weight or weight ranges for all environmental and human health effects endpoints. Since the time of the original submission by the sponsor, two additional dithiophosphate alkyl esters identified through the 2002 TSCA IUR as being HPV chemicals have been added to the category. These chemicals are: phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isopropyl) ester (CASRN 68909-92-2) and phosphorodithioic acid, 2-ethylhexyl 2-methylpropyl ester (CASRN 68389-47-9). A Peer Consultation Pilot Review Panel determined that the addition of these chemicals to the category was reasonable (see <http://www.tera.org/Peer/HPV/index.html>).

The sponsor proposed reduced health testing for these compounds based on their corrosive nature and on the claim that dithiophosphate alkyl esters are closed-system intermediates (CSIs). EPA's evaluation of the original information indicated insufficient evidence to support both of these claims and has determined that the chemical does not qualify for reduced testing. Therefore, EPA has concluded that data for repeated-dose and reproductive/developmental toxicity endpoints are needed for the purposes of the HPV Challenge Program.

The sponsor proposed the use of phosphorodithioic acid, mixed O,O-bis(isobutyl and isoctyl and pentyl) esters (no CASRN provided) as a supporting chemical for human health effects. In its original 2002 submission, the sponsor provided a robust summary for a study on the acute dermal toxicity endpoint using a chemical identified as phosphorodithioic acid, mixed O,O-bis(isobutyl and isoctyl and pentyl) esters, zinc salts (no CASRN). EPA determined that the use of this chemical was inappropriate for health effects evaluation as the sponsor failed to indicate whether or how the presence of zinc contributes to its toxicity.

In the 2005 submission, the sponsor provided the same robust summary for acute dermal toxicity as before, but indicated that they had previously submitted the study with the incorrect chemical name and that the actual name of the chemical tested was phosphorodithioic acid, mixed O,O-bis(isobutyl and isooctyl and pentyl) esters (no CASRN).

Although the use of this chemical, in the absence of zinc, would be acceptable as a supporting chemical on the basis of structural similarity with the sponsored category members, EPA has noted that this study appears to be both qualitatively and quantitatively identical to that reported in the robust summary for the acute dermal toxicity of phosphorodithioic acid, mixed O,O-bis(isobutyl and isooctyl and pentyl) esters, zinc salts (CASRN 68988-46-5) in the sponsor's zinc dialkyldithiophosphate category submission. EPA decided the data for this chemical in support of human health effects are considered to be inadequate. Therefore, studies submitted on this chemical in support of the category were not used in this hazard characterization.

1 Chemical Identity

1.1 Identification and Purity

The following is taken from the 2002 Test Plan and 2005 Robust Summary:

Substances in this category consist of a phosphorodithioic acid structure with alkyl ester substituent groups. The alkyl groups are saturated hydrocarbon chains that vary in length and extent of branching; the alkyl side chain may vary in length from C3 to C8. These substances are prepared by reacting phosphorous pentasulfide with one or more primary or secondary alcohols to form the phosphorodithioic acid ester. Residual phosphorus pentasulfide is removed and stored as a closed system intermediate. Test substance purity was noted in the Robust Summary as 'not provided'. The chemical structures of the dithiophosphate alkyl esters are depicted in Table 1.

