SCREENING-LEVEL HAZARD CHARACTERIZATION
Terpenoid Tertiary Alcohols and Related Esters

SPONSORED CHEMICALS
13 Chemicals and/or Mixtures (See Section 1.0)

The High Production Volume (HPV) Challenge Program[1] 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 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

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[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.

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.

Chemical Abstract Service Registry Number (CASRN)	**See Appendix**
Chemical Abstract Index Name	**See Appendix**
Structural Formula	**See Appendix**

Summary

The terpenoid tertiary alcohols and related esters category consists of substances that are primarily liquids at room temperature with moderate vapor pressure and moderate water solubility. The substances in this category are expected to possess moderate to high mobility in soil. Volatilization is expected to be moderate for all category members. The rate of atmospheric photooxidation is considered moderate to rapid. The rate of hydrolysis under environmental conditions is negligible for each member of the category. The substances contained in the terpenoid tertiary alcohols and related esters category are expected to have low to moderate persistence (P1-P2) and low bioaccumulation potential (B1).

Human Health Hazard

Subcategory 1: Terpenoid Alcohols

Subgroup 1: Noncyclic Saturated Tertiary Alcohols

The acute oral toxicity of CASRN 78-69-3 is low in rats and the acute dermal toxicity is low in rabbits.

The repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

The acute oral toxicity of subgroup 2 members is low in rats and the acute dermal toxicity is low in rabbits. The subgroup members induced gene mutations *in vitro,* but did not induce chromosomal aberrations. CASRNs 78-70-6 did not induce unscheduled DNA synthesis in rat hepatocytes. CASRN 78-70-6 was irritating to rabbit skin and eyes.

CASRN 78-70-6 showed no systemic toxicity in rats via immunotoxicity testing.

Repeated-dose, reproductive and developmental toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subgroup 3: Cyclic Unsaturated Tertiary Alcohols/Subgroup 4: Pinanols

The acute oral toxicity of subgroup 3 member (CASRN 98-55-5) is low in mice. The acute oral toxicity of subgroup 4 member (CASRN 4948-28-1) is low rats and the acute dermal toxicity is low in rabbits. CASRN 98-55-5 did not induce gene mutations *in vitro*.

Repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

The acute oral and dermal toxicity of CASRN 115-95-7 is low rats and rabbits, respectively. CASRN 115-95-7 did not induce gene mutations *in vitro*.

Repeated-dose, reproductive and developmental toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subgroup 2: Cyclic Unsaturated Tertiary Esters
A repeated-dose toxicity study in rats administered CASRN 115-95-7 via the diet showed no systemic toxicity. The NOAEL for systemic toxicity is 550 mg/kg-bw/day, the highest dose tested.

Acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory 3: Terpenoid Hydroperoxides

The acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

The acute oral toxicity of CASRN 8002-09-3 is low in rats, and the acute dermal and inhalation toxicity is moderate in rats and rabbits. In an oral prenatal developmental toxicity study in rats, decreases in body weight and food consumption and increases in clinical signs of toxicity were observed in the dams at 600 mg/kg-day; the NOAEL for maternal toxicity is 50 mg/kg-day. Delays in fetal ossification, decreases in brain and fetal body weights, and increases in resorptions were observed in the fetuses at 1200 mg/kg-day; the NOAEL for developmental toxicity is 600 mg/kg-day. CASRN 8002-09-3 did not induce gene mutations in vitro or chromosomal aberrations *in vivo*. CASRN did not induce unscheduled DNA synthesis *in vitro*.

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

The acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Hazard to the Environment

Subcategory 1: Terpenoid Alcohols

The evaluation of available toxicity data of terpenoid alcohols indicates that the 96 hour LC_{50} values to fish range 3.7-18 mg/L, the 48 hour EC_{50} values to daphnia range 7.0- 36 mg/L, and the algal 72-h EC_{50} value is > 15 mg/L for biomass.

Subcategory 2: Terpenoid Esters

The evaluation of available toxicity data of terpenoid esters indicates that the 96 hour LC_{50} to fish is 11 mg/L, the 48 hour EC_{50} to daphnia is 6.2 mg/L, and the algal 72-h EC_{50s} values are 4.2 mg/L for biomass and 16 mg/L for growth rate.

Subcategory 3: Terpenoid Hydroperoxides

The aquatic toxicity of terpenoid esters and terpenoid hydroperoxides could not be evaluated because no data on aquatic toxicity endpoints were available.

Subcategory 4: Terpenoid Allyl Alcohols

The evaluation of available toxicity data of CASRN 78-70-6 indicates that the 96 hour LC_{50} to fish is 28 mg/L, the 48 hour EC_{50} to daphnia is 20 mg/L, and the algal 96-h EC_{50s} values are 88 mg/L for biomass and 157 mg/L for growth rate.

The acute toxicity to fish and aquatic invertebrates and toxicity to aquatic plants endpoints for Subcategory 3: Terpenoid Hydroperoxides were identified as data gaps under the HPV Challenge Program.

The sponsor, The Flavor and Fragrance High Production Volume Chemical Consortia, submitted a Test Plan and Robust Summaries to EPA for terpenoid alcohols and related esters on January 29, 2001. EPA posted the submission on the ChemRTK HPV Challenge website on February 14, 2001 (http://www.epa.gov/oppt/chemrtk/pubs/summaries/tertestr/c12930tc.htm). EPA comments on the original submission were posted to the website on June 26, 2001. Public comments were also received and posted to the website.

Category Justification

The terpenoid tertiary alcohols and related esters category contains 13 terpenoid substances that are used extensively in flavors and fragrances. All but one of the substances is either a tertiary alcohol or an ester; the exception is 2-pinanol hydroperoxide. Seven of the substances are discrete alcohols: linalool (CASRN 78-70-6), tetrahydrolinalool (CASRN 78-69-3), myrcenol (CASRN 543-39-5), dihydromyrcenol (CASRN 18479-58-8), α-terpineol (CASRN 98-55-5), *cis*-2-pinanol (CASRN 4948-28-1) and *trans*-2-pinanol (CASRN 4948-29-2); two substances are acetate esters: linalyl acetate (CASRN115-95-7) and α-terpineol acetate (CASRN 80-26-2); one substance is a mixture of two chemicals: 2-pinanol (CASRN 473-54-1), a mixture of *cis*- and *trans*-2-pinanol; and two substances are complex mixtures: pine oil (CASRN 8002-09-3) and 2-pinanol thermal rearrangement products (CASRN 125252-49-5). EPA does not support the proposed category since it does not appear to cohere on the basis of structural considerations. The structural types may have different physiological and environmental properties. Although the sponsor provided information on metabolic pathways with respect to 7 of the 13 proposed category members, the incomplete discussion provides little support for the conclusion that all members of this group have a common metabolic fate in mammalian systems.

Therefore, for human health, EPA has separated this category into the following four subcategories: terpenoid alcohols (subcategory 1), terpenoid esters (subcategory 2), terpenoid hydroperoxides (subcategory 3) and terpenoid complex mixtures (subcategory 4). The presence of ester and peroxide functional groups are expected to result in differences in environmental fate and health effects for structures listed in subcategories 2 and 3 compared to the alcohol structures of subcategory 1. The complex mixtures are also treated separately since they are not comparable with the single structures listed in the other subcategories. Subcategories 1 and 2 have been further divided into subgroups on the basis of differences in cyclic nature and saturation since these differences may affect metabolic pathways as well as environmental degradation rates. The subcategory 1 include subgroup 1: noncyclic saturated tertiary alcohols; subgroup 2: noncyclic unsaturated tertiary alcohols; subgroup 3: cyclic unsaturated tertiary alcohols and subgroup 4: pinanols. Subcategory 2 consists of subgroup1: noncyclic unsaturated tertiary esters and subgroup 2: cyclic unsaturated tertiary esters. A read-across approach is supported between subgroup members residing within the same subcategory, but is not supported across subgroups or across subcategories. Subcategory 4 has been divided into subgroup 1: pine oil and subgroup 2: 2-pinanol thermal rearrangement products.

For ecotoxicity, EPA has separated this category into the following four subcategories: terpenoid alcohols (subcategory 1), terpenoid esters (subcategory 2), terpenoid hydroperoxides (subcategory 3) and terpenoid allyl alcohol (subcategory 4). The presence of ester and peroxide functional groups are expected to result in differences in environmental fate and environmental

effects for structures listed in subcategories 2 and 3 compared to the alcohol structures of subcategory 1. Also, terpenoid allyl alcohol has been delineated to a subcategory on the basis of differences in alcohol nature since these differences may affect the ecotoxicity. However, the complex mixtures are treated together since they are comparable with the single structures listed in subcategory1. A read-across approach is supported between subcategory members, but is not supported across subcategories.

1. Chemical Identity

1.1 Identification and Purity

The following description is taken from the 2001 Test Plan:

The chemical category designated "Tertiary Terpenoid Alcohols and Related Esters" includes eight terpenoid aliphatic tertiary alcohols and two related acetate esters. The group of alcohols consists of linalool (3,7&nethyl- 1,6-octadien-3-ol), tetrahydrolinalool (3,7-dimethyl-3-octanol), a tertiary alcohol isomer of linalool, myrcenol (2-methyl-6-methylene-7-octen-2-ol), dihydromyrcenol (3,7-dimethyl-7-octen-2-o1); *an* isomeric alicyclic tertiary alcohol *alpha-*terpineol (p-menth 1 -en-8-ol), 2-pinanol, and *cis-* and trans-2-pinanol. The two esters include the acetate ester of linalool (3,7dimethyl- 1,6-octadien-3-yl acetate) and acetate ester of *alpha-terpineol* (p-menth- 1-en-8-yl acetate).

