

SCREENING-LEVEL HAZARD CHARACTERIZATION

Bicyclic Terpene Hydrocarbons Category

SPONSORED CHEMICALS

(See Section 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 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, EXTOXNET, 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

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

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>.

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 provide information previously not readily available to the public.

<p>Chemical Abstract Service Registry Number (CASRN)</p>	<p>80-56-8 127-91-3 79-92-5 6876-13-7 473-55-2 7785-26-4 65996-96-5 65996-97-6 9005-90-7 8006-64-2</p>
<p>Chemical Abstract Index Name</p>	<p>See Section 1</p>
<p>Structural Formula</p>	<p>See Section 1</p>
<p style="text-align: center;">Summary</p> <p>Members of the bicyclic terpene hydrocarbons category are liquids, with the exception of CASRN 79-92-5, which forms colorless crystals at room temperature. The bicyclic terpene hydrocarbons have low to moderate water solubility and high vapor pressure. The bicyclic terpene hydrocarbons are expected to have moderate mobility in soil. Volatilization of the bicyclic terpene hydrocarbons is considered high based on their Henry's Law constants. The bicyclic terpene hydrocarbons are not expected to hydrolyze since these substances lack functional groups that hydrolyze under environmental conditions. The rate of atmospheric photooxidation is considered rapid to moderate. The chemicals in the bicyclic terpene hydrocarbons category are expected to have low persistence (P1) and low (B1) to moderate (B2) bioaccumulation potential.</p> <p>Members of the bicyclic terpene hydrocarbons category exhibit low acute toxicity via oral (rats) and dermal (rabbits) routes and moderate acute toxicity via inhalation (rats, mice and guinea pigs). In a 28-day oral repeated-dose toxicity study, rats treated with CASRN 79-92-5 showed vacuolization and increased liver weights in both sexes at 1000 mg/kg-day; the NOAEL for systemic toxicity is 250 mg/kg-day. A 14-week inhalation study with CASRN 80-56-8 in rats showed significant mortality (6/10) and organ weight changes in females treated at 400 ppm; the NOAEC for systemic toxicity is 200 ppm. A 14-week inhalation study with CASRN 80-56-8 in mice showed increased (absolute/relative) liver weights at concentrations ≥ 200 ppm and epithelial hyperplasia in the urinary bladder at concentrations ≥ 100 ppm; the NOAEC for systemic toxicity is 50 ppm. No specific reproductive toxicity data are available; however, no adverse effects were observed in the reproductive organs (ovaries, uterus, epididymides, seminal vesicles, testes) of rats or mice in the 14-week inhalation studies with CASRN 80-56-8. An oral prenatal developmental toxicity study with CASRN 80-56-8 showed no maternal or developmental effects in hamsters at 600 mg/kg-day (highest doses tested); the NOAEL for maternal/developmental toxicity is 600 mg/kg-day. Oral prenatal developmental toxicity studies with CASRN 80-56-8 in rats and mice showed no maternal effects, but a decrease in the number of live offspring was observed in rats and mice at 56 and 120 mg/kg-day, respectively. In rats, the NOAEL for maternal toxicity is 260 mg/kg-day (highest dose tested) and the NOAEL for</p>	

developmental toxicity is 12 mg/kg-day. In mice, the NOAEL for maternal toxicity is 560 mg/kg-day (highest dose tested) and the NOAEL for developmental toxicity is 26 mg/kg-day. An oral prenatal developmental toxicity study in rats showed increased resorptions in dams exposed to CASRN 79-92-5 at 1000 mg/kg-day (highest dose tested); the NOAELs for maternal and developmental toxicity are 1000 and 250 mg/kg-day, respectively. The bicyclic terpene hydrocarbons are irritating to rabbit skin and eyes. Skin irritation and allergic contact dermatitis have been reported in patients patch tested with CASRN 8006-64-2. Available genotoxicity studies showed no evidence of mutagenicity for members of this category. CASRNs 80-56-8, 127-91-3 and 79-92-5 did not induce gene mutations in bacteria *in vitro*. CASRNs 127-91-3 and 79-92-5 did not induce sister chromatid exchange in cultured Chinese hamster ovary cells *in vitro*. CASRN 80-56-8 did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro*. CASRN 79-92-5 did not induce micronuclei *in vivo*.

The 96-h LC₅₀ of CASRN's 80-56-8, 127-91-3, and 79-92-5 for fish are 0.28, 0.5, and 0.72, respectively. There were no effects at saturation after 96-hr exposure to CASRN 9005-90-7 for fish. The 48-h EC₅₀ of CASRNs 80-56-8 and 127-91-3 for aquatic invertebrates are 1.44 and 1.25 mg/L respectively. The 48-h EC₅₀ of CASRN 127-91-3 for aquatic plants is 1.44 mg/L. There were no effects at saturation after 96-h exposure to CASRN 9005-90-7 for aquatic plants.

The chronic aquatic toxicity endpoint is identified as a data gap under the HPV Challenge Program.

The sponsor, the Flavor and Fragrance High Production Volume Consortia, submitted a Test Plan and Robust Summaries to EPA for the Bicyclic Terpene Hydrocarbons category on February 20, 2002. EPA posted the submission on the ChemRTK HPV Challenge website on March 8, 2002 (<http://www.epa.gov/oppt/chemrtk/pubs/summaries/bictrphy/c13610tc.htm>). EPA comments on the original submission were posted to the website on November 12, 2002. Public comments were also received and posted to the website. The sponsor submitted revised documents on November 9, 2006, which were posted to the ChemRTK website on December 7, 2006. The Bicyclic Terpene Hydrocarbons category members are listed in Table 1.

Category Justification

The sponsor's rationale for grouping substances in the bicyclic terpene hydrocarbons category is based on similarities in chemical structure and pathways associated with absorption, distribution, metabolism and excretion. There is no evidence that any member of this category will be atypical in terms of its chemical behavior, environmental fate or toxicity. Based on similar molecular structures and comparable toxicological effects data, EPA agrees that this category grouping is justified.

Justification for Supporting Chemicals

The sponsor did not include a formal supporting chemical justification in either its original or revised test plan; however, data for two unsponsored chemicals, verbenone and myrcene, were included in the revised Robust Summaries, thus implying that these compounds are adequate supporting chemicals. The sponsor's revised Test Plan indicated that verbenone is the principal *in vivo* metabolite of *alpha*-pinene and that the sensitivity of current standardized toxicological assays show that aliphatic branched chain (myrcene), monocyclic (limonene) and bicyclic (pinene and camphene) hydrocarbons exhibit nearly equivalent toxicities. EPA generally does not support use of metabolites as supporting chemicals, because it is unclear that any toxicity exhibited by a metabolite adequately represents those that may be associated with the parent (and, in this case, sponsored) compound; therefore, use of verbenone as a supporting chemical is not justified. Since all sponsored members of this category have cyclic structures, EPA concludes that myrcene is not adequately justified as a supporting chemical due to its linear structure. Data supplied in the Robust Summaries for verbenone and myrcene are not included in this hazard characterization.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2006 Test Plan:

The bicyclic terpene hydrocarbons category includes six simple bicyclic terpene hydrocarbons and four mixtures composed primarily of *alpha*- and *beta*-pinene and smaller amounts of the other four chemically identified terpene hydrocarbons in this category. Both *alpha*-pinene and *beta*-pinene are bicyclic monounsaturated terpenes and positional isomers of each other; *alpha*-pinene is 2,6,6-trimethylbicyclo[3.1.1]hept-2-ene and *beta*-pinene is 2-methylene-6,6-

dimethylbicyclo [3.1.1]heptane. The combined concentration of *alpha*- and *beta*-Pinene in each of the four mixtures exceeds 80%. The remaining fraction is primarily composed of other bicyclic (*e.g.*, camphene and carene), monocyclic (*e.g.*, limonene) and monoaromatic (*e.g.*, *p*-cymene) terpene hydrocarbons and terpene tertiary alcohols. Two of these mixtures are distillation products of turpentine oil (CASRN 8006-64-2). One fraction, (CASRN 65996-96-5), is rich in *alpha*-pinene (92–97%) while the other fraction, (CASRN 65996-97-6), is rich in *beta*-pinene (78– 81%). The other two mixtures represent variations of the naturally occurring solvent turpentine, varying slightly in composition as a result of preparation. A typical analysis of turpentine oil (CASRN 8006-64-2) includes 59% *alpha*-pinene, 24% *beta*-pinene, 5% dipentene (racemic limonene), 2% *beta*-phellandrene, 2% *alpha*-Terpineol, 2% linalool, 1% methyl chavicol, 1% *cis*-Anethole, 1% *trans*-anethole [Arizona Chemical, 1999]. Turpentine gum (CASRN 9005-90-7) is composed of 60-65% *alpha*-pinene, 25-35% *beta*-pinene, and 5-8% monocyclic terpenes (*e.g.*, limonene). The substance *l*-*alpha*-pinene is a stereoisomer of *alpha*-pinene, whereas *cis*-pinane and dihydropinene are saturated derivatives of *alpha*- and *beta*-pinene. They differ in the sense that *cis*-pinane is one of two diastereoisomers of dihydropinene, in which the 2-methyl is *cis*-with respect to the geminal dimethyl moiety. Camphene is also a bicyclic terpene hydrocarbon with a [2.2.1] carbon skeleton, more specifically a 3-methylene-2,2-dimethylbicyclo[2.2.1] heptane. Camphene is structurally related to *beta*-pinene in that both are bicyclic C10 hydrocarbons that contain an exocyclic methylene function. Chemical structures for sponsored substances in the bicyclic terpene hydrocarbons category are provided in Table 1.