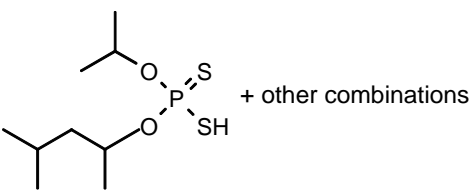
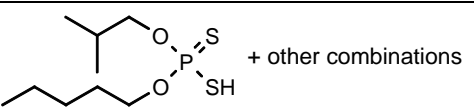
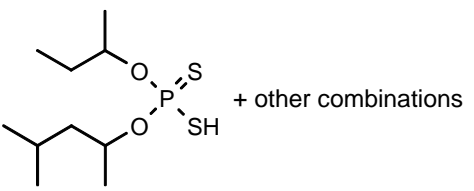
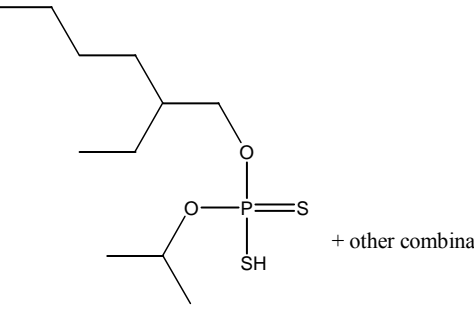
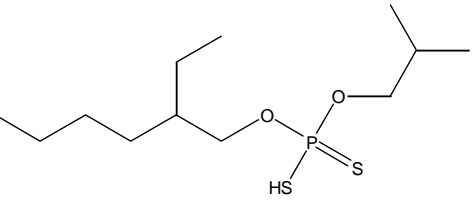
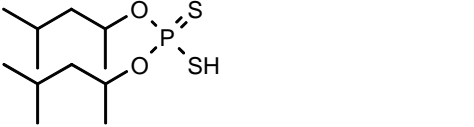
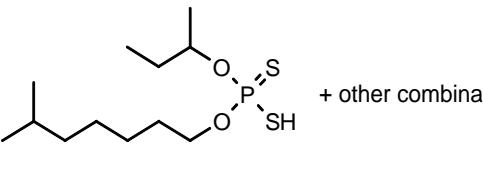
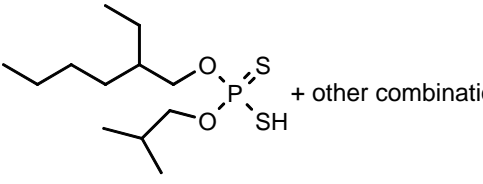
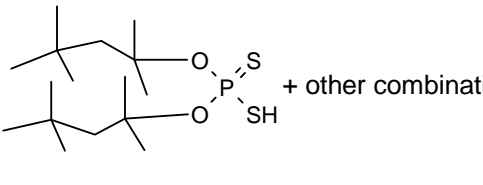
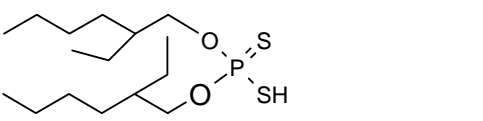
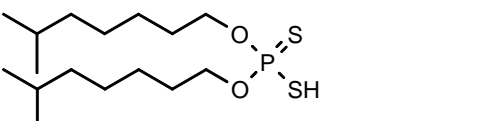
Table 1. Dithiophosphate Alkyl Esters Category Sponsored Chemical Structures in Estimated Lowest to Highest Molecular Weight Order			
Sponsored Chemicals			
Chemical Abstract Index Name	Molecular Weight	CASRN	Structure
Subcategory 1			
Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters	256	84605-28-7	 + other combinations
Phosphorodithioic acid, mixed O,O-bis(isobutyl and pentyl) esters	256	68516-01-8	 + other combinations
Phosphorodithioic acid, mixed O,O-bis(secbutyl and 1,3-dimethylbutyl) esters	270	68784-30-5	 + other combinations
Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isopropyl) esters	282	68909-92-2	 + other combinations
Subcategory 2			
Phosphorodithioic acid, 2-ethylhexyl 2-methylpropyl ester	296	68389-47-9	
2-Pentanol, 4-methyl-, 2-(hydrogen phosphorodithioate)	298	6028-47-3	

Table 1. Dithiophosphate Alkyl Esters Category Sponsored Chemical Structures in Estimated Lowest to Highest Molecular Weight Order			
Sponsored Chemicals			
Chemical Abstract Index Name	Molecular Weight	CASRN	Structure
Phosphorodithioic acid, mixed O,O-bis(secbutyl and isoctyl) esters	298	113706-14-2	 + other combinations
Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isobutyl) esters	298	68784-32-7	 + other combinations
Subcategory 3			
Phosphorodithioic acid, O,O-diioctyl ester, branched	354	68649-43-4	 + other combinations
Phosphorodithioic acid, O,O-bis(2-ethylhexyl) ester	354	5810-88-8	
Phosphorodithioic acid, O,O-diisoctyl ester	354	26999-29-1	

1.2 Physical-Chemical Properties

The physical-chemical properties of the dithiophosphate alkyl esters category are summarized in Table 2.

The substances in the dithiophosphate alkyl esters category are amber colored viscous liquids with moderate to high water solubility and low to moderate vapor pressure.