This chemical category also includes a site-restricted peroxide of a terpene tertiary alcohol (pinane hydroperoxide) that is efficiently reduced to the corresponding alcohol (2-pinanol). It also includes two mixtures consisting predominantly of tertiary terpenoid alcohols. These two mixtures are pine oil and "2,6,6-trimethylbicyclo[3.1.l]heptan-2-o1 thermal rearrangement products, linalool h-actions, acid-isomerized distillation residues, acid-isomerized distillation lights, terpenoids". The composition of these mixtures is discussed in the paragraph below.

Seven of the tertiary alcohols are isomers of the formula $C_{10}H_{18}O$, one is a dihydro homologue ($C_{10}H_{20}O$), and one is a tetrahydro homologue ($C_{10}H_{22}O$). The two acetate esters have the formula $C_{12}H_{20}O_2$. The pinane hydroperoxide has the formula $C_{10}H_{18}O_2$. The two mixtures are composed principally of terpenoid tertiary alcohols of the formula $C_{10}H_{18}O$. Purity of the individual chemicals and/or mixtures is specified in section 3.

1.2 Physical-Chemical Properties

The terpenoid tertiary alcohols and related esters category consists of substances that are primarily liquids at room temperature. 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-; bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-; bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-,

(1R,2S,5S)-rel-; and bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel- may appear as viscous liquids or solids at room temperature. All members of the category possess moderate vapor pressure and moderate water solubility.

The physical-chemical properties of Terpenoid Tertiary Alcohols and Related Esters are summarized in Table 1. Structures of all category members are provided in the Appendix.

Table 1. Physical-Chemical Properties of Terpenoid Tertiary Alcohols and Related Esters Category[1]

Property	3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, 1-acetate	3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-	7-Octen-2-ol, 2-methyl-6-methylene-	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2S,5S)-rel-	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel-
CASRN	80-26-2	98-55-5	473-54-1	543-39-5	4948-28-1	4948-29-2
Molecular Weight	196.29	154.25	154.25	154.25	154.25	154.25
Physical State[2]	Colorless clear liquid	Colorless viscous liquid to solid	White solid	Colorless to pale yellow clear liquid	White solid; Colorless crystals[3]	White solid; Colorless needles[3]
Melting Point	<25°C (liquid)	31–36.4°C (measured)	78–79.2°C (measured *cis*-isomer)[3]; 58–59°C (measured *trans*-isomer)[3]	<25°C (liquid)	78–79.2°C (measured)[3]	58–59°C (measured)[3]
Boiling Point	220°C (measured)	217–218°C (measured)	205°C (measured)	213°C (measured)	205°C (measured)	205–206°C (measured)
Vapor Pressure	0.13 at 25°C (estimated)[4]	0.04 mm Hg at 22–25°C (measured)	0.030 mm Hg at 25°C (estimated)[4]	0.033 mm Hg at 25°C (estimated)[4]	0.030 mm Hg at 25°C (estimated)[4]	0.030 mm Hg at 25°C (estimated)[4]

Table 1. Physical-Chemical Properties of Terpenoid Tertiary Alcohols and Related Esters Category[1]						
Property	**3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, 1-acetate**	**3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-**	**7-Octen-2-ol, 2-methyl-6-methylene-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2S,5S)-rel-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel-**
CASRN	80-26-2	98-55-5	473-54-1	543-39-5	4948-28-1	4948-29-2
Water Solubility	37 mg/L at 25°C (estimated)[4]	716 mg/L at 22–25°C (measured); 341 mg/L at 4–8°C (measured)	777 mg/L at 25°C (estimated)[4]	316 mg/L at 25°C (estimated)[4]	777 mg/L at 25°C (estimated)[4]	777 mg/L at 25°C (estimated)[4]
Dissociation Constant (pK_a)	Not applicable					
Henry's Law Constant	1.0×10^{-4} atm-m^3/mole (estimated)[4]	1.2×10^{-5} atm-m^3/mole (estimated)[4]	1.9×10^{-6} atm-m^3/mole (estimated)[4]	2.9×10^{-5} atm-m^3/mole (estimated)[4]	1.9×10^{-6} atm-m^3/mole (estimated)[4]	1.9×10^{-6} atm-m^3/mole (estimated)[4]
Log K_{ow}	4.3 (measured)	2.98 (measured)	2.85 (estimated)[4]	3.46 (estimated)	2.85 (estimated)[4]	2.85 (estimated)[4]

[1] The Flavor and Fragrance High Production Volume Consortia. The Terpene Consortium. January 29, 2001. Test Plan and Robust Summary for Terpenoid Tertiary Alcohols and Related Esters. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/tertestr/c12930tc.htm as of March 24, 2010.
[2] The Good Scents Company. CAS Indexed Botanic, Cosmetic, Flavor and Fragrance Ingredients. Available online from: http://www.thegoodscentscompany.com/allproc.html as of March 24, 2010.
[3] Ullmann's Encyclopedia of Industrial Chemicals. 2005. Terpenes. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.
[4] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of March 24, 2010.

Table 1 cont. Physical-Chemical Properties of Terpenoid Tertiary Alcohols and Related Esters Category[1]							
Property	**Oils, pine**	**7-Octen-2-ol, 2,6-dimethyl-**	**Hydroperoxide, 2,6,6-trimethyl-bicyclo[3.1.1] heptyl**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids**	**3-Octanol, 3,7-dimethyl-**	**1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)**	**1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)**
CASRN	8002-09-3	18479-58-8	28324-52-9	125252-49-5	78-69-3	78-70-6	115-95-7
Molecular Weight	154.25 (typical)	156.27	170.25	154.25 (typical for cyclopentanol, 1,2-dimethyl-3-(1-methylethenyl)- (CASRN 72402-00-7)	158.29	154	196
Physical State[2]	Colorless to pale yellow liquid	Colorless clear liquid	Colorless liquid[5]	Liquid	Colorless clear liquid	Liquid	Liquid
Melting Point	<25°C (liquid)	<25°C (liquid)	<25°C (liquid)	<25°C (liquid)	<25°C (liquid)	<20°C (measured)	<25°C (liquid)
Boiling Point	200–220°C (measured)	80°C at 213 mm Hg (measured); 188.4 (measured)[3]	Thermally unstable; Decomposes at >110°C, forming 1-((1*R*)- *cis*-3-ethyl-2,2-dimethyl-cyclobutyl) ethanone[5]	196°C (measured for CASRN 94346-09-5); 219°C (measured for CASRN 94346-09-5)	230°C (measured)	198°C (measured)	213 (measure); 220°C (measured)[4]
Vapor Pressure	0.04 mm Hg at 22–25°C (measured for CASRN 98-55-5)	0.14 mm Hg at 25°C (estimated)[4]	0.06 mm Hg at 25°C (estimated)[4]	0.81 mm Hg at 25°C (measured for CASRN 94346-09-5); 0.14 mm Hg at 22–25°C (measured for CASRN 72402-00-7)	0.012 mm Hg at 25°C (estimated)[4]	0.15 at 20°C (measured); 0.05027 at 20°C (measured); 0.16 at 22-25°C (measured)	0.07 at 20°C (estimated) ; 0.111 (measured)[4]
Water Solubility	716 mg/L at 22–25°C (measured for CASRN 98-55-5)	311 mg/L at 25°C (estimated)[4]	160 mg/L at 25°C (estimated)[4]	60.5 mg/L at 20°C (measured for CASRN 94346-09-5)	700 mg/L (measured at unspecified temperature)	1,450 at 20°C (measured); 867 at 22-25°C (measured)	140 at 20°C (measured)

Table 1 cont. Physical-Chemical Properties of Terpenoid Tertiary Alcohols and Related Esters Category[1]							
Property	**Oils, pine**	**7-Octen-2-ol, 2,6-dimethyl-**	**Hydroperoxide, 2,6,6-trimethyl-bicyclo[3.1.1] heptyl**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids**	**3-Octanol, 3,7-dimethyl-**	**1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)**	**1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)**
CASRN	8002-09-3	18479-58-8	28324-52-9	125252-49-5	78-69-3	78-70-6	115-95-7
Dissociation Constant (pK_a)	Not applicable						
Henry's Law Constant	1.2×10^{-5} atm-m^3/mole (estimated)[4]	4.1×10^{-5} atm-m^3/mole (estimated)[4]	1.7×10^{-5} atm-m^3/mole (estimated)[4]	1.9×10^{-5} atm-m^3/mole (estimated for measured for CASRN 72402-00-7)[4]	5.5×10^{-5} atm-m^3/mole (estimated)[4]	2.2×10^{-5} atm-m^3/mole (measured)[4]	1.7×10^{-3} atm-m^3/mole (estimated)[4]
Log K_{ow}	2.98 (measured for CASRN 98-55-5)	3.47 (estimated)	3.06 (estimated)[4]	4.09 at 21.5°C (measured for CASRN 94346-09-5); 2.87 (measured for CASRN 72402-00-7)	3.60 (estimated)	2.9 (measured); 2.97 (measured)[4]	3.93 (measured)[4]

[1] The Flavor and Fragrance High Production Volume Consortia. The Terpene Consortium. January 29, 2001. Test Plan and Robust Summary for Terpenoid Tertiary Alcohols and Related Esters. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/tertestr/c12930tc.htm as of March 24, 2010.
[2] The Good Scents Company. CAS Indexed Botanic, Cosmetic, Flavor and Fragrance Ingredients. Available online from: http://www.thegoodscentscompany.com/allproc.html as of March 24, 2010.
[3] Beilstein search. The Procter and Gamble Company Patent: US2007/280976, 2007.
[4] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of March 24, 2010.
[5] Ullmann's Encyclopedia of Industrial Chemicals. 2005. Terpenes. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

2. General Information on Exposure

2.1 Production Volume and Use Pattern

According to the 2006 IUR submissions, the t-Terpenols category chemicals had an aggregated production and/or import volume in the United States between 55.5 million pounds and 301 million pounds.