Table 1. Sponsored Chemicals of the Bicyclic Terpene Hydrocarbons Category			
Chemical Name	CASRN	Chemical Structure	
Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-	80-56-8		
Bicyclo[3.1.1]heptane, 6,6-dimethyl-2- methylene-	127-91-3		
Bicyclo[2.2.1]heptane, 2,2-dimethyl-3- methylene-	79-92-5		
Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-, (1R,2S,5R)-	6876-13-7	 (Stereochemistry not indicated)	
Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-	473-55-2		
Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-, (1S,5S)-	7785-26-4	 (Stereochemistry not indicated)	
Terpenes and terpenoids, terpentine oil <i>alpha</i> - pinene fraction	65996-96-5	<i>alpha</i> -pinene, 92–97% <i>beta</i> -pinene, 1–7%	
Terpenes and terpenoids, terpentine oil <i>beta</i> -pinene fraction	65996-97-6	<i>beta</i> -pinene, 78–81% <i>alpha</i> -pinene, 8–10% dipentene, 1–5%	camphene, 1–2% <i>beta</i> -phellandrene, 1–3% terpinolene 0–2%
Terpentine gum	9005-90-7	<i>alpha</i> -pinene, 60–65% <i>beta</i> -pinene, 25–35% monocyclic terpenes, 5–8%	
Terpentine oil	8006-64-2	<i>alpha</i> -pinene, 59% <i>beta</i> -pinene, 24% dipentene, 5% <i>beta</i> -phellandrene, 2% <i>alpha</i> -terpineol, 2%	linalool, 2% methyl chavicol, 1% <i>cis</i> -anethole, 1% <i>trans</i> -anethole, 1%

1.2 Physical-Chemical Properties

The physical-chemical properties of the bicyclic terpene hydrocarbons category are summarized in Table 2. Members of this category are liquids except for camphene which is a solid. These substances have low to moderate water solubility and high vapor pressure.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

The bicyclic terpene hydrocarbons category chemicals had an aggregated production and/or import volume in the United States between 171 million pounds and 710.5 million pounds in calendar year 2005.

- CASRN 80-56-8: 10 to <50 million pounds;
- CASRN 127-91-3: 10 to <50 million pounds;
- CASRN 473-55-2: 50 to <100 million pounds;
- CASRN 7785-26-4: <500,000 pounds;
- CASRN 8006-64-2: 100 to <500 million pounds;
- CASRN 9005-90-7: 1 to <10 million pounds;

CASRN 6876-13-7, 65996-96-5 and 65996-97-6 were not reported in the 2006 IUR.

CASRN 80-56-8:

Non-confidential information in the IUR indicated that its industrial processing and uses include other basic organic chemical manufacturing as odor agents. Non-confidential commercial and consumer uses of this chemical include soaps and detergents.

CASRN 127-91-3:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates and odor agents. No commercial and consumer uses were reported.

CASRN 473-55-2:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates. No commercial and consumer uses were reported.

CASRN 7785-26-4:

No industrial processing and uses, and commercial and consumer uses were reported.

CASRN 8006-64-2:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include all other chemical product and preparation manufacturing; other basic organic

chemical manufacturing as adhesives and binding agents, coloring agents (pigments), fuels, lubricants, odor agents, intermediates, processing aid (not otherwise listed), solvents (which become part of product formulation or mixture) and “other”; paperboard mills as intermediates and “other”; pulp mills as solvents (which become part of product formulation or mixture), functional fluids, and “other”; adhesive manufacturing as solvents (which become part of product formulation or mixture); cosmetic, beauty supplies, and perfume store; all other wood product manufacturing. Non-confidential commercial and consumer uses of this chemical include adhesive and sealants; lubricants, greases and fuel additives; paints and coatings; polishes and sanitation goods; soaps and detergents; not readily obtainable (NRO); and “other.”

CASRN 9005-90-7:

Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates and pulp mills as “other.” Non-confidential commercial and consumer uses of this chemical include not readily obtainable (NRO) and “other.”

Table 2. Physical-Chemical Properties of Bicyclic Terpene Hydrocarbons Category1

Property	Sponsored Chemicals									
	Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-(<i>alpha</i> -pinene) ²	Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-, (1 <i>S</i> ,5 <i>S</i>)-(1- <i>alpha</i> -pinene) ²	Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-methylene-(<i>beta</i> -pinene)	Bicyclo[2.2.1]heptane, 2,2-dimethyl-3-methylene-(camphene)	Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-, (1 <i>R</i> ,2 <i>S</i> ,5 <i>R</i>)(<i>cis</i> -pinane)	Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-(dihydro-pinene)	Terpenes and terpenoids, terpentine oil <i>alpha</i> -pinene fraction	Terpenes and terpenoids, terpentine oil <i>beta</i> -pinene fraction	Terpentine gum	Terpentine oil
CASRN	80-56-8	7785-26-4	127-91-3	79-92-5	6876-13-7	473-55-2	65996-96-5	65996-97-6	9005-90-7	8006-64-2
Molecular Weight	136		136	136	136	138	Not applicable for mixtures			
Physical State	Liquid		Liquid	Solid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid
Melting Point	-55°C (measured); -64°C (measured) ³		-61.5°C (measured) ³	51–52°C (measured)	-53°C (measured)	-53°C (measured)	-55°C (measured value for <i>alpha</i> -pinene); -61.5°C (measured value for <i>beta</i> -pinene) ³			
Boiling Point	155–156°C (measured)		165–166°C (measured)	156.5–159°C (measured)	169°C (measured)	164.5–165°C (measured)	155–156°C (measured value for <i>alpha</i> -pinene); 165–166°C (measured value for <i>beta</i> -pinene)			
Vapor Pressure (mm Hg)	4.75 at 25°C (measured) ³		2.93 at 25°C (measured) ³	28.5 at 20°C (measured)	5.47 at 25°C (measured)	2.2 at 25°C (estimated)	4.75 at 25°C (measured value for <i>alpha</i> -pinene) ³ ; 2.93 at 25°C (measured value for <i>beta</i> -pinene) ³			
Dissociation Constant (pK _a)	Not applicable									
Henry's Law Constant (atm-m ³ /mole)	0.29 (measured) ³		0.16 (estimated)	0.16 (estimated)	0.19 (estimated)	0.19 (estimated)	0.29 (measured value for <i>alpha</i> -pinene) ³ ; 0.16 (estimated value for <i>beta</i> -pinene) ⁴			
Water Solubility (mg/L)	0.65 at 25°C (measured); 2.49 at 25°C (measured) ³		2.1 at 25°C (measured)	4.2 at 20°C (measured)	1.58 at 25°C (measured) ⁵	1.58 at 25°C (measured) ⁵	0.65 at 25°C (measured value for <i>alpha</i> -pinene); 2.1 at 25°C (measured value for <i>beta</i> -pinene)			
Log K _{ow}	4.83 (measured)		4.16 (measured) ³	4.22 (measured) ⁶	4.35 (estimated)	4.35 (estimated)	4.83 (measured value for <i>alpha</i> -pinene); 4.16 (measured value for <i>beta</i> -pinene) ³			

¹The Flavor and Fragrance High Production Volume Consortia. The Terpene Consortium. November 9, 2006. Robust Summary and Test Plan for Bicyclic Terpene Hydrocarbons Category (posted December 7, 2006). <http://www.epa.gov/chemrtk/pubs/summaries/bictprhy/c13610tc.htm>.

²CASRN 7785-26-4 and the racemic mixture (CASRN 80-56-8) have identical physical properties.

³SRC. The Physical Properties Database (PHYSPROP). Syracuse, NY: SRC. Available from <http://www.srcinc.com/what-we-do/free-demos.aspx> as of January 23, 2009.

⁴U.S. EPA 2009. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. EPA, Washington, DC USA <http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm>

⁵Mueller, M.; Klein, W. 1992. Comparative evaluation of methods predicting water solubility for organic compounds. *Chemosphere* 25: 769–782.