Table 2. Physical -Chemical Properties of the Dithiophosphate Alkyl Esters Category¹

Property	Phosphoro-dithioic acid, mixed O,O-bis (1,3-dimethyl-butyl and isopropyl) esters	Phosphoro dithioic acid, mixed O,O-bis (isobutyl and pentyl) esters	Phosphoro dithioic acid, mixed,O,O-bis (secbutyl and 1,3-dimethyl-butyl) esters	Phosphoro dithioic acid, mixed O,O-bis (2-ethyl-hexyl and isopropyl) esters	Phosphoro dithioic acid, mixed O,O-bis (secbutyl and isoocetyl) esters	2-Pentanol, 4-methyl-, 2-(hydrogen phosphorodithioate)	Phosphoro dithioic acid, mixed O,O-bis (2-ethylhexyl and isobutyl) esters	Phosphoro-dithioic acid, 2-ethyl hexyl 2-methyl-propyl ester	Phosphoro dithioic acid, O,O-diocetyl ester, branched	Phosphorodithioic acid, O,O-bis (2-ethyl hexyl) ester	Phosphoro dithioic acid, O,O-diisooctyl ester
CASRN	84605-28-7	68516-01-8	68784-30-5	68909-92-2	113706-14-2	6028-47-3	68784-32-7	68389-47-9	68649-43-4	5810-88-8	26999-29-1
Molecular Weight	256	256	270	284	298	298	298	298	354	354	354
Physical State	Amber colored viscous liquids										
Melting Point	Not applicable (liquids)										
Boiling Point (°C) ⁶	289 (est.)	307 (est.)	304 (est.)	326 (est.)	339 (est.)	323 (est.)	339 (est.)	339 (est.)	353 (est.)	385 (est.)	385 (est.)
Vapor Pressure (mm Hg)	3.46×10 ⁻³ (est.)	1.34×10 ⁻³ (est.)	1.57×10 ⁻³ (est.)	4.84×10 ⁻⁴ (est.)	2.46×10 ⁻⁴ (est.)	5.6×10 ⁻⁴ (est.)	2.46×10 ⁻⁴ (est.)	2.46×10 ⁻⁴ (est.)	1.13×10 ⁻⁴ (est.)	1.9×10 ⁻⁵ (est.)	1.9×10 ⁻⁵ (est.)
Dissociation Constant (pK _a) ²	1.78 (est.)	1.77 (est.)	1.77 (est.)	1.76 (est.)	1.77 (est.)	1.78 (est.)	1.77 (est.)	1.77 (est.)	1.76 (est.)	1.77 (est.)	1.79 (est.)
Henry's Law Constant (atm·m ³ /mol) ^{3,4}	<1×10 ⁻¹⁰ (est.)										
Water Solubility (mg/L)	19,200 at 20°C	6,978 (est.) ^{4,5} (estimated) ^{4,5}	6,003 (est.) ^{4,5} (estimated) ^{4,5}	1,063 (est.) ^{4,5} (estimated) ^{4,5}	334 (est.) ^{4,5} (estimated) ^{4,5}	936 (est.) ^{4,5} (estimated) ^{4,5}	334 (est.) ^{4,5} (estimated) ^{4,5}	334 (est.) ^{4,5} (estimated) ^{4,5}	36 (est.) ^{4,5} (estimated) ^{4,5}	2.8 (est.) ^{4,5} (estimated) ^{4,5}	2.8 (est.) ^{4,5} (estimated) ^{4,5}
Log K _{ow} ^{3,4}	1.0 (est.)	1.92 (est.)	2.27 (est.)	2.83 (est.)	3.32 (est.)	3.18 (est.)	3.32 (est.)	3.32 (est.)	4.99 (est.)	5.29 (est.)	5.29 (est.)

Note: the estimated values are for the mixed ester where applicable; statistically, this would be the major component of the mixture.

¹American Chemistry Council Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTGT). December 5, 2005. Revised Robust Summary and Test Plan for Dithiophosphate Alkyl Esters Category. <http://www.epa.gov/chemrtk/pubs/summaries/dithipae/c14065tc.htm>.

²SPARC. 2008. Online pK_a and Property Calculator v. 4.2.1405-s4.2.1408. Accessed December 8, 2008. <http://ibmlc2.chem.uga.edu/sparc/>.

³U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v3.20. United States Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

⁴These estimates were performed using an ionized structure since these compounds are expected to exist as anions in solution and estimates for these properties will be more accurate using the conjugate base (ionized species) as opposed to the fully protonated acidic form.

⁵The WATERNT v.1.01 program contained in the EPIWIN suite was used for these estimations, along with the measured water solubility obtained for phosphorodithioic acid, mixed O,O-bis(1, 3-dimethyl and isopropyl) esters (CASRN 84605-28-7) for the experimental value adjustment.