CASRN 80-26-2:	1 to <10 million pounds;
CASRN 78-69-3:	500,000 to <1 million pounds;
CASRN 98-55-5:	1 to <10 million pounds;
CASRN 473-54-1:	10 to <50 million pounds;
CASRN 4948-28-1:	10 to <50 million pounds;
CASRN 4948-29-2:	1 to <10 million pounds;
CASRN 8002-09-3:	10 to <50 million pounds;
CASRN 18479-58-8:	1 to <10 million pounds;
CASRN 28324-52-9:	10 to <50 million pounds.
CASRN 78-70-6	10 to <50 million pounds.
CASRN 115-95-7	1 to <10 million pounds;

CASRN 543-39-5 and 125252-49-5 were not reported in the 2006 IUR.

CASRN 80-26-2:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing and soap and cleaning compound manufacturing as odor agents. Non-confidential commercial and consumer uses of this chemical include soaps and detergents.

CASRN 78-69-3:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include all other chemical product and preparation manufacturing as odor agents. Non-confidential commercial and consumer uses of this chemical include polishes and sanitation goods; soaps and detergents; and "other".

CASRN 98-55-5:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates; all other chemical product and preparation manufacturing and soap and cleaning compound manufacturing as odor agents; and all other chemical product and preparation manufacturing as "other". Non-confidential commercial and consumer uses of this chemical include polishes and sanitation goods; soaps and detergents; and "other".

CASRN 473-54-1, 4948-29-2 and CASRN 4948-28-1:
Non-confidential information in the IUR indicated that the industrial processing and uses of these chemicals include other basic organic chemical manufacturing as intermediates. No commercial and consumer uses were reported for these chemicals.

CASRN 8002-09-3:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include all other chemical product and preparation manufacturing, and soap and cleaning compound manufacturing as odor agents; all other chemical product and preparation manufacturing as "other"; and all other crop farming as non-pesticidal agricultural chemicals. Non-confidential commercial and consumer uses of this chemical include agricultural products (non-pesticidal); glass and ceramic products; polishes and sanitation goods; soaps and detergents; and "other".

CASRN 18479-58-8:
Non-confidential information in the IUR indicated that the industrial processing and uses of the chemical include other basic organic chemical manufacturing as intermediates; all other chemical product and preparation manufacturing; all other chemical product and preparation manufacturing as order agents; and all other food manufacturing. Non-confidential commercial and consumer uses of this chemical include polishes and sanitation goods; soaps and detergents; and "other".

CASRN 28324-52-9:
Non-confidential information in the IUR indicated that the industrial processing and uses of this chemical include other basic organic chemical manufacturing as process regulators (used in vulcanization or polymerization processes); and other basic organic chemical manufacturing as intermediates. No commercial and consumer uses were reported for this chemical.

CASRN 78-70-6:
Non-confidential information in the IUR indicated that the industrial processing and uses of this chemical include other basic organic chemical manufacturing as intermediates; all other chemical product and preparation manufacturing as odor agent and not readily obtainable (NRO); all other food manufacturing as not readily obtainable (NRO); all other miscellaneous manufacturing as odor agents; and soap and cleaning compound manufacturing as odor agents. Non-confidential commercial and consumer uses of this chemical include paper products; polishes and sanitation goods; soaps and detergents; and "other"

CASRN 115-95-7:
Non-confidential information in the IUR indicated that the industrial processing and uses of this chemical include all other chemical product and preparation manufacturing as odor agents. Non-confidential commercial and consumer uses of this chemical include polishes and sanitation goods; soaps and detergents; and "other".

2.2 Environmental Exposure and Fate

The terpenoid tertiary alcohols and related esters are expected to have moderate to high mobility in soil. Biodegradation studies on several category members suggest that the terpenoid tertiary alcohols and related esters are not expected to be highly persistent in the environment. 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, 1-acetate was readily biodegradable using both a manometric respirometry test (OECD 301F) in which greater than 60% degradation was achieved in 4 weeks and a modified Sturm test (OECD 301D) in which 87% mineralization was

observed in 4 weeks. 3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl- also achieved 85% of its theoretical biochemical oxygen demand (BOD) in 4 weeks using an activated sludge inoculum and the modified MITI test (OECD 301C) and is considered readily biodegradable. 7-Octen-2-ol, 2-methyl-6-methylene- was degraded 66% in 20 days using a closed bottle test (OECD 301D) and was considered readily biodegradable. Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids was not readily biodegradable using a manometric respirometry test (OECD 301F), degrading only 6% in 28 days. Hydroperoxide, 2,6,6-trimethylbicyclo[3.1.1]heptyl was also not readily biodegradable using a modified MITI test (OECD 301C), achieving only 3% of its theoretical BOD in 28 days; however, over 70% primary degradation was observed during the incubation period with the test substance transforming to bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl- in the sludge. In aqueous biodegradation screening tests, linalool reached 90% of its theoretical biological oxygen demand after 28 days in one MITI test (OECD 301C), and in another, 80% in 28 days. Linalyl actetate reached 75% of its theoretical biological oxygen demand after 28 days in a MITI test. Estimated Henry's Law constants suggest volatilization is moderate for the terpenoid tertiary alcohols and related esters. The rate of hydrolysis under environmental conditions is considered negligible for these compounds. However, linalyl acetate hydrolyzed with half-lives of <= 2.5 min at pH 1.2 and 112 min at pH 7, in artificial gastric fluid with and without peptic enzymes. The main product was linalool, with smaller amounts of alpha-terpineol and geraniol. The overall weight of evidence suggests that terpenoid tertiary alcohols and related esters are expected to have low to moderate persistence (P1-P2) and low bioaccumulation potential (B1).

The environmental fate properties are provided in Table 2.

Table 2. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]						
Property	**3-Cyclohexene-1-methanol, .alpha.,.alpha., 4-trimethyl-, 1-acetate**	**3-Cyclohexene-1-methanol, .alpha.,.alpha., 4-triethyl-**	**Bicyclo[3.1.1] heptan-2-ol, 2,6,6-trimethyl-**	**7-Octen-2-ol, 2-methyl-6-methylene-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2S,5S)-rel-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel-**
CASRN	**80-26-2**	**98-55-5**	**473-54-1**	**543-39-5**	**4948-28-1**	**4948-29-2**
Photodegradation Half-life	1.3 hours (estimated)	1.2 hours (estimated)	9.1 hours (estimated)	1.1 hours (estimated)	9.1 hours (estimated)	9.1 hours (estimated)
Hydrolysis Half-life	2.1 years at pH 8 (estimated)[2]; 21 years at pH 7 (estimated)[2]; 6 hours at 37°C and pH 7.5; 14 hours at 37°C and pH 7.0	Stable	Stable	Stable	Stable	Stable
Biodegradation	63% after 28 days (readily biodegradable); 87.3% after 28 days (readily biodegradable)	84.6% after 14 days (readily biodegradable)[3]	No data	66% after 20 days (readily biodegradable)	No data	No data

Table 2. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]						
Property	**3-Cyclohexene-1-methanol, .alpha.,.alpha., 4-trimethyl-, 1-acetate**	**3-Cyclohexene-1-methanol, .alpha.,.alpha., 4-triethyl-**	**Bicyclo[3.1.1] heptan-2-ol, 2,6,6-trimethyl-**	**7-Octen-2-ol, 2-methyl-6-methylene-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2S,5S)-rel-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel-**
CASRN	**80-26-2**	**98-55-5**	**473-54-1**	**543-39-5**	**4948-28-1**	**4948-29-2**
Bioaccumulation factor	BAF = 158 (estimated)[2]	BAF = 74 (estimated)[2]	BCF = 3.6–7.9 (measured in carp)[3]; BCF = <5.7 (measured in carp)[3]; BCF = 3.0–5.2 (measured in carp)[3]; BCF = <1.9–5.8 (measured in carp)[3]; BAF = 65 (estimated)[2]	BAF = 157 (estimated)[2]	BCF = 3.6–7.9 (measured in carp)[3]; BCF = <5.7 (measured in carp)[3]; BCF = 3.0–5.2 (measured in carp)[3]; BCF = <1.9–5.8 (measured in carp)[3]; BAF = 65 (estimated)[2]	BCF = 3.6–7.9 (measured in carp)[3]; BCF = <5.7 (measured in carp)[3]; BCF = 3.0–5.2 (measured in carp)[3]; BCF = <1.9–5.8 (measured in carp)[3]; BAF = 65 (estimated)[2]
Log K_{oc}	2.6 (estimated)[2]	1.9 (estimated)[2]	1.9 (estimated)[2]	2.4 (estimated)[2]	1.9 (estimated)[2]	1.9 (estimated)[2]
Fugacity (Level III Model)[2]						
Air	<0.1	<0.1	0.9	0.2	0.9	0.9
Water	15.8	25.9	26.3	25.8	26.3	26.3
Soil	83.8	73.9	72.6	73.9	72.6	72.6
Sediment	0.4	0.1	0.1	0.1	0.1	0.1
Persistence[4]	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation[4]	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)

Table 2. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]						
Property	**3-Cyclohexene-1-methanol, .alpha.,.alpha., 4-trimethyl-, 1-acetate**	**3-Cyclohexene-1-methanol, .alpha.,.alpha., 4-triethyl-**	**Bicyclo[3.1.1] heptan-2-ol, 2,6,6-trimethyl-**	**7-Octen-2-ol, 2-methyl-6-methylene-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2S,5S)-rel-**	**Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel-**
CASRN	**80-26-2**	**98-55-5**	**473-54-1**	**543-39-5**	**4948-28-1**	**4948-29-2**

[1] The Flavor and Fragrance High Production Volume Consortia. The Terpene Consortium. January 29, 2001. Test Plan and Robust Summary for Terpenoid Tertiary Alcohols and Related Esters. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/tertestr/c12930tc.htm as of March 24, 2010.
[2] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. United States Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of March 24, 2010.
[3] National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available online from: http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html as of March 24, 2010.
[4] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.