⁶Griffin, S.; Wyllie, S.G.; Markham, J. 1999. Determination of octanol-water partition coefficient for terpenoids using reversed-phase high-performance liquid chromatography. *J. Chromatogr.* 864: 221–228.

2.2 Environmental Exposure and Fate

Members of the bicyclic terpene hydrocarbons category are expected to have moderate mobility in soil based on the estimated K_{oc} values for these compounds. Using manometric respirometry tests, CASRN 80-56-8 was degraded approximately 38% over the course of a 28-day incubation period and did not pass either ready or inherent biodegradability criteria. However, CASRN 80-56-8 achieved 91–95% of its theoretical biochemical oxygen demand using the modified MITI test (OECD 301C) and was considered readily biodegradable. This compound was also completely degraded within 6–8 days using soil slurries prepared from samples collected from coniferous and mixed hardwood forest watersheds. A mixture consisting of approximately 50.9% CASRN 80-56-8 and 36.8% CASRN 127-91-3 achieved 52% degradation after a 28-day incubation period using a modified Sturm test (OECD 301B). CASRN 79-92-5 was not readily biodegradable using a closed bottle test (OECD 301D); however, the low biodegradation percentage was attributed to volatilization of the test substance in the upper parts of the test vessel. Volatilization of the bicyclic terpene hydrocarbons is considered high based on their Henry's Law constants. The bicyclic terpene hydrocarbons are not expected to hydrolyze since these substances lack functional groups that hydrolyze under environmental conditions. The rate of atmospheric photooxidation is considered moderate to rapid. Based on the weight of evidence, the chemicals in this category are expected to have low persistence (P1). The bioaccumulation potential for members of this category is expected to range from low (B1) to moderate (B2).

Conclusion: Members of the bicyclic terpene hydrocarbons category are liquids, with the exception of CASRN 79-92-5, which forms colorless crystals at room temperature. The bicyclic terpene hydrocarbons have low to moderate water solubility and high vapor pressure. The bicyclic terpene hydrocarbons are expected to have moderate mobility in soil. Volatilization of the bicyclic terpene hydrocarbons is considered high based on their Henry's Law constants. The bicyclic terpene hydrocarbons are not expected to hydrolyze since these substances lack functional groups that hydrolyze under environmental conditions. The rate of atmospheric photooxidation is considered rapid to moderate. The chemicals in the bicyclic terpene hydrocarbon category are expected to have low persistence (P1) and low (B1) to moderate (B2) bioaccumulation potential.

Table 3. Environmental Fate Characteristics of Bicyclic Terpene Hydrocarbons Category¹

Property	Sponsored Chemicals									
	Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl- (<i>alpha</i> -pinene) ²	Bicyclo[3.1.1]hept-2-ene, 2,6,6-trimethyl-, (1 <i>S</i> ,5 <i>S</i>)- (<i>l-alpha</i> -pinene) ²	Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-methylene- (<i>beta</i> -pinene)	Bicyclo[2.2.1]heptane, 2,2-dimethyl-3-methylene- (camphene)	Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-, (1 <i>R</i> ,2 <i>S</i> ,5 <i>R</i>)- (<i>cis</i> -pinane)	Bicyclo[3.1.1]heptane, 2,6,6-trimethyl- (dihydro-pinene)	Terpenes and terpenoids, terpentine oil <i>alpha</i> -pinene fraction	Terpenes and terpenoids, terpentine oil <i>beta</i> -pinene fractionl	Terpentine gum	Terpentine oil
CASRN	80-56-8	7785-26-4	127-91-3	79-92-5	6876-13-7	473-55-2	65996-96-5	65996-97-6	9005-90-7	8006-64-2
Photodegradation Half-life	1.4 hours (estimated)		2.3 hours (estimated)	2.2 hours (estimated)	9.4 hours (estimated)	9.4 hours (estimated)	1.4 hours (estimated for <i>alpha</i> -pinene); 2.3 hours (estimated for <i>beta</i> -pinene)			
Hydrolysis Half-life	Stable									
Biodegradation	38% after 28 days (not readily biodegradable); 37% after 31 days (not inherently biodegradable) 2.2% after 28 days (not readily biodegradable); 100% in 120 hrs; 52% after 28 days (50.9% <i>alpha</i> -pinene and 36.8% <i>beta</i> -pinene mixture) (not readily biodegradable); 91–95% in 28 days (readily biodegradable) ⁴		52% after 28 days (mixture consisting of 50.9% <i>alpha</i> -pinene and 36.8% <i>beta</i> -pinene) (not readily biodegradable)	<20% in 28 days (not readily biodegradable; however, volatilization occurred)	No data	No data	52% after 28 days (mixture consisting of 50.9% <i>alpha</i> -pinene and 36.8% <i>beta</i> -pinene) (not readily biodegradable)			
Bioaccumulation	BAF = 3,072 (estimated) ³		BAF = 923 (estimated) ³	BAF = 1,230 (estimated) ³	BAF = 1,357 (estimated) ³	BAF = 1,357 (estimated) ³	BAF = 3,072 (estimated for <i>alpha</i> -pinene) ³ ; BAF = 923 (estimated for <i>beta</i> -pinene) ³			
Log K _{oc}	3.0 (estimated) ³		3.0 (est.) ³	3.0 (est.) ³	3.0 (est.) ³	3.0 (est.) ³	3.0 (estimated for <i>alpha</i> - and <i>beta</i> -pinene) ³			
Fugacity (Level III Model)										
Air (%)										
Water (%)	2.53		3.1	5.0	17.3	17.3	2.53–3.1			
Soil (%)	84.6		79.2	71.8	72.6	72.6	89.2–84.6			
Sediment (%)	8.1		13.2	19.1	6.0	6.0	8.1–13.2			
	4.8		4.5	4.1	4.1	4.1	4.5–4.8 (estimates for <i>alpha</i> - and <i>beta</i> -pinene)			
Persistence ⁵	P1 (low)		P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)			
Bioaccumulation ⁵	B2 (moderate)		B1 (low)	B2 (moderate)	B2 (moderate)	B2 (moderate)	B2 (moderate)			

¹The Flavor and Fragrance High Production Volume Consortia. Terpene Consortium. Nov. 9, 2006. Robust Summary and Test Plan for Bicyclic Terpene Hydrocarbons Category (posted December 7, 2006).

²CASRN 7785-26-4 and the racemic mixture (CASRN 80-56-8) have identical physical properties.

³U.S. EPA. 2009. Estimation Programs Interface Suite™ for Microsoft® Windows v4.0. U.S. EPA, Washington, DC, USA. <http://www.epa.gov/opptintr/exposure/pubs/episuite.html>.

⁴National Institutes 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.

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

Acute Oral Toxicity

alpha-Pinene (CASRN 80-56-8)

Wistar rats (10 males/dose) were administered *alpha*-pinene via the oral route at 0, 2020, 3200, 5000 or 7800 mg/kg and observed for at least two days following dosing. Mortalities were observed in all treatment groups.

LD₅₀ = 3700 mg/kg

beta-Pinene (CASRN 127-91-3)

Wistar rats (10/dose; sex not specified) were administered *beta*-pinene via the oral route at 5000 mg/kg and observed for at least seven days after dosing. One death occurred.

LD₅₀ > 5000 mg/kg

Camphene (CASRN 79-92-5)

Wistar rats (10 animals; sex not specified) were administered camphene via an unspecified oral route at 5000 mg/kg. Two mortalities occurred.

LD₅₀ > 5000 mg/kg

Turpentine oil (CASRN 8006-64-2)

(1) Wistar rats (10 males/dose) were administered turpentine oil (59% *alpha*-pinene, 24% *beta*-pinene, 5% dipentene, 2% each *beta*-phellandrene, *alpha*-terpineol and linalool, 1% each methyl chavicol, *cis*-anethole, *trans*-anethole) via the oral route at 2752, 3440, 4300 or 5375 mg/kg. Mortalities were observed at all dose levels.

LD₅₀ = 3956 mg/kg

(2) Wistar rats (10 males) were administered turpentine oil (59% *alpha*-pinene, 24% *beta*-pinene, 5% dipentene, 2% each *beta*-phellandrene, *alpha*-terpineol and linalool, 1% each methyl chavicol, *cis*-anethole, *trans*-anethole) via the oral route at 5000 mg/kg. Six mortalities were observed.

LD₅₀ < 5000 mg/kg

(3) Sprague-Dawley albino rats (two – three/sex/dose) were administered turpentine oil (undiluted) via the oral route at 1260, 1580, 2000, 2510, 3160 or 3980 mg/kg and observed for 14 days following dosing. Mortalities were observed at all dose levels.