⁶For reference, boiling point values were obtained from Beilstein for Phosphorodithioic acid, O,O-diisopropyl ester of 71-72°C at 3 torr (which NOMO5 converts to 213°C at 760 torr), for Phosphorodithioic acid, O,O-dibutyl ester of 108-110°C at 3 torr (which NOMO5 converts to 269°C at 760 torr), and for Phosphorodithioic acid, O,O-diisobutyl ester of 93°C at 4 torr (which NOMO5 converts to 234°C at 760 torr). The chemicals are representative of the low weight components for some of the mixed esters in the table above.

2 General Information on Exposure

2.1 Production Volume and Use Pattern

Eight of the 11 dithiophosphate alkyl esters category chemicals had aggregated production and/or import volumes in the United States during calendar year 2005 between 25.5 and 151 million pounds. This aggregated volume range excludes CASRNs 113706-14-2, 68649-43-4 and 68784-32-7, which do not have IUR submissions.

- CASRN 68389-47-9 1-10 million pounds
- CASRN 68909-92-2 1-10 million pounds
- CASRN 84605-28-7 10-50 million pounds
- CASRN 68784-30-5 1-10 million pounds
- CASRN 6028-47-3 10-50 million pounds
- CASRN 68516-01-8 1-10 million pounds
- CASRN 5810-88-8 1-10 million pounds
- CASRN 26999-29-1 500,000-1 million pounds

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemicals include intermediates and lubricants. Non-confidential information in the IUR indicated that the commercial and consumer products containing the chemicals include lubricants, greases, and fuel additives. The HSDB for CASRN 5810-88-8 states that the chemical was formerly a lubricating oil additive and rust inhibitor. The HPV and eHPV submissions for the dithiophosphate alkyl esters category states that the chemicals are primarily used by lubricant additive manufacturers as reaction intermediates to produce components for lubricating oils such as the zinc dialkyldithiophosphates.

2.2 Environmental Exposure and Fate

There is potential for environmental releases to various media including water, land and air.

The environmental fate properties are provided in Table 3. The substances in this category are expected to possess low to moderate mobility in soil. No biodegradation data are available for the substances in this category; however, data provided for phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters, zinc salts (CASRN 84605-29-8) and phenol, dodecyl-, hydrogen phosphorodithiolate, zinc salt (CASRN 54261-67-5) suggest the substances in this category are not readily biodegradable. Furthermore, a structurally similar compound O,O-diethyl dithiophosphate (CASRN 298-06-6) was not readily biodegradable using a modified MITI test (OECD 301C). Volatilization is expected to be low since these compounds are expected to dissociate in water and exist as anions under environmental conditions and anions do not volatilize. The rate of hydrolysis was shown to be negligible at pH 7 for phosphorodithioic acid, O,O-bis(2-ethylhexyl) ester (CASRN 5810-88-8); however, structurally similar thiophosphate pesticides are known to undergo hydrolysis under alkaline conditions. The rate of atmospheric photooxidation is expected to be rapid. The category members in the dithiophosphate alkyl esters are expected to have moderate (P2) to high (P3) persistence. These category members are expected to have low bioaccumulation potential (B1), with the exception

of phosphorodithioic acid, O,O-dioctyl ester, branched (CASRN 68649-43-4), and phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isopropyl) esters (CASRN 68909-92-2) which may have moderate (B2) bioaccumulation potential.

Table 3. Environmental Fate Characteristics of the Dithiophosphate Alkyl Esters Category¹