Table 2 cont. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]

Property	Oils, pine	7-Octen-2-ol, 2,6-dimethyl-	Hydroperoxide, 2,6,6-trimethylbicyclo [3.1.1] heptyl	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids	3-Octanol, 3,7-dimethyl-	1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)	1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)
CASRN	**8002-09-3**	**18479-58-8**	**28324-52-9**	**125252-49-5**	**78-69-3**	**78-70-6**	**115-95-7**
Photodegradation Half-life	1.2 hours (estimated)[2]	3.4 hours (estimated)	6.8 hours (estimated)	2.0 hours (estimated for CASRN 72402-00-7)[2]	9.0 hours (estimated)	1.1 hours (estimated)[2]	1.1 hours (estimated)[2]

Table 2 cont. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]

Property	Oils, pine	7-Octen-2-ol, 2,6-dimethyl-	Hydroperoxide, 2,6,6-trimethylbicyclo [3.1.1] heptyl	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids	3-Octanol, 3,7-dimethyl-	1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)	1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)
CASRN	**8002-09-3**	**18479-58-8**	**28324-52-9**	**125252-49-5**	**78-69-3**	**78-70-6**	**115-95-7**
Hydrolysis Half-life	Stable	Stable	Stable	Stable	Stable	Stable	Base-catalyzed second-order hydrolysis rate constant of 4.6X10-2 L/mole-sec was estimated using a structure estimation method (4); this corresponds to half-lives of 4.8 years and 174 days at pH values of 7 and 8, respectively.[5] However hydrolyzed with half-lives of <= 2.5 min at pH 1.2 and 112 min at pH 7, in artificial gastric fluid (HPVIS) with and without peptic enzymes. The main product

Table 2 cont. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]

Property	Oils, pine	7-Octen-2-ol, 2,6-dimethyl-	Hydroperoxide, 2,6,6-trimethylbicyclo [3.1.1] heptyl	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids	3-Octanol, 3,7-dimethyl-	1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)	1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)
CASRN	**8002-09-3**	**18479-58-8**	**28324-52-9**	**125252-49-5**	**78-69-3**	**78-70-6**	**115-95-7**
Biodegradation	50% after 5 days (readily biodegradable)	72% in 28 days (readily biodegradable)	3% after 28 days (not readily biodegradable)[3]; 76–100% was transformed to 2,6,6-trimethylbicyclo [3.1.1] heptan-2-ol in the sludge[3]	6% after 28 days (not readily biodegradable);	>100% in 28 days (readily biodegradable)	90% in 28 days[3]; 80% in 28 days (readily biodegradable)[6]	75% in 28 days (readily biodegradable)[6]
Bioaccumulation factor	BAF = 74 (estimated)[2]	BAF = 132 (estimated)[2]	BAF = 234 (estimated)[2]	BAF = 424 (estimated for CASRN 72402-00-7)[2]	BAF = 152 (estimated)[2]	BAF = 74 (estimated)[2]	BAF = 125 (estimated)[2]
Log K_{oc}	1.9 (estimated)[2]	1.9 (estimated)[2]	3.6 (estimated)[2]	1.9 (estimated for CASRN 72402-00-7)[2]	1.9 (estimated)[2]	1.9 (estimated)[2]	2.6 (estimated)[2]
Fugacity (Level III Model)[2]				(estimated for CASRN 72402-00-7)			
Air	<0.1	0.4	0.8		1.4	0.0	0.1
Water	25.9	25.5	15.6	0.2	25.0	25.8	21.6
Soil	73.9	73.9	79.3	26.1	73.5	74.0	77.8
Sediment	0.1	0.1	4.3	73.5	0.1	0.1	0.5
				0.1			

Table 2 cont. Environmental Fate Characteristics of Terpenoid Tertiary Alcohols and Related Esters Category[1]

Property	Oils, pine	7-Octen-2-ol, 2,6-dimethyl-	Hydroperoxide, 2,6,6-trimethylbicyclo [3.1.1] heptyl	Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids	3-Octanol, 3,7-dimethyl-	1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)	1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)
CASRN	**8002-09-3**	**18479-58-8**	**28324-52-9**	**125252-49-5**	**78-69-3**	**78-70-6**	**115-95-7**
Persistence[4]	P1 (low)	P1 (low)	P1 (low)	P2 (moderate)	P1 (low)	P1 (low)	P1 (low)
Bioaccumulation[4]	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)	B1 (low)

[1] The Flavor and Fragrance High Production Volume Consortia. The Terpene Consortium. January 29, 2001. Test Plan and Robust Summary for Terpenoid Tertiary Alcohols and Related Esters. Available online from: http://www.epa.gov/chemrtk/pubs/summaries/tertestr/c12930tc.htm as of March 24, 2010.
[2] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.0. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuite.htm as of March 24, 2010.
[3] National Institute of Technology and Evaluation. 2002. Biodegradation and Bioaccumulation of the Existing Chemical Substances under the Chemical Substances Control Law. Available online from: http://www.safe.nite.go.jp/english/kizon/KIZON_start_hazkizon.html as of March 24, 2010.
[4] Federal Register. 1999. Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances. *Federal Register* 64, Number 213 (November 4, 1999) pp. 60194–60204.
[5] Hazardous Substances Data Bank (HSDB), accessed 7 May 2010.
[6] High Production Volume Information System (HPVSI), accessed 7 May 2010.
[a]Data from: http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
[b]Data from: http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf

Conclusions: The terpenoid tertiary alcohols and related esters category consists of substances that are primarily liquids at room temperature with moderate vapor pressure and moderate water solubility. The substances in this category are expected to possess moderate to high mobility in soil. Volatilization is expected to be moderate for all category members. The rate of atmospheric photooxidation is considered moderate to rapid. The rate of hydrolysis is negligible for each member of the category. The substances contained in the terpenoid tertiary alcohols and related esters category are expected to have low to moderate persistence (P1-P2) and low bioaccumulation potential (B1).

3. Human Health Hazard

A summary of health effects data submitted for SIDS endpoints is provided in Table 3. The table also indicates where data for tested category members are read-across (RA) to untested members of the category. For CASRNs 78-70-6 and 115-95-7, the SIARs, SIAPs and Dossiers were finalized and published by the UNEP at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf and http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf

Acute Oral Toxicity

Subcategory 1: Terpenoid Alcohols

Subgroup 1: Noncyclic Saturated Tertiary Alcohols

Tetrahydrolinalool (CASRN 78-69-3)
Rats (10/sex; strain nor dose identified) were administered tetrahydrolinalool by the oral route at unspecified doses. No other details were provided.
LD_{50} > 5000 mg/kg-bw

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
LD_{50} = 2790 mg/kg-bw

Myrcenol (CASRN 543-39-5)
Male Wistar rats (10/dose) were administered myrcenol by an unspecified oral route at 4000, 5000, 6250 and 7800 mg/kg-bw. Mortalities were observed in all dose groups, with 2/10 at 4000, 4/10 at 5000, 7/10 at 6250, and 10/10 at 7800 mg/kg-bw.
LD_{50} = 5300 mg/kg-bw

Dihydromyrcenol (CASRN 18479-58-8)
Male Wistar rats (10/dose) were administered dihydromyrcenol via an unspecified oral route at 2560, 3200, 4000 and 5000 mg/kg-bw. Mortalities were observed in all groups, with 1/10 at

2560; 5/10 at 3200; 4/10 at 4000 and 10/10 at 5000 mg/kg-bw.
LD_{50} = 3600 mg/kg-bw

Subgroup 3: Cyclic Unsaturated Tertiary Alcohols

α-Terpineol (CASRN 98-55-5)
Male CD-1 mice (10/dose) were administered α-terpineol via an unspecified oral route at unspecified doses and observed for 7 days after dosing. No other data were provided.
LD_{50} = 2830 mg/kg-bw

Subgroup 4:Pinanols

cis-2-Pinanol (CASRN 4948-28-1)
Wistar albino rats (5/sex/dose) were administered *cis*-2-pinanol via oral gavage at 0, 1260, 2000, 2520 and 3140 mg/kg-bw after 18 hours of fasting. The test substance was diluted in 25% corn oil. Animals were observed at 1, 3, 6 and 24 hours daily for 14 days. Mortalities were observed at all doses, with 2/5 at 1260, 2/5 males and 3/5 females at 2000, 2/5 males and 4/5 females at 2520, and 4/5 males and 3/5 females at 3140. All animals were necropsied. There were no remarkable necropsy findings.
LD_{50} = 2050 mg/kg-bw

Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

Linalyl acetate (CASRN 115-95-7)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
LD_{50} = 14,550 mg/kg-bw

Subcategory 3: Terpenoid Hydroperoxides

No data were provided. Testing is recommended.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