(<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384> OTS0545856).

LD₅₀ = 2600 mg/kg

Acute Inhalation Toxicity

Turpentine oil (CASRN 8006-64-2)

(1) Sprague-Dawley rats (four animals/group; sex not specified) were exposed to turpentine oil via inhalation at 2.4, 4.8, 9.5, 19.5 or 38.0 mg/L for 6 hours and observed for 14 days following dosing. Mortalities were observed at 19.5 and 38.0 mg/L.

LC₅₀ = 13.5 mg/L

(2) Albino guinea pigs (two animals/group; strain and sex not specified) were exposed to turpentine oil via inhalation at 2.4, 4.8, 9.5, 19.5 or 38.0 mg/L for 6 hours and observed for 14 days following dosing. Mortalities were observed at 19.5 and 38.0 mg/L.

LC₅₀ = 13.5 mg/L

(3) Swiss white mice (four animals/group; sex not specified) were exposed to turpentine oil via inhalation at 2.2, 4.5, 9, 18 or 36 mg/L for 6 hours and observed for 14 days following dosing. Mortalities were observed at 9, 18 and 36 mg/L.

LC₅₀ = 9.0 mg/L

Acute Dermal Toxicity

alpha-Pinene (CASRN 80-56-8)

New Zealand White rabbits (10 animals; sex not specified) were administered *alpha*-pinene via the dermal route at 5000 mg/kg-bw on clipped abraded skin for 24 hours and observed for 7 days following dosing. No mortalities were observed.

LD₅₀ > 5000 mg/kg-bw

beta-Pinene (CASRN 127-91-3)

New Zealand White rabbits (10 animals; sex not specified) were administered *beta*-pinene via the dermal route. Test material was applied to clipped abraded skin at 5000 mg/kg-bw for 24 hours and observed for 7 days following dosing. No mortalities were observed.

LD₅₀ > 5000 mg/kg-bw

Camphene (CASRN 79-92-5)

New Zealand White rabbits (two – three/sex/dose) were administered camphene via the dermal route at 2500 or 5000 mg/kg-bw on clipped abraded skin for 24 hours and observed for 7 days following dosing. One mortality was observed at 5000 mg/kg-bw.

LD₅₀ > 2500 mg/kg-bw

Turpentine oil (CASRN 8006-64-2)

(1) New Zealand White rabbits (10 animals; sex not specified) were administered turpentine oil via the dermal route at 2000 mg/kg-bw on clipped abraded skin for 24 hours and observed for 7 days following dosing. No mortalities were observed.

LD₅₀ > 2000 mg/kg-bw

(2) New Zealand White rabbits (one male or female/dose) were administered turpentine oil (undiluted) via the dermal route at 1260, 2000, 3160, 5010 or 7940 mg/kg-bw for 24 hours and

observed for 14 days following dosing. Mortalities were observed at 5010 and 7940 mg/kg-bw. (<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384> OTS0545856).

LD₅₀ > 3160 mg/kg-bw

Repeated-Dose Toxicity

alpha-Pinene (CASRN 80-56-8)

In a 14-week NTP study, F344/N rats (10/sex/dose) were administered *alpha*-pinene (purity \geq 97%) via inhalation at 0, 25, 50, 100, 200 or 400 ppm for 6 hours/day, 5 days/week. Tissues examined for histopathology included: adrenal glands, brain, clitoral glands, esophagus, eyes, femur, Harderian glands, heart, large and small intestines, kidneys, larynx, liver, lungs, lymph nodes, mammary gland, thigh muscle, nasal cavity and nasal turbinates, ovaries, pancreas, parathyroid glands, pituitary glands, preputial glands, prostate, salivary glands, seminal vesicles, spleen, epididymides, stomach, thymus, thyroid gland, trachea, urinary bladder and uterus. Mortality (6/10) occurred in females treated at 400 ppm. All exposed males showed decreased body weight gain; females exposed at concentrations $<$ 170 mg/kg-bw/day showed slightly increased body weight gain compared to controls. Treatment-related effects observed in males included increased absolute/relative kidney weights at or above 100 ppm and increased (absolute/relative) liver weights at concentrations \geq 200 ppm. Significant treatment effects observed in females included increased (absolute/relative) liver weights at concentrations \geq 50 ppm and decreased (absolute/relative) thymus weights and increased relative lung weight at 400 ppm. Males showed significant reductions in liver enzymes (alanine aminotransferase at concentrations \geq 50 ppm; alkaline phosphatase at concentrations \geq 100 ppm and decreased sorbitol dehydrogenase at 400 ppm). Females showed significant reductions in alanine aminotransferase and alkaline phosphatase activities at 200 and 400 ppm, respectively. Histopathologic examination revealed granular casts and hyaline droplet accumulation in treated males, indicative of α -2 μ -globulin nephropathy⁴; this treatment effect is not relevant to humans. No evidence of histopathology was observed in treated females (NTP draft 2006).

LOAEC = 400 ppm (based on mortality and clinical chemistry)

NOAEC = 200 ppm

(2) In a 14-week NTP study, B6C3F1 mice (10/sex/dose) were administered *alpha*-pinene (purity \geq 97%) via inhalation at 0, 25, 50, 100, 200 or 400 ppm for 6 hours/day, 5 days/week. Tissues examined for histopathology included adrenal glands, brain, clitoral glands, esophagus, eyes, femur, gallbladder, Harderian glands, heart, large and small intestines, kidneys, larynx, liver, lungs, lymph nodes, mammary gland, thigh muscle, nasal cavity and nasal turbinates, ovaries, pancreas, parathyroid glands, pituitary glands, preputial glands, prostate, salivary glands, seminal vesicles, spleen, epididymides, stomach, thymus, thyroid gland, trachea, urinary bladder and uterus. No mortalities were observed. Changes in organ weights included significantly increased (absolute/relative) liver weights in both sexes at concentrations \geq 200 ppm and decreased (absolute/relative) thymus weights in males at 400 ppm. Treatment-related

⁴ Nephropathy seen in male rats may be occurring by an alpha 2 μ -globulin-mediated mechanism (which is male rat-specific and not considered relevant to humans). EPA's Risk Assessment Forum has outlined key events and data that are necessary to demonstrate this mode of action (Alpha 2 μ -Globulin: Association with Chemically Induced Renal Toxicity and Neoplasia in the Rat, EPA/625/3-91/019F).

histopathology included hyperplasia of transitional epithelia in the urinary bladder in both sexes at or above 100 ppm. No other signs of histopathology were reported (NTP draft 2006).

LOAEC = 100 ppm (based on hyperplasia of transitional epithelia in the urinary bladder)

NOAEC = 50 ppm

Camphene (CASRN 79-92-5)

Wistar rats (5/sex/group) were administered camphene in sesame oil via gavage at 0, 62.5, 250 or 1000 mg/kg-day for 28 days. Treatment-related effects observed at 1000 mg/kg-day included increased salivation, vacuolization of hepatocytes and increased liver weights in both sexes. In addition, treated males exhibited histopathological changes indicative of α -2 μ -globulin nephropathy at all dose levels⁵.

LOAEL = 1000 mg/kg-day (based on increased liver weight and vacuolization of hepatocytes)

NOAEL = 250 mg/kg-day

Reproductive Toxicity

No specific reproductive toxicity data are available; however, no adverse effects were observed in the reproductive organs (ovaries, uterus, epididymides, seminal vesicles, testes) of rats or mice during the 14-week inhalation studies with CASRN 80-56-8, described above.

Developmental Toxicity

alpha-Pinene (CASRN 80-56-8)

In a prenatal developmental toxicity study, pregnant CD-1 outbred mice (20-22 females/group) were administered an essential oil consisting of 85-90% terpene hydrocarbons and < 10% oxygenated terpene hydrocarbons (*alpha*-pinene (20-25%), *beta*-pinene (15-18%) and sabinene (38-42%)) in corn oil (10 mL/kg) via gavage at 0, 6, 26, 120 or 560 mg/kg-day on gestation day (GD) 6-15. Positive controls received aspirin (in corn oil) at 150 mg/kg-day; negative controls received corn oil vehicle. Dams were subjected to caesarian section on GD 17 and the number of implantation sites, resorption sites, live/dead offspring and the body weight of live pups were recorded. The urogenital tract of each dam was also examined for anatomical abnormalities. Gestational index, mortality, gross pathology, number of implantation sites, number of corpora lutea, litter size and sex ratio of pups were evaluated. One third of the offspring from each litter underwent a detailed visceral examination; the rest were stained with alizarin red and examined for skeletal anomalies. No pregnant females died or aborted before scheduled sacrifice. There was no evidence of reproductive toxicity based on the average number of corpora lutea, implantation sites or partial resorptions in treated versus control animals. No effects on maternal body weight or urogenital tract abnormalities were observed in treated dams; however, the number of live offspring per dam was significantly decreased at or above 120 mg/kg-day. There was no evidence of developmental toxicity based on gross, visceral or skeletal examinations of live offspring and no treatment-related effects on pup body weight or sex ratio.