Property	Phosphoro-dithioic acid, mixed O,O-bis (1,3-dimethylbutyl and isopropyl) esters	Phosphoro dithioic acid, mixed O,O-bis (isobutyl and pentyl) esters	Phosphoro dithioic acid, mixed,O,O-bis (secbutyl and 1,3-dimethylbutyl) esters	Phosphoro dithioic acid, mixed O,O-bis (2-ethylhexyl and isopropyl) esters	Phosphoro dithioic acid, mixed O,O-bis (secbutyl and isoocetyl) esters	2-Pentanol, 4-methyl-, 2-(hydrogen phosphorodithioate)	Phosphoro dithioic acid, mixed O,O-bis (2-ethylhexyl and isobutyl) esters	Phosphoro-dithioic acid, 2-ethyl hexyl 2-methyl-propyl ester	Phosphoro dithioic acid, O,O-dioctyl ester, branched	Phosphoro dithioic acid, O,O-bis (2-ethyl hexyl) ester	Phosphoro dithioic acid, O,O-diisooctyl ester
CASRN	84605-28-7	68516-01-8	68784-30-5	68909-92-2	113706-14-2	6028-47-3	68784-32-7	68389-47-9	68649-43-4	5810-88-8	26999-29-1
Molecular Wt.	256	256	270	284	298	298	298	298	354	354	354
Photodegradation Half-life	0.877 hours (est.)	1.216 hours (est.)	0.832 hours (est.)	1.021 hours (est.)	0.948 hours (est.)	0.805 hours (est.)	1.147 hours (est.)	1.147 hours (est.)	2.23 hours (est.)	1.086 hours (est.)	1.098 hours (est.)
Biodegradation	<ul style="list-style-type: none"> 5.9% after 28 days (not readily biodegradable). Data provided for phosphorodithioic acid, mixed O,O-bis(1, 3-dimethylbutyl and isopropyl) esters, zinc salts (CASRN 84605-29-8) and phenol, dodecyl-, hydrogen phosphorodithiolate, zinc salt (CASRN 54261-67-5); 1% after 28 days (not readily biodegradable). Data provided for O,O-diethyl dithiophosphate (CASRN 298-06-6)² 										
Hydrolysis	Stable at pH 7 and room temperature										
Log K _{oc} ^{3,4}	2.7 (est.)	2.8 (est.)	2.9 (est.)	3.3 (est.)	3.5 (est.)	3.4 (est.)	3.6 (est.)	3.6 (est.)	4.0 (est.)	4.7 (est.)	4.7 (est.)
Bioconcentration ^{3,4}	BCF = 5 (est.)	BCF = 6 (est.)	BCF = 11 (est.)	BCF = 3,630 (est.)	BCF = 72 (est.)	BCF = 56 (est.)	BCF = 71 (est.)	BCF = 71 (est.)	BCF = 1,388 (est.)	BCF = 236 (est.)	BCF = 236 (est.)
Fugacity (Level III Model) ^{3,4}											
Air (%)	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	0.1	0.1	<0.1	0.1	0.1
Water (%)	27.4	23.8	19.0	18.6	14.3	14.5	19.1	19.1	4.1	14.5	14.5
Soil (%)	72.5	76.1	80.9	81.2	85.0	85.0	80.2	80.2	76.5	54.9	54.9
Sediment (%)	0.1	0.1	0.1	0.2	0.7	0.5	0.6	0.6	19.4	30.4	30.4
Persistence ⁵	P2 to P3 (moderate to (high))										
Bioaccumulation ⁵	B1 (low)	B1 (low)	B1 (low)	B2 (moderate)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B2 (moderate)	B1 (low)	B1 (low)

Note: the estimated values are for the mixed ester where applicable; statistically, this would be the major component of the mixture.

¹American Chemistry Council Petroleum Additives Panel Health, Environmental, and Regulatory Task Group (HERTG). December 5, 2005. Revised Robust Summary and Test Plan for Dithiophosphate Alkyl Esters Category. <http://www.epa.gov/chemrtk/pubs/summaries/dithipae/c14065tc.htm>.

²National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html.

³U.S. EPA. 2008. Estimation Programs Interface Suite™ for Microsoft® Windows, v3.20. United States Environmental Protection Agency, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.htm>.

⁴These estimates were performed using an ionized structure since these compounds are expected to exist as anions in solution and estimates for these properties will be more accurate using the conjugate base (ionized species) as opposed to the fully protonated acidic form.

⁵Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

3 Human Health Hazard

A summary of the available health effects data submitted for SIDS endpoints is provided in Table 4. Data are only available for genetic toxicity endpoints. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Acute Oral/Dermal/Inhalation Toxicity

Subcategories 1/2/3: Low-, Mid-, and High-Range Molecular Weight

No data are available.

Repeated-Dose/Reproductive/Developmental Toxicity

Subcategories 1/2/3: Low-, Mid-, and High-Range Molecular Weight

No data are available.

Genetic Toxicity – Gene Mutation

Subcategory 1: Low-Range Molecular Weight

In vitro

Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters (CASRN 84605-28-7)

Salmonella typhimurium strains TA98, TA100, TA102, TA1535 and TA1537 were exposed to phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters at 0, 50, 150, 500, 1500 or 5000 µg/plate in the presence and absence of metabolic activation. No cytotoxicity was observed. An oily precipitate was observed at concentrations ≥ 1500 µg/plate, but this did not prevent the scoring of plates. Positive and negative controls were included and responded appropriately.

Phosphorodithioic acid mixed O,O-bis(isobutyl and isooctyl and pentyl) esters was not mutagenic in this assay.

Subcategories 2 and 3: Mid- and High-Range Molecular Weight

No data are available.