Pine oil (CASRN 8002-09-3)
(1) Wistar albino rats (5/sex/dose) were administered pine oil (20% pine oil disinfectant in water at 5.0 g/kg; pine oil contained 76.7% α- and γ-terpineol) by an unspecified oral route at a concentration of 5000 mg/kg-bw and observed for 1, 2, and 4 hours immediately after dosing and after 14 days. No other information was provided.
LD_{50} (undiluted pine oil) > 1000 mg/kg-bw

(2) Albino Sprague Dawley rats (4/females/dose) were administered a single dose of Hercules 70L Pine Oil Disinfectant directly into the stomach at 0, 1350, 2025, 3038, 4556, and 15380 mg/kg-bw. Mortalities occurred at 4456 (3/4), and 15380 (4/4) mg/kg-bw. No gross pathological alterations were noted.
LD_{50}= 4118 mg/kg-bw

(3) Sprague-Dawley rats (4/females/dose) were administered a single dose of pine oil Hercules Fortified Pine-Odor Disinfectant (60% terpineol isomers, mainly α-terpineol) by an unspecified oral route at concentrations of 1350, 4556, 6834, 10,250 or 15,380 mg/kg-bw. Mortalities were observed at 6834 (1/4), 10250 (1/4) and 15380 (4/4). Examination of the surviving animals did not reveal any gross pathologic alterations. No other details were provided.
LD_{50} = 6834 mg/kg-bw

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

This mixture was not approved for testing. No adequate data were provided on this complex mixture. Testing is recommended.

Acute Inhalation Toxicity

Subcategory 1: Terpenoid Alcohols

No data were provided.

Subcategory 2: Terpenoid Esters

No data were provided.

Subcategory 3: Terpenoid Hydroperoxides
No data were provided.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

Pine oil (CASRN 8002-09-3)
Sprague-Dawley rats (5/sex/dose) were administered pine oil (100%; 62.7% α-terpineol, 83.4% total terpene alcohol content) via the inhalation route for 4 hours to a nominal concentration of 9.2 mg/L air. The actual concentrations measured in the breathing zone 3 times during the exposure were 3.98, 3.92 and 3.48 mg/L. No other details were provided.
LD_{50} > 3.79 mg/L

Acute Dermal Toxicity

Subcategory 1: Terpenoid Alcohols

Subgroup 1: Noncyclic Saturated Tertiary Alcohols

Tetrahydrolinalool (CASRN 78-69-3)
Rabbits (10/dose; sex and strain not provided) were administered tetrahydrolinalool by the dermal route at unspecified doses under unspecified conditions. No mortalities were observed.
LD_{50} > 5000 mg/kg-bw

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
LD_{50} = 5610 mg/kg-bw

Myrcenol (CASRN 543-39-5)
New Zealand White rabbits (10/dose, sex not specified) were administered myrcenol via the dermal route at unspecified doses. No other details were provided. No mortalities were reported.
LD_{50} > 5000 mg/kg-bw

Dihydromyrcenol (CASRN 18479-58-8)
New Zealand White rabbits (10, sex and dose not specified) were administered dihydromyrcenol via the dermal route at unspecified doses. No other details were provided. No mortalities were reported.
LD_{50} > 5000 mg/kg-bw

Subgroup 3: Cyclic Unsaturated Tertiary Alcohols

No data were provided.

Subgroup 4: Pinanols

cis-2-Pinanol (CASRN 4948-28-1)
New Zealand White rabbits (3/sex; dose not specified) were administered *cis*-2-pinanol via the dermal route at unspecified doses. The skin of two males and one female rabbit were intact and the skin of one male and 2 females were abraded. The material was applied in a close patch test. Animals were observed at 1, 3, 6, and 24 hours after treatment, followed by daily observations for 14 days. All rabbits were necropsied. No mortalities were reported.
LD_{50} > 5000 mg/kg-bw

Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

Linalyl acetate (CASRN 115-95-7)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
LD_{50} = > 5000 mg/kg-bw

Subgroup 2: Cyclic Unsaturated Tertiary Esters

No data were provided.

Subcategory 3: Terpenoid Hydroperoxides

No data were provided.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

Pine oil (CASRN 8002-09-3)
(1)Albino New Zealand rabbits (5/sex/dose) were administered pine oil (20% pine oil disinfectant, contained 76.7% α- and γ-terpineol) by the dermal route at concentrations of 2000 mg/kg-bw and applied to unabraded skin under semi-occluded conditions for 24 hours. Dermal responses were observed on day 1, 7, and 14. No mortalities were reported.
LD_{50} (undiluted) = 400 mg/kg-bw

(2)New Zealand White rabbits (4 males) were administered Hercules 70L pine oil disinfectant, via the dermal route on unabraded skin at 3000 mg/kg-bw for 24 hours. Animals were observed for local skin reactions for 14 days. No mortalities were reported.
LD_{50} (undiluted) > 3000 mg/kg-bw

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

No data were provided.

Repeated-Dose Toxicity

Subcategory 1: Terpenoid Alcohols

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
NOAEL > 375 mg/kg-bw/day (highest dose tested)
Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

Linalyl acetate (CASRN 115-95-7)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
NOAEL > 750 mg/kg-bw/day (highest dose tested)

Subgroup 2: Cyclic Unsaturated Tertiary Esters

α-Terpineol acetate (CASRN 80-26-2)
Osborne-Mendel rats (10/sex/dose) were administered α-terpineol acetate in the diet at concentrations of 0, 1000, 2500, or 10,000 ppm (~ 55, 138, or 550 mg/kg-bw/day) continuously

for 20 weeks. No vehicle was used. Measurements of body weight, food intake and general condition were recorded weekly. Hematological examinations (white and red cell counts, hemoglobin and hematocrit) were performed at the end of the study. Macroscopic examination of all tissues was performed. Histopathological examination was performed on the liver, kidneys, spleen, heart and testes of 6 – 8 rats (evenly divided by sex) from the high dose and controls. Tissues from rats that died during treatment were examined for gross changes. Dietary concentration of test substance was lost at a rate of 7% per week. The resulting mean exposure level over the 20-week period was 5697 ppm (~ 313 mg/kg-bw/day). No significant differences between treatment groups and controls for any endpoint were observed. Mortalities were not reported.
NOAEL = 550 mg/kg-bw/day (highest dose tested)

Subcategory 3: Terpenoid Hydroperoxides

No data were provided. Testing is recommended.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

No data were provided. Testing is recommended.

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

No adequate data were provided. See Section 6, Additional Comments.

Reproductive/Developmental Toxicity

Subcategory 1: Terpenoid alcohols

No data were provided. Testing is recommended.

Subcategory 2: Terpenoid esters
No data were provided. Testing is recommended.

Subcategory 3: Terpenoid Hydroperoxides

No data were provided. Testing is recommended.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

Pine oil (CASRN 8002-09-3)
Pregnant Sprague-Dawley rats (25/dose) were administered pine oil blend (composed of five commercial pine oil samples; range of composition was 35 – 76.7% α- and γ-terpineol, 1 – 1.3%

other terpineol isomers, 0 – 14.6% secondary terpene alcohols, 0.1 – 10% terpene hydrocarbons) in corn oil by oral gavage at concentrations of 0, 50, 600 or 1200 mg/kg-day on gestation days 6 through 20 (14 days). On day 20 of presumed gestation, rats were sacrificed and examined for pregnancy, number and placement of implantations, early and late resorptions, live and dead fetuses, and number of corpora lutea. Fetuses were weighed and evaluated for soft and hard tissue anomalies. At 600 and 1200 mg/kg-day, decreased food consumption and body weight gains, excess salivation, alopecia, ungroomed coat, ataxia, decreased motor activity and impaired righting reflex, and urine stained abdominal fur were observed in the dams. Statistical significance was not reported. Six out of 25 dams died at 1200 mg/kg-day. Necropsy showed significantly increased adrenal weights (statistical significance and absolute/relative not specified). At 1200 mg/kg-day, increased incidence of resorptions (early/late not specified), delayed ossification, and decreased brain and body weights were reported in the fetuses; statistical significance was not provided.
LOAEL (maternal toxicity) = 600 mg/kg-day (based on decreases in body weight and food consumption and increases in clinical signs of toxicity)
NOAEL (maternal toxicity) = 50 mg/kg-day
LOAEL (developmental toxicity) = 1200 mg/kg-day (based on increased incidence of resorptions, delayed ossification, and decreased brain and body weights)
NOAEL (developmental toxicity) = 600 mg/kg-day

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

No data were provided for this complex mixture.

Genetic Toxicity – Gene Mutation

In vitro

Subcategory 1: Terpenoid Alcohols

Subgroup 1: Noncyclic Saturated Tertiary Alcohols
Tetrahydrolinalool (CASRN 78-69-3)
Salmonella typhimurium strains TA1535, TA100, TA1537, TA1538 and TA98 were exposed to tetrahydrolinalool at concentrations up to 3600 µg/plate in a reverse mutation assay.
Tetrahydrolinalool was not mutagenic in this assay.

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
(1) See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
Linalool was not mutagenic in this assay.

(2) See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
Linalool was mutagenic in this assay.

Subgroup 3: Cyclic Unsaturated Tertiary Alcohols

α-Terpineol (CASRN 98-55-5)
(1) *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98 and TA100 were exposed to α-terpineol at 10,000 μg/plate with and without metabolic activation.
α-Terpineol was not mutagenic in this assay.

(2) L5178y mouse lymphoma cells were exposed to α-terpineol at concentrations of 250 – 300 nL/mL in a mouse lymphoma forward mutation assay with and without metabolic activation.
α-Terpineol was not mutagenic in this assay.