NOAEL (maternal toxicity) = 560 mg/kg-day (highest dose tested)

LOAEL (developmental toxicity) = 120 mg/kg-day (based on decreased number of live offspring)

NOAEL (developmental toxicity) = 26 mg/kg-day

⁵ See footnote 4.

(2) In a prenatal developmental toxicity study, pregnant golden hamsters (26-28 females/dose) were administered an essential oil consisting of 85-90% terpene hydrocarbons and < 10% oxygenated terpene hydrocarbons (*alpha*-pinene (20-25%), *beta*-pinene (15-18%) and sabinene (38-42%)) in corn oil vehicle (10 mL/kg) via gavage at 0, 6, 28, 130 or 600 mg/kg-day on GD 6-10. The positive control group received aspirin (in corn oil) at 250 mg/kg-day; the negative control group received corn oil. Dams were subjected to caesarian section on GD 14 and the number of implantation sites, resorption sites, live/dead offspring and the body weight of live pups were recorded. The urogenital tract of each dam was also examined for anatomical abnormalities. Gestational index, mortality, gross pathology, number of implantation sites, number of corpora lutea, litter size and sex ratio of pups were evaluated. One third of the offspring from each litter underwent a detailed visceral examination; the rest were examined for skeletal anomalies. Two control and two high-dose females died before scheduled sacrifice. No treatment-related effects were observed on nidation, maternal survival or fetal survival. The number and type of tissue abnormalities seen in treated animals were comparable to those seen in control animals.

NOAEL (maternal toxicity) = 600 mg/kg-day (highest dose tested)

NOAEL (developmental toxicity) = 600 mg/kg-day (highest dose tested)

(3) In a prenatal developmental toxicity study, pregnant Wistar rats (22-23 females/dose) were administered an essential oil consisting of 85-90% terpene hydrocarbons and < 10% oxygenated terpene hydrocarbons (*alpha*-pinene (20-25%), *beta*-pinene (15-18%) and sabinene (38-42%)) in corn oil vehicle (10 mL/kg) via gavage at 0, 3, 12, 56 or 260 mg/kg-day on GD 6-15. Positive controls received aspirin at 250 mg/kg-day in corn oil; negative controls received corn oil vehicle. Dams were subjected to caesarian section on GD 20 and the number of implantation sites, resorption sites, live/dead offspring and the body weight of live pups were recorded. The urogenital tract of each dam was also examined for anatomical abnormalities. Gestational index, mortality, gross pathology, number of implantation sites, number of corpora lutea, litter size and sex ratio of pups were evaluated. One third of the offspring from each litter underwent a detailed visceral examination; the rest were stained with alizarin red and examined for skeletal anomalies. No pregnant females died or aborted before scheduled sacrifice. There was no evidence of reproductive toxicity based on the average number of corpora lutea, implantation sites or partial resorptions in treated versus control animals. No effects on maternal body weight or urogenital tract abnormalities were observed in treated dams; however, the number of live offspring per dam was significantly decreased at or above 56 mg/kg-day. There was no evidence of developmental toxicity based on gross, visceral or skeletal examinations of live offspring and no treatment-related effects on pup body weight or sex ratio. The number and type of tissue abnormalities seen in treated animals were comparable to those seen in control animals.

NOAEL (maternal toxicity) = 260 mg/kg-day (highest dose tested)

LOAEL (developmental toxicity) = 56 mg/kg-day (based on decreased number of live offspring)

NOAEL (developmental toxicity) = 12 mg/kg-day

Camphene (CASRN 79-92-5)

In a prenatal developmental toxicity study, pregnant Sprague-Dawley rats (20/dose) were administered camphene (78%) via gavage at 0, 250 or 1000 mg/kg-day on GD 6-15. No maternal mortalities were observed. Treatment-related clinical symptoms included reduced motor activity and salivation at 1000 mg/kg-day. A slight increase in resorptions was also observed at 1000 mg/kg-day.

LOAEL (maternal toxicity) = 1000 mg/kg-day (based on reduced motor activity and salivation; highest dose tested)

NOAEL (maternal toxicity) = 250 mg/kg-day

NOAEL (developmental toxicity) = 1000 mg/kg-day (highest dose tested)

Genetic Toxicity – Gene Mutation

In vitro

(-)-alpha-Pinene (CASRN 80-56-8)

Salmonella typhimurium strains TA97a, TA98, TA100 and TA1535 were exposed to (-)-alpha-pinene in ethanol at 0, 1, 5, 10, 25, 50, 75, 100, 200, 250, 300, 400, 500, 600, 700, 750, 800, 900, 1000, 1250, 1500, 2000 or 4000 µg/plate with and without metabolic activation. Cytotoxicity was observed at ≥ 1250 µg/plate in TA100 with and without metabolic activation and TA97a without activation, ≥ 5000 µg/plate for TA98 with and without activation and TA97a with activation and ≥ 100 µg/plate for TA1535 without activation. Negative and positive controls were included, but these responses were not provided in the Robust Summaries.

(-)-alpha-Pinene was not mutagenic in this assay.

(+)-alpha-Pinene (CASRN 80-56-8)

S. typhimurium strains TA97a, TA98, TA100 and TA1535 were exposed to (+)-alpha-pinene in ethanol at concentrations ranging from 0-1000 µg/plate with and without metabolic activation. Cytotoxicity was observed at concentrations ≥ 1250 µg/plate in TA100, ≥ 600 µg/plate for TA98, > 400 µg/plate for TA97a and 1000 µg/plate for TA1535. Negative and positive controls were included, but these responses were not provided in the Robust Summaries.

(+)-alpha-Pinene was not mutagenic in this assay.

alpha-Pinene (CASRN 80-56-8)

(1) *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to alpha-pinene in ethanol at 0, 0.1, 0.25, 0.5, 1.0, 2.5, 5.0, 10.0 or 25 µL/plate with and without metabolic activation. In a preliminary toxicity study, cytotoxicity was observed at concentrations ≥ 4.69µL/plate. Positive and negative controls were included; however, these responses were not reported in the Robust Summaries.

alpha-Pinene was not mutagenic in this assay.

(2) *S. typhimurium* strains TA98 and TA100 and *Escherichia coli* strain pKM101 were exposed to alpha-pinene at concentrations ranging from 0-10,000 µg/plate in the presence and absence of metabolic activation. Positive and negative controls were included and responded appropriately. For TA98, precipitation and toxicity occurred at 40 and 500 µg/plate, respectively, in the absence of metabolic activation.

alpha-Pinene was not mutagenic in this assay.

beta-Pinene (CASRN 127-91-3)

S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 were exposed to *beta*-pinene in dimethylsulfoxide at 0, 0.01, 0.05, 0.1, 0.5, 1.0, 2.5 or 5.0 $\mu\text{L}/\text{plate}$ in the presence and absence of metabolic activation. Cytotoxicity was observed at concentrations $\geq 4.69 \mu\text{L}/\text{plate}$. Positive and negative controls were included, but these responses were not reported.

beta-Pinene was not mutagenic in this assay.

Camphene (CASRN 79-92-5)

S. typhimurium strains TA98, TA100, UTH8413 and UTH8414 were exposed to camphene in dimethylsulfoxide at five concentrations ranging from 10 to 1000 $\mu\text{g}/\text{plate}$ in the presence and absence of metabolic activation. Positive controls were included; however, no other information was provided in the Robust Summaries.

Camphene was not mutagenic in this assay.

Dihydropinene (CASRN 473-55-2)

S. typhimurium strains TA97, TA98, TA100 and TA1535 were exposed to dihydropinene at 0, 1, 3, 10, 33, 100, 333, 1000, 3333 or 10,000 $\mu\text{g}/\text{plate}$ with and without metabolic activation. Positive and negative controls were included and responded appropriately. Toxicity was observed at 10,000 $\mu\text{g}/\text{plate}$ with metabolic activation in TA1535 and TA98. No precipitation occurred.

Dihydropinene was not mutagenic in this assay.

Turpentine oil (CASRN 8006-64-2)

S. typhimurium strains TA98, TA100 and TA102 were exposed to turpentine oil at 0, 1, 3.3, 10, 33, 75, 100 or 333 $\mu\text{g}/\text{plate}$ with and without metabolic activation. Positive and negative controls were included and responded appropriately. Cytotoxicity was observed at 333 $\mu\text{g}/\text{plate}$ in the presence of metabolic activation and at concentrations $\geq 33 \mu\text{g}/\text{plate}$ in the absence of metabolic activation. No precipitation occurred.