Genetic Toxicity – Chromosomal Aberrations

Subcategory 1: Low-Range Molecular Weight

In vitro

Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters (CASRN 84605-28-7)

Human peripheral blood lymphocytes were exposed to phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters at concentrations of 0 – 1250 or 0 – 937.5 µg/plate in the presence and absence of metabolic activation, respectively, over the course of two experiments. In experiment one, lymphocytes were exposed for 4 hours both with and without metabolic activation and given a 20-hour harvest time. In experiment two, lymphocytes were exposed for 24 hours with a 0-hour harvest without activation or for 4 hours with a 20-hour harvest with activation. In the pretest toxicity assay, a precipitate of the test material was observed in parallel blood free cultures at the end of exposure at concentrations ≥ 1250 µg/mL under all exposure conditions. Toxicity was observed under all exposure conditions. Positive and vehicle controls were included and responded appropriately in both experiments.

Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters did not induce chromosomal aberrations in this assay.

Subcategories 2 and 3: Mid- and High-Range Molecular Weight

No data are available.

Additional Information

Skin and Eye Irritation

Subcategories 1/2/3: Low-, Mid-, and High-Range Molecular Weight

No data are available.

Conclusion:

Subcategory 1: Low-Range Molecular Weight

Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters (CASRN 84605-28-7) was not mutagenic in an in vitro assay conducted in bacterial cells and did not induce chromosomal aberrations in human peripheral blood lymphocytes *in vitro*. The acute oral, repeated-dose, reproductive and developmental toxicity endpoints remain as data gaps.

Subcategories 2 and 3: Mid- and High-Range Molecular Weight

The potential human health hazard could not be evaluated because no data were available. The acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints remain as data gaps.

Conclusion: No acute/repeated-dose/reproductive/developmental/genetic toxicity or skin and eye irritation data are available for any category member, with the exception of CASRN 84605-28-7, which did not induce gene mutations or chromosomal aberrations *in vitro*.

Table 4. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Summary of Human Health

Endpoints	Subgroup 1 Low-range Molecular Weight (Carbon numbers: C6 – C12; C8 – 10; C8 – 12; C12)				Subgroup 2 Mid-range Molecular Weight (Carbon number range: C8 – 16)				Subgroup 3 High-range Molecular Weight (Carbon number: C16)		
	Phosphoro dithioic acid, mixed O,O-bis(1, 3-di- methylbut yl and iso- propyl) esters	Phosphoro dithioic acid, mixed O,O-bis(is o-butyl and pentyl) esters	Phosphoro dithioic acid, mixed O,O-bis(se c-butyl and 1,3-dimeth ylbutyl) esters	Phosphorodi thioic acid, mixed O,O- bis(2-ethyl- hexyl and iso-Pr) esters	2- Pentanol, 4-methyl- hydrogen phosphor odithioate	Phosphorodi thioic acid, 2-ethylhexyl 2-methyl- propyl ester	Phosphoro- dithioic acid, mixed O,O-bis(sec- butyl and isooctyl) mixed esters	Phosphoro dithioic acid, mixed O,O-bis(2- ethylhexyl and iso- butyl) esters	Phosphoro dithioic acid, O,O- dioctyl ester, branched	Phosphoro dithioic acid, O,O-bis(2- ethylhexyl) esters	Phosphoro- dithioic acid, O,O-diisooctyl ester
CASRN	84605-28-7	68516-01-8	68784-30-5	68909-92-2	6028-47-3	68389-47-9	113706-14-2	68784-32-7	68649-43-4	5810-88-8	26999-29-1
Acute Oral toxicity LD₅₀ (mg/kg-bw)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Repeated-Dose Toxicity NOAEL/ LOAEL Oral (mg/kg-bw/day)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Reproductive Toxicity NOAEL/ LOAEL Oral (mg/kg- bw/day)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No data	No Data	No Data	No data
Developmental Toxicity NOAEL/ LOAEL Oral (mg/kg- bw/day)	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No data	No data	No data
Genetic Toxicity- Gene Mutation <i>In vitro</i>	Negative	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data	No Data	No Data	No Data	No Data	No Data	No Data
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	Negative	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data	No Data	No Data	No Data	No Data	No Data	No Data

Measured data in bold text; (RA) = Read Across

4 Hazards to the Environment

Environmental Effects – Aquatic Toxicity

A summary of aquatic toxicity data submitted for SIDS endpoints is provided in Table 5. The table also indicates where data for tested category members are read-across (RA) to untested members of the category.