Subgroup 4: Pinanols

No data were provided. Testing is recommended.

Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

Linalyl acetate (CASRN 115-95-7)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
Linalyl acetate was not mutagenic in this assay.

Subgroup 2: Cyclic Unsaturated Tertiary Esters

No data were provided. Testing is recommended.

Subcategory 3: Terpenoid Hydroperoxides

No data were provided. Testing is recommended.
Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine oil

Pine oil (CASRN 8002-09-3)
Chinese hamster ovary cells were exposed to pine oil (referred to as pine oil blend; no details of composition provided) at 100, 130, 170, 200 and 250 nL/mL without metabolic activation and 50, 100, 200, 300 and 400 nL/mL with metabolic activation. Positive controls produced an appropriate response.
Pine oil was not mutagenic in this assay.

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

No data were provided. Testing is recommended.

Genetic Toxicity – Chromosomal Aberrations

In vitro

Subcategory 1: Terpenoid Alcohols

Subgroup 1: Noncyclic Saturated Tertiary Alcohols

No data were provided.

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
Linalool did not induce chromosomal aberrations in this assay.

Subgroup 3: Cyclic Unsaturated Tertiary Alcohols

No data were provided.

Subgroup 4: Pinanols

No data were provided.

Subcategory 2: Terpenoid Esters

No data were provided.

Subcategory 3: Terpenoid Hydroperoxides
No data were provided.

Subcategory 4: Terpenoid Complex Mixtures
No data were provided.

Genetic Toxicity – Chromosomal Aberrations

In vivo

Subcategory 1: Terpenoid Alcohols

No data were provided.

Subcategory 2: Terpenoid Esters

No data were provided.

Subcategory 3: Terpenoid Hydroperoxides

No data were provided.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine oil

Pine oil (CASRN 8002-09-3)
CD-1 mice (number not specified; males and females at each dose) were exposed to pine oil (76% α- and γ- terpineol) at concentrations of 116, 578 or 1155 mg/kg-bw by intraperitoneal injection. Bone marrow polychromatic erythrocytes were collected at 24, 48 and 72 hours after treatment in a micronucleus cytogenetic assay.
Pine oil did not induce formation of micronuclei in this assay.

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

No data were provided.

Genetic Toxicity – Other

In vitro

Subcategory 1: Terpenoid Alcohols

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
Linalool did not induce unscheduled DNA synthesis in this assay.

Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

Linalyl acetate (CASRN 115-95-7)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
Linalyl acetate did not induce unscheduled DNA synthesis in this assay.

Subcategory 3: Terpenoid Hydroperoxides

No data were provided.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

Pine oil (CASRN 8002-09-3)
Primary rat hepatocytes were isolated from male rats and exposed to pine oil (76.7% α- and γ-terpinol) at 10 concentrations of 0.0003 – 10 µL/mL in DMSO in a test for unscheduled DNA synthesis. Concentrations of 3 and 10 µL/mL were described as cytotoxic.
Pine oil did not induce unscheduled DNA synthesis in this assay.

Additional Information

Skin Irritation

Subcategory 1: Terpenoid Alcohols

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
Linalool was slightly irritating to rabbit skin in this assay.

Eye Irritation

Subcategory 1: Terpenoid Alcohols

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

Linalool (CASRN 78-70-6)
See human health hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
Linalool was moderately irritating to rabbit eyes in this assay.

Conclusions:

Subcategory 1: Terpenoid Alcohols

Subgroup 1: Noncyclic Saturated Tertiary Alcohols

The acute oral toxicity of CASRN 78-69-3 is low in rats and the acute dermal toxicity is low in rabbits.

The repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subgroup 2: Noncyclic Unsaturated Tertiary Alcohols

The acute oral toxicity of subgroup 2 members is low in rats and the acute dermal toxicity is low in rabbits. The subgroup members induced gene mutations *in vitro,* but did not induce chromosomal aberrations. CASRNs 78-70-6 did not induce unscheduled DNA synthesis in rat hepatocytes. CASRN 78-70-6 was irritating to rabbit skin and eyes.

CASRN 78-70-6 showed no systemic toxicity in rats via immunotoxicity testing.

Repeated-dose, reproductive and developmental toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subgroup 3: Cyclic Unsaturated Tertiary Alcohols/Subgroup 4: Pinanols

The acute oral toxicity of subgroup 3 member (CASRN 98-55-5) is low in mice. The acute oral toxicity of subgroup 4 member (CASRN 4948-28-1) is low rats and the acute dermal toxicity is low in rabbits. CASRN 98-55-5 did not induce gene mutations *in vitro*.

Repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory 2: Terpenoid Esters

Subgroup 1: Noncyclic Unsaturated Tertiary Esters

The acute oral and dermal toxicity of CASRN 115-95-7 is low rats and rabbits, respectively. CASRN 115-95-7 did not induce gene mutations *in vitro*.

Repeated-dose, reproductive and developmental toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subgroup 2: Cyclic Unsaturated Tertiary Esters
A repeated-dose toxicity study in rats administered CASRN 115-95-7 via the diet showed no systemic toxicity. The NOAEL for systemic toxicity is 550 mg/kg-bw/day, the highest dose tested.

Acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory 3: Terpenoid Hydroperoxides

The acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Subcategory 4: Terpenoid Complex Mixtures

Subgroup 1: Pine Oil

The acute oral toxicity of CASRN 8002-09-3 is low in rats, and the acute dermal and inhalation toxicity is moderate in rats and rabbits. In an oral prenatal developmental toxicity study in rats, decreases in body weight and food consumption and increases in clinical signs of toxicity were observed in the dams at 600 mg/kg-day; the NOAEL for maternal toxicity is 50 mg/kg-day. Delays in fetal ossification, decreases in brain and fetal body weights, and increases in resorptions were observed in the fetuses at 1200 mg/kg-day; the NOAEL for developmental toxicity is 600 mg/kg-day. CASRN 8002-09-3 did not induce gene mutations in vitro or chromosomal aberrations *in vivo*. CASRN did not induce unscheduled DNA synthesis *in vitro*.

Subgroup 2: 2-Pinanol Thermal Rearrangement Products

The acute oral, repeated-dose, reproductive, developmental and genetic toxicity endpoints were identified as data gaps under the HPV Challenge Program.

Table 3. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health Data

Endpoints	Subcategory 1: Terpenoid Alcohols							
	Subgroup 1	Subgroup 2			Subgroup 3	Subgroup 4		
	Tetrahydro-linalool	Linalool	Myrcenol	Dihydro-myrcenol	α-Terpineol	*cis*-2-Pinanol	*trans*-2-Pinanol	2-Pinanol
CASRN	(78-69-3)	(78-70-6)	(543-39-5)	(18479-58-8)	(98-55-5)	(4948-28-1)	(4948-28-2)	(473-54-1)
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**> 5000**	**2200**[a]	**5300**	**3600**	**2830**	**2050**	No Data 2050 (RA)	No Data 2050 (RA)
Acute Inhalation Toxicity LC_{50} (mg/L)	–	–	–	–	–	–	–	–
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**> 5000 (m)**	**5610**[a]	**> 5000**	**> 5000**	–	**> 5000**	No Data > 5000 (RA)	No Data > 5000 (RA)
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	No data				No data	No data	No data	No data
Systemic toxicity		> 375	> 375 (RA)	> 375 (RA)				
Reproductive/ Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day)	No data	No data	No data	No data	No data	No data	No data	No data
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**	**Positive**[a]	No Data Positive (RA)	No Data Positive (RA)	**Negative**	No data	No data	No data

Table 3. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health Data

Endpoints	Subcategory 1: Terpenoid Alcohols							
	Subgroup 1	Subgroup 2			Subgroup 3	Subgroup 4		
	Tetrahydro-linalool	Linalool	Myrcenol	Dihydro-myrcenol	α-Terpineol	*cis*-2-Pinanol	*trans*-2-Pinanol	2-Pinanol
CASRN	(78-69-3)	(78-70-6)	(543-39-5)	(18479-58-8)	(98-55-5)	(4948-28-1)	(4948-28-2)	(473-54-1)
Genetic Toxicity – Chromosomal Aberrations *In vitro*	–	**Negative[a]**	No Data Negative (RA)	No Data Negative (RA)	–	–	–	–
Genetic Toxicity – Chromosomal Aberrations *In vivo*	–	–	–	–	–	–	–	–
Genetic Toxicity – Other *In vitro* Unscheduled DNA synthesis	–	**Negative[a]**	No Data Negative (RA)	No Data Negative (RA)	–	–	–	–
Additional Information **Skin irritation** **Eye irritation**	–	**Slightly irritating[a]** **Moderately irritating[a]**	No Data Slightly irritating Moderately irritating (RA)	No Data Slightly irritating Moderately irritating (RA)	–	–	–	–