Turpentine oil was not mutagenic in this assay.

Genetic Toxicity – Chromosomal Aberrations

In vitro

beta-Pinene (CASRN 127-91-3)

Chinese hamster ovary cells (CHO K-1) were exposed to *beta*-pinene in dimethylsulfoxide at 0, 3.3, 10, 33.3, 100, 333 or 1000 μM in the absence of metabolic activation. No other information was provided regarding cytotoxicity, precipitation or control responses.

beta-Pinene did not induce sister chromatid exchange in this assay.

Camphene (CASRN 79-92-5)

Chinese hamster ovary cells (CHO K-1) were exposed to camphene in dimethylsulfoxide at 0, 3.3, 10, 33.3, 100, 333 or 1000 μM without metabolic activation. No other information was provided regarding cytotoxicity, precipitation or control responses.

Camphene did not induce sister chromatid exchange in this assay.

In vivo

Camphene (CASRN 79-92-5)

In a micronucleus assay, NMRI mice (5/sex/group) were administered camphene via gavage at 0 or 4000 mg/kg. No other information was provided.

Camphene did not induce micronuclei in this assay.

(-)-alpha-Pinene (CASRN 80-56-8)

In an NTP study, B6C3F1 mice (5/sex/group) were administered (-)-alpha-pinene via inhalation at 0, 25, 50, 100, 200 or 400 ppm (~ 0, 0.14, 0.28, 0.58, 1.1 and 2.2 mg/L, respectively) for 6 hours/day, 5 days/week for 14 weeks. Blood samples were taken following the 14-week dosing period and erythrocytes were scored for the presence of micronuclei. No information was provided regarding control responses.

(-)-alpha-Pinene did not induce micronuclei in this assay.

Genetic Toxicity – Other

In vitro

alpha-Pinene (CASRN 80-56-8)

In an unscheduled DNA synthesis assay, hepatocytes taken from male rats (Fischer and Sprague-Dawley) were exposed to alpha-pinene at 0.001, 0.003, 0.01, 0.03, 0.1 or 10 µL/mL in the absence of metabolic activation. Positive and negative controls were included and responded appropriately. Cytotoxicity was not observed at any tested concentration.

alpha-Pinene did not induce unscheduled DNA synthesis in this assay.

Additional Information

Eye Irritation

Turpentine oil (CASRN 8006-64-2)

Six New Zealand White rabbits were given an ocular administration of turpentine oil undiluted at 0.1 mL with an exposure time of 24 hours and observed for at least 168 hours following dosing. Treatment-related effects included slight erythema, slight edema and copious discharge. All rabbits received an eye irritation score of 0 after 168 hours. (<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384> OTS0545856).

Turpentine oil was slightly irritating to rabbits in this assay.

Skin Irritation

Turpentine oil (CASRN 8006-64-2)

Six New Zealand White rabbits were exposed to turpentine oil undiluted via the dermal route at 0.5 mL for 24 hours and observed for 14 days following dosing. Treatment-related effects included the sloughing off of skin in 10 – 14 days. (<http://www.srcinc.com/what-we-do/databaseforms.aspx?id=384> OTS0545856).

Turpentine oil was severely irritating to rabbits in this assay.

Skin Sensitization

Turpentine oil (CASRN 8006-64-2)

There are several case reports of patients who present with irritation of the eyes, skin and/or mucous membranes following turpentine exposure. Two multicenter studies evaluated patients with suspected contact dermatitis related to turpentine exposure. In one study conducted by the German-Austrian Information Network of Departments of Dermatology, patch testing was performed on 45,005 patients. Data on patch test reactions to turpentine (10% in petrolatum) were collected from 30 dermatological centers in Germany and Austria for five years (1992-1997). Readings were carried out according to guidelines set forth by the German Contact Dermatitis Research Group. Positive reactions were considered as +, ++, or +++ reactions with erythematous papules, vesicles and/or a spreading reaction to surrounding skin. From 1992-1995, positive reactions to turpentine were reported in approximately 0.3-0.6% of patients tested. This incidence increased to 3.2% in 1997. Allergic contact dermatitis was confirmed in 54.3% of turpentine positive versus 25.3% of turpentine negative patients ($p < 0.001$) examined during this study (Tredler *et al.*, 2000).

An earlier study conducted in Portugal used a specific formulation of turpentine which lacked turpentine peroxides and other known sensitizers, such as Δ_3 -carene to determine whether other components commonly found in turpentine induced skin reactions. From 1979 – 1983, 4316 patients were evaluated for allergic sensitization to oil of turpentine (10% in olive oil). Positive skin reactions were noted in 101 patients. A subsequent study enrolled 30 patients that had previously developed positive skin reactions to oil of turpentine (20 men and 10 women). These individuals were subsequently tested with a series of six pure terpenes (α -pinene, β -pinene, dipentene, α -terpineol, myrcene and Δ_3 -carene) and a standard series of 25 allergens which included the European Standard. All test substances were delivered via topical administration in olive oil, except dipentene which was administered in petrolatum. Patch tests were performed using Leukotest[®] (Beiersdorf) and results were read within 2-4 days of administration, according to recommendations set forth by the International Contact Dermatitis Research Group. Positive skin reactions were observed with α -pinene (17 patients), dipentene (15 patients), α -terpineol (3 patients) and β -pinene (2 patients) (Cachao, 1986).

Conclusion: Members of the bicyclic terpene hydrocarbons category exhibit low acute toxicity via oral (rats) and dermal (rabbits) routes and moderate acute toxicity via inhalation (rats, mice and guinea pigs). In a 28-day oral repeated-dose toxicity study, rats treated with CASRN 79-92-5 showed vacuolization and increased liver weights in both sexes at 1000 mg/kg-day; the NOAEL for systemic toxicity is 250 mg/kg-day. A 14-week inhalation study with CASRN 80-56-8 in rats showed significant mortality (6/10) and organ weight changes in females treated at 400 ppm; the NOAEC for systemic toxicity is 200 ppm. A 14-week inhalation study with CASRN 80-56-8 in mice showed increased (absolute/relative) liver weights at concentrations \geq 200 ppm and epithelial hyperplasia in the urinary bladder at concentrations \geq 100 ppm; the NOAEC for systemic toxicity is 50 ppm. No specific reproductive toxicity data are available; however, no adverse effects were observed in the reproductive organs (ovaries, uterus, epididymides, seminal vesicles, testes) of rats or mice in the 14-week inhalation studies with CASRN 80-56-8. An oral prenatal developmental toxicity study with CASRN 80-56-8 showed no maternal or developmental effects in hamsters at 600 mg/kg-day (highest doses tested); the

NOAEL for maternal/developmental toxicity is 600 mg/kg-day. Oral prenatal developmental toxicity studies with CASRN 80-56-8 in rats and mice showed no maternal effects, but a decrease in the number of live offspring was observed in rats and mice at 56 and 120 mg/kg-day, respectively. In rats, the NOAEL for maternal toxicity is 260 mg/kg-day (highest dose tested) and the NOAEL for developmental toxicity is 12 mg/kg-day. In mice, the NOAEL for maternal toxicity is 560 mg/kg-day (highest dose tested) and the NOAEL for developmental toxicity is 26 mg/kg-day. An oral prenatal developmental toxicity study in rats showed increased resorptions in dams exposed to CASRN 79-92-5 at 1000 mg/kg-day (highest dose tested); the NOAELs for maternal and developmental toxicity are 1000 and 250 mg/kg-day, respectively. The bicyclic terpene hydrocarbons are irritating to rabbit skin and eyes. Skin irritation and allergic contact dermatitis have been reported in patients patch tested with CASRN 8006-64-2. Available genotoxicity studies showed no evidence of mutagenicity for members of this category. CASRNs 80-56-8, 127-91-3 and 79-92-5 did not induce gene mutations in bacteria *in vitro*. CASRNs 127-91-3 and 79-92-5 did not induce sister chromatid exchange in cultured Chinese hamster ovary cells *in vitro*. CASRN 80-56-8 did not induce unscheduled DNA synthesis in rat hepatocytes *in vitro*. CASRN 79-92-5 did not induce micronuclei *in vivo*.