Three aquatic toxicity studies (acute fish and invertebrate toxicity and toxicity to aquatic plants) were provided by the sponsor on the sponsored chemical, CASRN 84605-28-7. However, all of these studies were performed using the water accommodated fraction method at concentrations that appear to be below saturation. The sponsor reported a measured water solubility of 19,000 mg/L at 20 °C. The highest WAF concentration used in each of the aquatic toxicity studies was 100 mg/L. These three studies are unacceptable for use in this hazard characterization without a proper explanation of why the substance was insoluble at 100 mg/L given the very high measured water solubility reported.

Acute Toxicity to Fish

Subcategory I and 2: Low-and mid-range Molecular Weights

There are no data available. RA from CASRN 68649-43-4 is used.

Subcategory 3: High-range Molecular Weight

Phosphorodithioic acid, O,O-dioctyl ester, branched (CAS No. 68649-43-4)

Fathead minnows (*Pimephales promelas*) were exposed to phosphorodithioic acid, O,O-dioctyl ester, branched at nominal concentrations of 0.1, 1, 5 or 10 mg/L under static conditions for 96 hours. A dilution water control and solvent control (0.1 mL dimethylformamide/L) were included. Observations of stress or mortality were made at 6, 24, 48, 72 and 96 hours. Temperature, dissolved oxygen and pH were measured at 0, 24, 48, 72 and 96 hours. This study summary is from a TSCATS submission (OTS0570825).

96-h LC₅₀ = 9.2 mg/L

96-h NOEC = 5 mg/L

Acute Toxicity to Aquatic Invertebrates

Subcategory I and 2: Low-and mid-range Molecular Weights

There are no data available. RA from CASRN 68649-43-4 is used.

Subcategory 3: High-range Molecular Weight

Phosphorodithioic acid, O,O-dioctyl ester, branched (CAS No. 68649-43-4)

(1) Water fleas (*Daphnia magna*) were exposed to phosphorodithioic acid, O,O-dioctyl ester, branched at nominal concentrations of 0.16, 0.32, 0.63, 1.25, 2.50 or 5.00 mg/L under static

conditions for 48 hours. A dilution water control and solvent control (0.5 mL dimethylformamide/L) were included. Dissolved oxygen, pH, alkalinity, hardness and temperature were monitored at test initiation and conclusion. This study summary is from a TSCATS submission (OTS0546283).

48-h EC₅₀ = 0.62 mg/L

(2) Water fleas (*Daphnia magna*) were exposed to phosphorodithioic acid, O,O-dioctyl ester, branched at nominal concentrations of 0.1, 1, 5 or 10 mg/L under static conditions for 48 hours. A dilution water control and solvent control (0.1 mL dimethylformamide/L) were included. Temperature, dissolved oxygen and pH were measured at 0, 24 and 48 hours. Animals were observed for both immobilization and mortality. This study summary is from a TSCATS submission (OTS0570825).

48-h EC₅₀ = 0.25 – 0.32 mg/L

48-h NOEC = 0.1 mg/L

Toxicity to Aquatic Plants

Subcategory 1: Low-range Molecular Weight

There are no data available. A 96-hour EC₅₀ for aquatic plants on CASRN 68909-92-2, estimated by ECOSAR (v. 1.00a), is provided to evaluate the aquatic toxicity of these chemicals.

Algae 96-h EC₅₀ = 10.71 mg/L (e)

Subcategory 2: Mid-range Molecular Weight

There are no data available. A 96-hour EC₅₀ for aquatic plants on CASRN 68389-47-9, estimated by ECOSAR (v. 1.00a), is provided to evaluate the aquatic toxicity of these chemicals.

Algae 96-h EC₅₀ = 5.74 mg/L (e)

Subcategory 3: High-range Molecular Weight

There are no data available. A 96-hour EC₅₀ for aquatic plants on CASRN 68649-43-4, estimated by ECOSAR (v. 1.00a), is provided to evaluate the aquatic toxicity of these chemicals.

Algae 96-h EC₅₀ = 0.69 mg/L (e)

Chronic Toxicity to Aquatic Invertebrates

There are no data available. A 21-day chronic toxicity to aquatic invertebrates on CASRN 68649-43-4, estimated by ECOSAR (v. 1.00a), is provided to evaluate the chronic toxicity of these chemicals.