Table 3. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health Data

	Subcategory 2		Subcategory 3	Subcategory 4	
	Subgroup 1	Subgroup 2		Subgroup 1	Subgroup 2
Endpoints	**Linalyl acetate (115-95-7)**	**α-Terpineol acetate (80-26-2)**	**2-Pinanol hydroper-oxide (28324-52-9)**	**Pine oil (8002-09-3)**	**2-Pinanol thermal rearrangement products (125252-49-5)**
Acute Oral Toxicity LD_{50} (mg/kg-bw)	**14,550**[b]	No data	No data	**> 1000**	No data
Acute Inhalation Toxicity LC_{50} (mg/L)	–	–	–	**3.79**	–
Acute Dermal Toxicity LD_{50} (mg/kg-bw)	**> 5000**[b]	–	–	**400**	–
Repeated-Dose Toxicity NOAEL/LOAEL Oral (mg/kg-bw/day)	**> 750**[b]	> 550	No data	No data	No data
Developmental Toxicity NOAEL/LOAEL Oral (mg/kg-day)					
Reproductive Toxicity	No data	No data	No data	**NOAEL = 600**	No data
	No data	No data	No data	**LOAEL = 1200**	No data
Maternal Toxicity	No data	No data	No data	**NOAEL = 600**	
				LOAEL = 1200	
Developmental Toxicity				**NOAEL = 600**	
				LOAEL = 1200	
Genetic Toxicity – Gene Mutation *In vitro*	**Negative**[b]	No data	No data	**Negative**	No data
Genetic Toxicity – Chromosomal Aberrations *In vitro*	–	–	–	–	–

Table 3. Summary Table of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program: Human Health Data

	Subcategory 2		Subcategory 3	Subcategory 4	
	Subgroup 1	Subgroup 2		Subgroup 1	Subgroup 2
Endpoints	**Linalyl acetate (115-95-7)**	**α-Terpineol acetate (80-26-2)**	**2-Pinanol hydroper-oxide (28324-52-9)**	**Pine oil (8002-09-3)**	**2-Pinanol thermal rearrangement products (125252-49-5)**
Genetic Toxicity – Chromosomal Aberrations *In vivo*	–	–	–	**Negative**	–
Genetic Toxicity – Other *In vitro* Unscheduled DNA synthesis	**Negative**[b]	–	–	**Negative**	–

Measured data in bold text; (RA) = Read Across; – indicates that endpoint was not evaluated for this substance.

[a]Data from: http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf

[b]Data from: http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf

4. Hazard to the Environment

Subcategory 1: Terpenoid Alcohols

Tetrahydrolinalool	CASRN 78-69-3
Myrcenol	CASRN 543-39-5
Dihydromyrcenol	CASRN 18479-58-8
α-Terpineol	CASRN 98-55-5
cis-2-Pinanol	CASRN 4948-28-1
trans-2-Pinanol	CASRN 4948-29-2
2-Pinanol	CASRN 473-54-1
Pine oil	CASRN 8002-09-3
2,6,6-Trimethylbicyclo[3.1.1]heptan-2-ol	CASRN 125252-49-5

Subcategory 2: Terpenoid Esters

Linalyl acetate	CASRN 115-95-7
α-Terpineol acetate	CASRN 80-26-2

Subcategory 3: Terpenoid Hydroperoxides

2-Pinanol hydroperoxide	CASRN 28324-52-9

Subcategory 4: Terpenoid Allyl Alcohols

Linalool	CASRN 78-70-6

A summary of aquatic toxicity 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. For CASRNs 78-70-6 and 115-95-7, the SIARs, SIAPs and Dossiers were finalized and published by the UNEP at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf and http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf

Acute Toxicity to Fish

Subcategory 1: Terpenoid Alcohols

Myrcenol (CASRN 543-39-5)
(1) Fathead minnows (*Pimephales promelas*) were exposed to myrcenol at unspecified concentrations under static conditions for 96 hours. No further information was provided.
96-h LC_{50} = 3.7 mg/L

(2) A 96-hour LC_{50} for fish, estimated by ECOSAR (v1.00a), was provided to support the evaluation of the acute toxicity of myrcenol. The estimated concentration is consistent with measured results.
96-h LC_{50} = 6.17 mg/L (estimated)

α-Terpineol (CASRN 98-55-5)
Coho salmon (*Oncorhynchus kisutch*) and rainbow trout (*Oncorhynchus mykiss*) (5 or 10/species) were exposed to α-terpineol (90% with 10% emulsifier) at five unspecified concentrations below 100 mg/L under static conditions for 96 hours. No further information was provided.
96-LC_{50} (Coho salmon) = 6.8 mg/L
96-LC_{50} (rainbow trout) = 6.7 mg/L

Pine oil (CASRN 8002-09-3)
(1) Rainbow trout (*Oncorhynchus mykiss*) were exposed to pine oil (62.7% α-terpinol, 83.4% total terpene alcohol content) at nominal concentrations of 25, 50, 75, 100, 200 or 1000 mg/L under static conditions for 96 hours. No further information was provided.
96-h LC_{50} = 71 mg/L

(2) Rainbow trout (*Oncorhynchus mykiss*) were exposed to pine oil (62.7% α-terpinol, 83.4% total terpene alcohol content) at nominal concentrations of 6.5, 11, 18, 30 or 50 mg/L under static conditions for 96 hours. Measured concentrations were 6.2, 10, 17, 28 and 48 mg/L. No mortalities were observed at ≤ 10 mg/L.
96-h LC_{50} = 18 mg/L

(3) Bluegills (*Lepomis macrochirus*) were exposed to pine oil (62.7% α-terpinol, 83.4% total terpene alcohol content) at nominal concentrations of 7.8, 13, 22, 36 or 60 mg/L under static conditions for 96 hours. Measured concentrations were 6.4, 11, 21, 36 and 58 mg/L. No mortalities were observed at ≤ 36 mg/L.
96-h LC_{50} = 53 mg/L

2,6,6-Trimethylbicyclo[3.1.1]heptan-2-ol therma rearrangement products (CASRN 125252-49-5)
Rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance at measured concentrations of 1.47, 2.55, 4.53, or 13.9 mg/L under unstated test conditions for 96 hours.
96-h LC_{50} = 11 mg/L

Subcategory 2: Terpenoid Esters

Linalyl acetate (CASRN 115-95-7)
See environmental hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
96-h LC_{50} = 11 mg/L

Subcategory 3: Terpenoid Hydroperoxides

No experimental data were provided.

Subcategory 4: Terpenoid Allyl Alcohol

Linalool (CASRN 78-70-6)
See environmental hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
96-h LC_{50} = 28 mg/L

Acute Toxicity to Aquatic Invertebrates

Subcategory 1: Terpenoid Alcohols

Myrcenol (CASRN 543-39-5)
(1) Water fleas (*Daphnia magna*) were exposed to myrcenol at unspecified concentrations under static conditions for 48 hours. No pH measurements were provided. Mortalities were recorded at 24 and 48 hours.
48-h EC_{50} = 36 mg/L

(2) A 48-hour LC_{50} for water fleas (*Daphnia magna*), estimated by ECOSAR (v1.00a), was provided to support evaluation of the acute toxicity of myrcenol.
48-h LC_{50} = 4.32 mg/L (estimated)

Pine oil (CAS No. 8002-09-3)
Water fleas (*Daphnia magna*) were exposed to pine oil (62.7% α-terpineol, 83.4% total terpene alcohol content) at nominal concentrations of 3.9, 6.5, 11, 18 or 30 mg/L for 48 hours. Measured concentrations were 3.7, 7.3, 11, 17 and 28 mg/L.
48-h EC_{50} = 24 mg/L

2,6,6-Trimethylbicyclo[3.1.1]heptan-2-ol thermal rearrangement products (CASRN 125252-49-5)
Water fleas (*Daphnia magna*) were exposed to the test substance at nominal concentrations of 0.15, 0.27, 0.48, 0.85, 1.5, 2.7, 4.8, 8.5 or 15mg/L under static conditions for 48 hours. The numbers of immobilized Daphnia were recorded at 24 and 48 hours.
48-h EC_{50} = 7.0 mg/L

Subcategory 2: Terpenoid Esters

Linalyl acetate (CASRN 115-95-7)
See environmental hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
48-h EC_{50} = 6.2 mg/L

Subcategory 3: Terpenoid Hydroperoxides

No experimental data were provided.

Subcategory 4: Terpenoid Allyl Alcohol

Linalool (CASRN 78-70-6)
See environmental hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
48-h EC_{50} = 20 mg/L

Toxicity to Aquatic Plants

Subcategory 1: Terpenoid Alcohols

2,6,6-Trimethylbicyclo[3.1.1]heptan-2-ol therma rearrangement products (CASRN 125252-49-5)
Green algae (*Scenedesmus subspicatus*) were exposed to the test substance at unspecified concentrations under static conditions for 72 hours.
72-h EC_{50} > 15 mg/L (Biomass)

Subcategory 2: Terpenoid Esters

Linalyl acetate (CASRN 115-95-7)
See environmental hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
72-h E_bC_{50} = 4.2 mg/L
72-h ErC_{50} = 16 mg/L
Subcategory 3: Terpenoid Hydroperoxides

No experimental data were provided.

Subcategory 4: Terpenoid Allyl Alcohol

Linalool (CASRN 78-70-6)
See environmental hazard data at http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf
96-h E_bC_{50} = 88 mg/L
96-h ErC_{50} = 157 mg/L

Conclusions:

Subcategory 1: Terpenoid Alcohols

The evaluation of available toxicity data of terpenoid alcohols indicates that the 96 hour LC_{50} values to fish range 3.7-18 mg/L, the 48 hour EC_{50} values to daphnia range 7.0- 36 mg/L, and the algal 72-h EC_{50} value is > 15 mg/L for biomass.

Subcategory 2: Terpenoid Esters

The evaluation of available toxicity data of terpenoid esters indicates that the 96 hour LC_{50} to fish is 11 mg/L, the 48 hour EC_{50} to daphnia is 6.2 mg/L, and the algal 72-h EC_{50s} values are 4.2 mg/L for biomass and 16 mg/L for growth rate.