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

Endpoints	Bicyclo[3.1.1] hept-2-ene, 2,6,6-trimethyl – (<i>alpha</i> -pinene) (80-56-8)	Bicyclo[3.1.1] heptane, 6,6-dimethyl -2-ethylene (<i>beta</i> -pinene) (127-91-3)	Bicyclo[2.2.1] heptane, 2,2-dimethyl-3-methylene- (camphene) (79-92-5)	Bicyclo[3.1.1] heptane, 2,6,6-trimethyl-, (1R,2S,5R) (<i>cis</i> -pinane) (6876-13-7)	Bicyclo[3.1.1] heptane, 2,6,6 -trimethyl- (dihydro-pinene) (473-55-2)	Bicyclo[3.1.1] hept-2-ene,2,6,6-trimethyl-(1S,5S)- (<i>l-alpha</i> -pinene) (7785-26-4)	Terpenes and terpenoids, terpenine oil <i>alpha</i> -pinene fraction (65996-96-5)	Terpenes and terpenoids, terpenine oil <i>beta</i> -pinene fraction (65996-97-6)	Turpentine gum (9005-90-7)	Turpentine oil (8006-64-2)
Acute Oral Toxicity LD ₅₀ (mg/kg-bw)	3700	>5000	> 5000	No Data 2600 (RA)	No Data 2600 (RA)	No Data 2600 (RA)	No Data 2600 (RA)	No Data 2600 (RA)	No Data 2600 (RA)	2600
Acute Inhalation Toxicity LC ₅₀ (mg/L)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	No Data 9 (RA)	9
Acute Dermal Toxicity LD ₅₀ (mg/kg-bw)	> 5000	> 5000	> 2500	No Data > 2000 (RA)	No Data > 2000 (RA)	No Data > 2000 (RA)	No Data > 2000 (RA)	No Data > 2000 (RA)	No Data > 2000 (RA)	> 2000
Repeated-Dose Toxicity NOAEL/ LOAEL Oral(mg/kg-day)	No Data NOAEL= 250 LOAEL= 1000 (RA)	No Data NOAEL = 250 LOAEL=1000 (RA)	NOAEL= 250 LOAEL=1000	No Data NOAEL= 250 LOAEL=1000 (RA)	No Data NOAEL = 250 LOAEL = 1000 (RA)	No Data NOAEL = 250 LOAEL = 1000 (RA)	No Data NOAEL = 250 LOAEL = 1000 (RA)	No Data NOAEL = 250 LOAEL = 1000 (RA)	No Data NOAEL = 250 LOAEL = 1000 (RA)	No Data NOAEL = 250 LOAEL = 1000 (RA)
Repeated-Dose Toxicity NOAEL/ LOAEL Inhalation (ppm)	(rat) NOAEC= 200 LOAEC =400 (mouse) NOAEC=50 LOAEC=100	No Data (rat) NOAEC= 200 LOAEC = 400 (mouse) NOAEC= 100 LOAEC= 200 (RA)	No Data (rat) NOAEC = 200 LOAEC = 400 (mouse) NOAEC = 100 LOAEC = 200 (RA)	No Data (rat) NOAEC= 200 LOAEC = 400 (mouse) NOAEC = 100 LOAEC = 200 (RA)	No Data (rat) NOAEC = 200 LOAEC = 400 (mouse) NOAEC = 100 LOAEC = 200 (RA)	No Data (rat) NOAEC = 200 LOAEC = 400 (mouse) NOAEC = 100 LOAEC = 200 (RA)	No Data (rat) NOAEC = 200 LOAEC = 400 (mouse) NOAEC = 100 LOAEC = 200 (RA)	No Data (rat) NOAEC = 200 LOAEC = 400 (mouse) NOAEC = 100 LOAEC = 200 (RA)	No Data (rat) NOAEC=200 LOAEC=400 (mouse) NOAEC= 100 LOAEC= 200 (RA)	No Data (rat) NOAEC=200 LOAEC=400 (mouse) NOAEC=100 LOAEC= 200 (RA)

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

Endpoints	Bicyclo[3.1.1] hept-2-ene, 2,6,6-trimethyl – (<i>alpha</i> -pinene) (80-56-8)	Bicyclo[3.1.1] heptane, 6,6-dimethyl -2-ethylene (<i>beta</i> -pinene) (127-91-3)	Bicyclo[2.2.1] heptane, 2,2-dimethyl-3-methylene- (camphene) (79-92-5)	Bicyclo[3.1.1] heptane, 2,6,6-trimethyl-, (1R,2S,5R) (<i>cis</i> -pinane) (6876-13-7)	Bicyclo[3.1.1] heptane, 2,6,6 -trimethyl- (dihydro-pinene) (473-55-2)	Bicyclo[3.1.1] hept-2-ene,2,6,6-trimethyl- (1S,5S)- (<i>l-alpha</i> -pinene) (7785-26-4)	Terpenes and terpenoids, terpenine oil <i>alpha</i> -pinene fraction (65996-96-5)	Terpenes and terpenoids, terpenine oil <i>beta</i> -pinene fraction (65996-97-6)	Turpentine gum (9005-90-7)	Turpentine oil (8006-64-2)
Reproductive Toxicity NOAEL/ LOAEL Oral (mg/kg-day)	No specific reproductive toxicity data are available; however, no adverse effects were observed in the reproductive organs of rats or mice during the 14-week inhalation studies with CASRN 80-56-8.									
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day)										
Maternal Toxicity	(mouse) NOAEL = 560 (highest dose tested)	No Data (mouse) NOAEL = 560	(rat) NOAEL=250 LOAEL = 1000	No Data (mouse) NOAEL = 560	No Data (mouse) NOAEL = 560	No Data (mouse) NOAEL = 560	No Data (mouse) NOAEL = 560	No Data (mouse) NOAEL = 560	No Data (mouse) NOAEL = 560	No Data (mouse) NOAEL = 560
Developmental Toxicity	NOAEL = 26 LOAEL = 120	NOAEL = 26 LOAEL = 120 (RA)	NOAEL=1000 (highest dose tested)	NOAEL = 26 LOAEL = 120 (RA)	NOAEL = 26 LOAEL = 120 (RA)	NOAEL = 26 LOAEL = 120 (RA)	NOAEL = 26 LOAEL = 120 (RA)	NOAEL = 26 LOAEL = 120 (RA)	NOAEL = 26 LOAEL = 120 (RA)	NOAEL = 26 LOAEL = 120 (RA)
Maternal Toxicity	(hamster) NOAEL= 600 (highest dose tested)	No Data (hamster) NOAEL= 600		No Data (hamster) NOAEL= 600	No Data (hamster) NOAEL= 600	No Data (hamster) NOAEL= 600	No Data (hamster) NOAEL= 600	No Data (hamster) NOAEL= 600	No Data (hamster) NOAEL= 600	No Data (hamster) NOAEL= 600
Developmental Toxicity	NOAEL= 600 (highest dose tested)	NOAEL= 600 (RA) No Data		NOAEL= 600 (RA) No Data	NOAEL= 600 (RA) No Data	NOAEL= 600 (RA) No Data	NOAEL= 600 (RA) No Data	NOAEL= 600 (RA) No Data	NOAEL= 600 (RA) No Data	NOAEL= 600 (RA) No Data

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

Endpoints	Bicyclo[3.1.1] hept-2-ene, 2,6,6-trimethyl – (<i>alpha</i>-pinene) (80-56-8)	Bicyclo[3.1.1] heptane, 6,6-dimethyl -2-ethylene (<i>beta</i>-pinene) (127-91-3)	Bicyclo[2.2.1] heptane, 2,2-dimethyl-3-methylene- (camphene) (79-92-5)	Bicyclo[3.1.1] heptane, 2,6,6-trimethyl-, (1R,2S,5R) (<i>cis</i>-pinane) (6876-13-7)	Bicyclo[3.1.1] heptane, 2,6,6 -trimethyl- (<i>dihydro</i>-pinene) (473-55-2)	Bicyclo[3.1.1] hept-2-ene,2,6,6-trimethyl- (1S,5S)- (<i>l-alpha</i>-pinene) (7785-26-4)	Terpenes and terpenoids, terpine oil <i>alpha</i>-pinene fraction (65996-96-5)	Terpenes and terpenoids, terpine oil <i>beta</i>-pinene fraction (65996-97-6)	Turpentine gum (9005-90-7)	Turpentine oil (8006-64-2)
Maternal Toxicity	(rat) NOAEL= 260 (highest dose tested)	(rat) NOAEL = 260		(rat) NOAEL = 260	(rat) NOAEL = 260	(rat) NOAEL = 260	(rat) NOAEL = 260	(rat) NOAEL = 260	(rat) NOAEL = 260	(rat) NOAEL = 260
Developmental Toxicity	NOAEL = 56 LOAEL = 12	NOAEL = 56 LOAEL =12 (RA)		NOAEL = 56 LOAEL =12 (RA)	NOAEL = 56 LOAEL =12 (RA)	NOAEL = 56 LOAEL =12 (RA)	NOAEL = 56 LOAEL =12 (RA)	NOAEL = 56 LOAEL =12 (RA)	NOAEL = 56 LOAEL =12 (RA)	NOAEL = 56 LOAEL =12 (RA)
Genetic Toxicity- Gene Mutation <i>In-vitro</i>	Negative	Negative	Negative	No Data Negative (RA)	Negative	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	Negative
Genetic Toxicity – Chromosomal Aberrations <i>In vitro</i>	No Data Negative (RA)	Negative	Negative	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)
Genetic Toxicity – Chromosomal Aberrations <i>In vivo</i>	Negative	No Data Negative (RA)	Negative	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)
Genetic Toxicity – Other <i>In vitro</i> Unscheduled DNA Synthesis	Negative	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)	No Data Negative (RA)