Daphnia 21-d ChV = 0.0001 mg/L (e)

Conclusion:

Subcategory 1: Low-range Molecular Weight

For the low-range molecular weight subcategory 1 chemicals, the 96-hour LC₅₀ to fish is 9.2 mg/L and the 48-hour EC₅₀ for aquatic invertebrates ranges from 0.25 – 0.62 mg/L, based on RA data from CASRN 68649-43-4. The estimated 96-hour EC₅₀ for aquatic plants is 10.71 mg/L from the representative chemical CASRN 68909-92-2. The aquatic plant toxicity remains as a data gap.

Subcategory 2: Mid-range Molecular Weight

For the mid-range molecular weight subcategory 2 chemicals, the 96-hour LC₅₀ to fish is 9.2 mg/L and the 48-hour EC₅₀ for aquatic invertebrates ranges from 0.25 – 0.62 mg/L, based on RA data from CASRN 68649-43-4. The estimated 96-hour EC₅₀ for aquatic plants is 5.74 mg/L from the representative chemical CASRN 68784-32-7. The aquatic plant toxicity remains as a data gap.

Subcategory 3: High-range Molecular Weight

For the high-range molecular weight subcategory 3 chemicals, the measured 96-hour LC₅₀ to fish is 9.2 mg/L and the measured 48-hour EC₅₀ for aquatic invertebrates ranges from 0.25 – 0.62 mg/L, using the data from CASRN 68649-43-4. The estimated 96-hour EC₅₀ for aquatic plants is 0.76 mg/L, and the estimated 21-day chronic toxicity to aquatic invertebrates is 0.0001 mg/L from the representative chemical 68649-43-4. Aquatic plant toxicity and chronic invertebrate toxicity endpoints remain as data gaps.

Endpoints	Subgroup 1 Low-range Molecular Weight (Carbon numbers: C6 – C12; C8 – 10; C8 – 12; C12)				Subgroup 2 Mid-range Molecular Weight (Carbon number range: C8 – 16)				Subgroup 3 High-range Molecular Weight (Carbon number: C16)		
	Phosphorodithioic acid, mixed O,O-bis(1,3-dimethylbutyl and isopropyl) esters	Phosphorodithioic acid, mixed O,O-bis(isobutyl and pentyl) esters	Phosphorodithioic acid, mixed O,O-bis(sec-butyl and 1,3-dimethylbutyl) esters	Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and iso-Pr) esters	2-Pentanol, 4-methylhydrogen phosphorodithioate	Phosphorodithioic acid, 2-ethylhexyl 2-methylpropyl ester	Phosphorodithioic acid, mixed O,O-bis(sec-butyl and isoctyl) mixed esters	Phosphorodithioic acid, mixed O,O-bis(2-ethylhexyl and isobutyl) esters	Phosphorodithioic acid, O,O-diethyl ester, branched	Phosphorodithioic acid, O,O-bis(2-ethylhexyl) esters	Phosphorodithioic acid, O,O-diisooctyl ester
CASRN	84605-28-7	68516-01-8	68784-30-5	68909-92-2	6028-47-3	68389-47-9	113706-14-2	68784-32-7	68649-43-4	5810-88-8	26999-29-1
Fish 96-h LC ₅₀ (mg/L)	Inadequate Data 9.2 (RA)	No Data 9.2 (RA)	No Data 9.2 (RA)	No Data 9.2 (RA)	No Data 9.2 (RA)	No Data 9.2 (RA)	No Data 9.2 (RA)	No Data 9.2 (RA)	9.2 (m) 0.03 (e)	No Data 9.2 (RA)	No Data 9.2 (RA)
Aquatic Invertebrates 48-h EC ₅₀ (mg/L)	Inadequate Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)	.25-0.62 (m) 0.001 (e)	No Data 0.25-0.62 (RA)	No Data 0.25-0.62 (RA)
Aquatic Plants 96-h EC ₅₀ (mg/L)	Inadequate Data 40.66 (e)	No Data 33.56 (e)	No Data 21.92 (e)	No Data 10.71 (e)	No Data 6.96 (e)	No Data 5.74 (e)	No Data 5.74 (e)	No Data 5.74 (e)	No Data 0.69 (e)	No Data 0.46 (e)	No Data 0.46 (e)
Chronic Toxicity to Invertebrates 21-day EC ₅₀ (mg/L)	—	—	—	—	—	—	—	—	No Data 0.0001 (e)	No Data 0.0001 (e)	No Data 0.0001 (e)

(m) = measured data (i.e., derived from testing); (RA) = Read Across; — = endpoint is not required to be addressed

Testing is recommended on one low-range molecular weight compound.

Testing is recommended on one mid-range molecular weight compound.

Algae and chronic aquatic invertebrates' toxicity tests are recommended on one high-range molecular weight compound.