Subcategory 3: Terpenoid Hydroperoxides

The aquatic toxicity of terpenoid esters and terpenoid hydroperoxides could not be evaluated because no data on aquatic toxicity endpoints were available.
The acute toxicity to fish and aquatic invertebrates and toxicity to aquatic plants endpoints remain as data gaps under the HPV Challenge Program.

Subcategory 4: Terpenoid Allyl Alcohols

The evaluation of available toxicity data of CASRN 78-70-6 indicates that the 96 hour LC_{50} to fish is 28 mg/L, the 48 hour EC_{50} to daphnia is 20 mg/L, and the algal 96-h EC_{50s} values are 88 mg/L for biomass and 157 mg/L for growth rate.

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

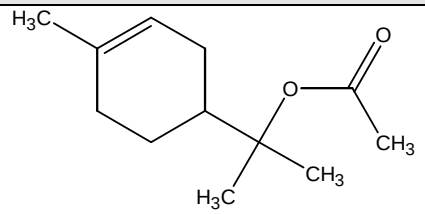
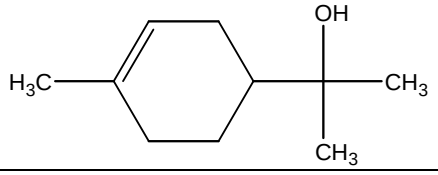
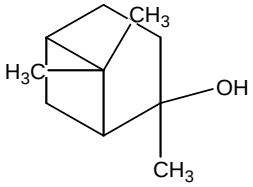
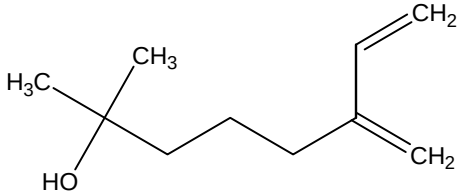
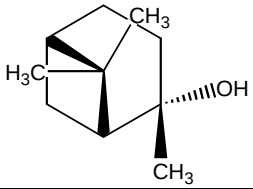
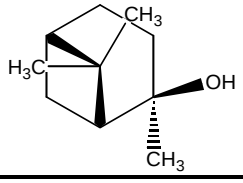
Subcategory 1: Terpenoid Alcohols

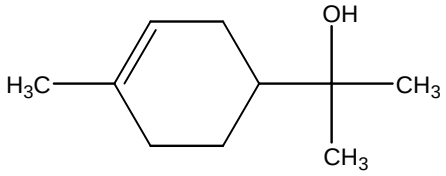
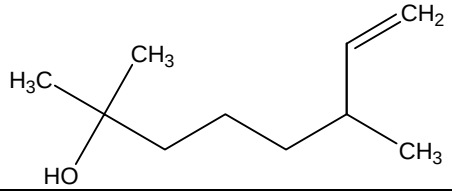
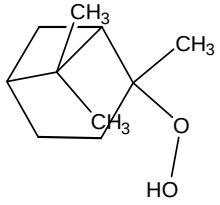
Endpoints	Tetrahydro-linalool (78-69-3)	Myrcenol (543-39-5)	Dihydro-myrcenol (18479-58-8)	α-Terpineol (98-55-5)	*cis*-2-Pinanol (4948-28-1)	*trans*-2-Pinanol (4948-28-2)	2-Pinanol (473-54-1)	Pine oil (8002-09-3) 50-60% (98-55-5)	2-Pinanol thermal rearrange-ment products (125252-49-5) Major isomer plinol 72402-00-7
Fish 96-h LC_{50} (mg/L)	No data (RA) 3.7- 18 4.74 (e)	**3.7 (m)** 6.17 (e)	No Data (RA) 3.7- 18 6.17 (e)	**6.7 – 6.8 (m)** 8.00 (e)	No data (RA) 3.7- 18 21.18 (e)	No data (RA) 3.7- 18 21.18 (e)	No data (RA) 3.7- 18 21.18 (e)	**18 (m)** 8.00 (e)	**11 (m)** 7.92 (e)
Aquatic Inverte-brates 48-h EC_{50} (mg/L)	No data (RA) 7.0- 36 3.39 (e)	**36 (m)** 4.32 (e)	No Data (RA) 7.0- 36 4.32 (e)	No data (RA) 7.0- 36 5.50 (e)	No data (RA) 7.0- 36 13.55 (e)	No data (RA) 7.0- 36 13.55 (e)	No data (RA) 7.0- 36 13.55 (e)	**24 (m)** 5.50 (e)	**7.0 (m)** 5.44 (e)
Aquatic Plants 72-h EC_{50} (mg/L)	No data (RA) >15 3.23 (e)	No data (RA) >15 3.87 (e)	No data (RA) >15 3.88 (e)	No data (RA) >15 4.65 (e)	No data (RA) >15 9.31 (e)	No data (RA) >15 9.31 (e)	No data (RA) >15 9.31 (e)	No data (RA) >15 4.65 (e)	**>15 (m)** 4.62 (e)

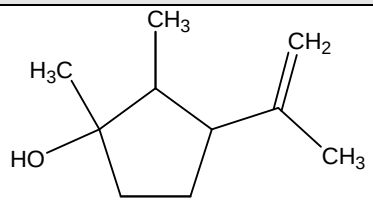
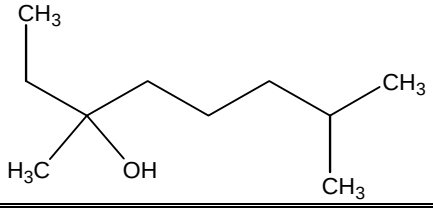
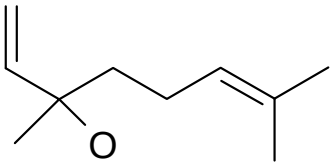
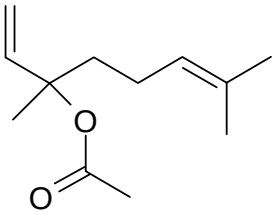
Table 4 cont. Summary of the Screening Information Data Set as Submitted under the U.S. HPV Challenge Program- Aquatic Toxicity Data				
	Subcategory 2: Terpenoid Esters		Subcategory 3: Terpenoid Hydroperoxides	Subcategory 4: Terpenoid Allyl Alcohol
Endpoints	**Linalyl acetate (115-95-7)**	**α-Terpineol acetate (80-26-2)**	**2-Pinanol hydroper-oxide (28324-52-9)**	**Linalool (78-70-6)**
Fish 96-h LC_{50} (mg/L)	**11 (m)[a]**	No data (RA) 11	No data 0.31 (e)	**28 (m)[b]**
Aquatic Invertebrates 48-h EC_{50} (mg/L)	**6.2 (m)[a]**	No data (RA) 6.2	No data 2.28 (e)	**20 (m)[b]**
Aquatic Plants 72/96-h EC_{50} (mg/L)		No data (RA)	No data	
Biomass	**4.2 (m)[a]**	4.2		**88 (m)[b]**
Growth rate	**16 (m)[a]**	16		**157 (m)[b]**

(m) = measured data (i.e., derived from testing); (e) = estimated data (i.e., derived from modeling); (RA) = Read Across
[a]Data from http://www.chem.unep.ch/irptc/sids/OECDSIDS/115957.pdf
[b]Data from http://www.chem.unep.ch/irptc/sids/OECDSIDS/78706.pdf

APPENDIX

Sponsored Chemical		
Chemical Name	**CASRN**	**Structure**
3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-, 1-acetate	80-26-2	
3-Cyclohexene-1-methanol, .alpha.,.alpha.,4-trimethyl-	98-55-5	
Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-	473-54-1	 Mixture of *cis*- and *trans*-isomers
7-Octen-2-ol, 2-methyl-6-methylene-	543-39-5	
Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2S,5S)-rel-	4948-28-1	
Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, (1R,2R,5S)-rel-	4948-29-2	

Sponsored Chemical		
Chemical Name	**CASRN**	**Structure**
Oils, pine	8002-09-3	 Representative structure. Complex mixture composed mainly of 50–60% of CASRN 98-55-5. Naturally occurring pine oils typically contain[1]: 50–70% alpha-terpineol (CASRN 98-55-5) 5–10% borneal (CASRN 464-45-9) and isoborneol (CASRN 124-76-5) 5–10% fenchol (CASRN 2217-02-9) 5–15% other terpene alcohols (e.g., *p*-menthan-8-ol, beta-terpineol, terpin) 0–10% terpinyl and bornyl acetates 0–3% monoterpenes (e.g., pinenes, dipentene, terpinolene) 5–10% other components (e.g., cineols, camphor, anethole, estragole, sesquiterpenes)
7-Octen-2-ol, 2,6-dimethyl-	18479-58-8	
Hydroperoxide, 2,6,6-tri-methylbicyclo[3.1.1]heptyl	28324-52-9	 Approximately 75% *cis*- and 25% *trans*-isomers

Sponsored Chemical		
Chemical Name	**CASRN**	**Structure**
Bicyclo[3.1.1]heptan-2-ol, 2,6,6-trimethyl-, thermal-rearrangement products, linalool fractions, acid-isomerized, distillation residues, acid-isomerized, distillation lights, terpenoids	125252-49-5	 Representative structure. Complex mixture containing 47–50% cyclopentanol, 1,2-dimethyl-3-(1-methylethenyl)- (common name plinol) (CASRN 72402-00-7)
3-Octanol, 3,7-dimethyl-	78-69-3	
1,6-Octadien-3-ol, 3,7-dimethyl- (Linalool)	78-70-6	
1,6-Octadien-3-ol, 3,7-dimethyl-, acetate (Linalyl acetate)	115-95-7	

[3]Ullmann's Encyclopedia of Industrial Chemicals. 2005. Turpentine's. Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.