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

Endpoints	Bicyclo[3.1.1] hept-2-ene, 2,6,6-trimethyl – (<i>alpha</i>-pinene) (80-56-8)	Bicyclo[3.1.1] heptane, 6,6-dimethyl -2-ethylene (<i>beta</i>-pinene) (127-91-3)	Bicyclo[2.2.1] heptane, 2,2-dimethyl-3-methylene- (<i>camphene</i>) (79-92-5)	Bicyclo[3.1.1] heptane, 2,6,6-trimethyl, (1R,2S,5R) (<i>cis</i>-pinane) (6876-13-7)	Bicyclo[3.1.1] heptane, 2,6,6 -trimethyl- (<i>dihydro</i>-pinene) (473-55-2)	Bicyclo[3.1.1] hept-2-ene,2,6,6-trimethyl- (1S,5S)- (<i>l-alpha</i>-pinene) (7785-26-4)	Terpenes and terpenoids, turpentine oil <i>alpha</i>-pinene fraction (65996-96-5)	Terpenes and terpenoids, turpentine oil <i>beta</i>-pinene fraction (65996-97-6)	Turpentine gum (9005-90-7)	Turpentine oil (8006-64-2)
Additional Information										
Eye Irritation	–	–	–	–	–	–	–	–	–	Slightly Irritating
Skin Irritation	–	–	–	–	–	–	–	–	–	Severely Irritating
Skin Sensitization	–	–	–	–	–	–	–	–	–	Positive

Measured data in bold; RA = read across; – indicates endpoint not addressed for this chemical

4. Hazard to the Environment

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.

Acute Toxicity to Fish

alpha-Pinene (CASRN 80-56-8)

Fathead minnow (*Pimephales promelas*) were exposed to *alpha*-pinene (91% pure) at measured concentrations of 0.058, 0.14, 0.23, 0.30 and 0.65mg/L under semi-static conditions for 96 hours. Analytical monitoring was conducted every 24 hours. An LC₅₀ of 0.28 was reported.

96-h LC₅₀ = 0.28 mg/L

beta-Pinene (CASRN 127-91-3)

Fathead minnow (*Pimephales promelas*) were exposed to *beta*-pinene (97% pure) at measured concentrations of 0.24, 0.58, 1.0, 1.2 and 1.8 mg/L under semi-static conditions for 96 hours. Analytical monitoring was conducted every 24 hours.

96-h LC₅₀ = 0.5 mg/L

Camphene (CASRN 79-92-5)

(1) Zebrafish (*Brachydanio rerio*) were exposed to camphene (86.7% pure) at unspecified concentrations under flow-through conditions for 96 hours.

96-h LC₅₀ = 0.72 mg/L

(2) Sheepshead minnow (*Cyprinodon variegatus*) were exposed to CASRN 79-92-5 (≥ 80%) at nominal concentration ranging from 1.6 to 2.2 mg/L under static conditions for 96 hours.

96-h LC₅₀ = 1.9 mg/L

Acute Toxicity to Aquatic Invertebrates

alpha-Pinene (CASRN 80-56-8)

Water fleas (*Daphnia magna*) were exposed to *alpha*-pinene (91% pure) at unspecified concentrations under static conditions for 48 hours. Analytical monitoring was conducted every 24 hours. A negative control was included and responded appropriately.

48-h LC₅₀ = 1.44 mg/L

beta-Pinene (CASRN 127-91-3)

Water fleas (*Daphnia magna*) were exposed to *beta*-pinene (97% pure) at measured concentrations of 0.30, 0.70, 0.85, 1.18 and 1.66 mg/L under static conditions for 48 hours. Analytical monitoring was conducted every 24 hours. A negative control was included and responded appropriately.

48-h EC₅₀ = 1.25 mg/L

Toxicity to Aquatic Plants

alpha-Pinene (CASRN 80-56-8)

(1) Green algae (species not specified) were exposed to *alpha*-pinene at unspecified concentrations for 48 hours. No additional information was provided.

No effects at saturation.

(2) A 96-hour LC₅₀ for aquatic plants, estimated by ECOSAR (Version 1.00a), was provided to support evaluation of the toxicity of *alpha*-pinene.

96-h LC₅₀ = 0.22 mg/L (estimated)

beta-Pinene (CASRN 127-91-3)

(1) Green algae (species not specified) were exposed to *beta*-pinene at unspecified concentrations for 48 hours. No additional information was provided.

48-h LC₅₀ = 1.44 mg/L

(2) A 96-hour LC₅₀ for aquatic plants, estimated by ECOSAR (Version 1.00a), was provided to support evaluation of the toxicity of *beta*-pinene.

96-h LC₅₀ = 0.79 mg/L (estimated)

Turpentine gum (CASRN 9005-90-7)

Green algae (*Pseudokirchneriella subcapitata*) were exposed to turpentine gum as WAFs under unspecified conditions for 72 hours. The loading rates were 0, 1, 10 or 100 mg/L and no analytical measurements were made on the WAFs. No effects were noted at any of the WAF loading rates. EPA does not consider the loading rate as the no-effect concentration when the concentration exceeds the water solubility of the substance. Assuming that the exposure concentration in the WAF is the water solubility limit (saturation) for turpentine gum, the no-effect concentration would be approximately 1.1 mg/L.

No effects at saturation.

Conclusion: The 96-h LC₅₀ of CASRN's 80-56-8, 127-91-3, and 79-92-5 for fish are 0.28, 0.5, and 0.72, respectively. There were no effects at saturation after 96-hr exposure to CASRN 9005-90-7 for fish. The 48-h EC₅₀ of CASRNs 80-56-8 and 127-91-3 for aquatic invertebrates are 1.44 and 1.25 mg/L respectively. The 48-h EC₅₀ of CASRN 127-91-3 for aquatic plants is 1.44 mg/L. There were no effects at saturation after 96-h exposure to CASRN 9005-90-7 for aquatic plants.

5. References

Treudler R., Richter G, Geier J., Schnuch A., Orfanos C., Tebbe B. Increase in sensitization to oil of turpentine: recent data from a Multicenter Study on 45,005 patients from the German-Austrian Information Network of Departments of Dermatology. *Contact Dermatitis* 2000 (42) 68-73.

Cachão P, Menezes Brandão F, Carmo M, Frazão S, Silva M. Allergy to oil of turpentine in Portugal. *Contact Dermatitis* 1986 Apr; 14(4):205-8.

Table 5. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program - Aquatic Toxicity Data

Endpoints	<i>alpha</i> -Pinene (80-56-8)	<i>beta</i> -Pinene (127-91-3)	Camphene (79-92-5)	<i>cis</i> -Pinane (6876-13-7)	Dihydro- pinene (473-55-2)	<i>l-alpha</i> - Pinene (7785-26-4)	Terpenes and Terpenoids, Turpentine oil, <i>alpha</i> -Pinene (65996-96-5)	Terpenes and Terpenoids, Turpentine oil, <i>beta</i> -Pinene (65996-97-6)	Turpentine gum (9005-90-7)	Turpentine oil (8006-64-2)
Fish 96-h LC₅₀ (mg/L)	0.28	0.5	0.72	No Data 0.28 (RA)	No Data 0.28 (RA)	No Data 0.28 (RA)	No Data 0.28 (RA)	No Data 0.28 (RA)	No Data 0.28 (RA)	No Data 0.28 (RA)
Aquatic Invertebrates 48-h EC₅₀ (mg/L)	1.44	1.25	No Data 1.25 (RA)	No Data 1.25 (RA)	No Data 1.25 (RA)	No Data 1.25 (RA)	No Data 1.25 (RA)	No Data 1.25 (RA)	No Data 1.25 (RA)	No Data 1.25 (RA)
Aquatic Plants 48-h EC₅₀ (mg/L) 96-hr Predicted	No Adequate Data 1.44 (RA)	1.44	No Data 1.44 (RA)	No Data 1.44 (RA)	No Data 1.44 (RA)	No Data 1.44 (RA)	No Data 1.44 (RA)	No Data 1.44 (RA)	No Data 1.44 (RA)	No Data 1.44 (RA)
Aquatic Chronic 21-day NOEC	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data	No Data

bold = measured data (i.e., derived from testing); (RA) = Read Across