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**The Flavor and Fragrance High Production Volume  
Consortia**

**The Terpene Consortium**

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**Revised Robust Summaries for Terpenoid Primary  
Alcohols and Related Esters**

<b>3,7-Dimethyl-6-octen-1-ol (dl-Citronellol)</b>	<b>CAS No. 106-22-9</b>
<b><i>trans</i>-3,7-Dimethyl-2,6-octadien-1-ol (Geraniol)</b>	<b>CAS No. 106-24-1</b>
<b><i>cis</i>-3,7-Dimethyl-2,6-octadien-1-ol (Nerol)</b>	<b>CAS No. 106-25-2</b>
<b>Acetylated myrcene (Process name for mixture containing <i>cis</i>- and <i>trans</i>-3,7-dimethyl-2,6-octadien-1-yl acetate)</b>	<b>CAS No. 68412-04-4</b>

**FFHPVC Terpene Consortium Registration Number**

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# Robust Summaries for Terpenoid Primary Alcohols and Related Esters

The evaluation of the quality of the following data uses a systematic approach described by Klimisch [Klimisch *et al.*, 1996]. Based on criteria relating to international testing standards for categorizing data reliability, four reliability categories have been established. The following categories are:

- Reliability code 1. Reliable without restrictions
- Reliability code 2. Reliable with restrictions
- Reliability code 3. Not reliable
- Reliability code 4. Not assignable

## 1 Chemical and Physical Properties

### 1.1 Boiling Point

<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>GLP</b>	NG
<b>Year</b>	1989
<b>Boiling Point</b>	225 °C
<b>Pressure</b>	1013 (760 mm Hg)
<b>Pressure Unit</b>	Millibars
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Givaudan-Roure (1989) Determination of the ready biodegradability of d,l-citronellol. Unpublished report to Fragrance Materials Association.
<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>GLP</b>	NG

<b>Boiling Point</b>	230 °C (measured)
<b>Pressure</b>	760
<b>Pressure Unit</b>	mm Hg
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA) Reported values for boiling point.

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<b>Substance Name</b>	Nerol
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<b>CAS</b>	106-25-2
<b>GLP</b>	NG
<b>Boiling Point</b>	225 °C (measured)
<b>Pressure</b>	760
<b>Pressure Unit</b>	mm Hg
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA) Reported values for boiling point.

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<b>Substance Name</b>	Citral
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<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS
<b>GLP</b>	NG
<b>Boiling Point</b>	230 °C (measured)
<b>Pressure</b>	760
<b>Pressure Unit</b>	mm Hg
<b>Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA) Reported values for boiling point.

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, geranyl acetate)
<b>CAS</b>	68412-04-4
<b>GLP</b>	NG
<b>Boiling Point</b>	244 °C (measured)
<b>Pressure</b>	760
<b>Pressure Unit</b>	mm Hg
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA) Reported values for boiling point.

<b>Substance Name</b>	Acetylated myrcene (data given for major component, neryl acetate)
<b>CAS</b>	68412-04-4
<b>GLP</b>	NG
<b>Boiling Point</b>	231 °C (measured)
<b>Pressure</b>	760
<b>Pressure Unit</b>	mm Hg
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA) Reported values for boiling point.

## 1.2 Vapor Pressure

<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	Measured
<b>Year</b>	1995
<b>Vapor Pressure</b>	0.0095 kPa (0.071 mm Hg)
<b>Temperature</b>	30 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions

**Remarks for Data Reliability** Basic data given and comparable to guidelines/standards.

**References** Vuilleumier C., Flament I. And Sauvegrain P. (1995)  
Headspace analysis study of evaporation rate of perfume ingredients applied onto skin. International Journal of Cosmetic Science 17, 61-76.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Method/guideline</b>	Calculated
<b>Vapor Pressure</b>	0.003 kPa (0.023 mm Hg)
<b>Temperature</b>	20 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA). Reported values for vapor pressure.

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<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Method/guideline</b>	Calculated
<b>Vapor Pressure</b>	0.008 kPa (0.060 mm Hg)
<b>Temperature</b>	20 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA). Reported values for vapor pressure.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for substance.</b>	Substance supported under SIDS
<b>Method/guideline</b>	Calculated
<b>Vapor Pressure</b>	0.009 kPa (0.068 mm Hg)
<b>Temperature</b>	20 °C

<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA). Reported values for vapor pressure.

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<b>Substance Name</b>	Acetylated myrcene (data for principal component geranyl acetate)
<b>CAS</b>	68412-04-4
<b>Remarks for substance.</b>	Substance supported under SIDS
<b>Method/guideline</b>	Calculated
<b>Vapor Pressure</b>	0.004 kPa (0.03 mm Hg)
<b>Temperature</b>	25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA). Reported values for vapor pressure.

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<b>Substance Name</b>	Acetylated myrcene (data for principal component neryl acetate)
<b>CAS</b>	68412-04-4
<b>Remarks for substance.</b>	Substance supported under SIDS
<b>Method/guideline</b>	Calculated
<b>Vapor Pressure</b>	0.003 kPa (0.02 mm Hg)
<b>Temperature</b>	25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Fragrance Materials Association (FMA). Reported values for vapor pressure.

### 1.3 Octanol/Water Partition Coefficient

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9

<b>Method/guideline</b>	OECD Guideline No. 117; Reference substances = Thiourea, Acetophenone, Benzophenone, Naphthalene, 1,2,4-Trichlorobenzene
<b>GLP</b>	Yes
<b>Year</b>	1991
<b>Remarks for Test Conditions</b>	Reverse phase HPLC
<b>Log Pow</b>	3.1
<b>Remarks for Results</b>	Average retention time: 5.01
<b>Conclusion Remarks</b>	Good correlation with calculated log Pow of 3.56
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study. The log Kow compares well with the calculated value. Data are considered reliable.
<b>References</b>	Givaudan-Roure (1991) Partition coefficient n-octanol/water of d,l-citronellol. Private communication to FMA.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Method/guideline</b>	Calculated
<b>GLP</b>	NG
<b>Log Pow</b>	3.47
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Calculated Log Kow compares well with the measured value for the very closely related citronellol. Data are considered reliable.
<b>References</b>	Syracuse Research Corporation (SRC). Private communication to FMA.

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<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Method/guideline</b>	Calculated
<b>Log Pow</b>	3.47
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Calculated Log Kow compares well with the measured value for the very closely related citronellol. Data are considered reliable.

**References** Syracuse Research Corporation (SRC). Private communication to FMA.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for substance</b>	Substance supported under SIDS.
<b>Method/guideline</b>	Calculated
<b>Log Pow</b>	3.45
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Calculated Log Kow compares well with the measured value for the very closely related citronellol. Data are considered reliable.
<b>References</b>	Syracuse Research Corporation (SRC). Private communication to FMA.

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<b>Substance Name</b>	Acetylated myrcene (data for principal component neryl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	Calculated
<b>Log Pow</b>	4.48
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Calculated Log Kow compares well with the measured value for the very closely related citronellol. Data are considered reliable.
<b>References</b>	Syracuse Research Corporation (SRC). Private communication to FMA.

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<b>Substance Name</b>	Acetylated myrcene (data for principal component geranyl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	Calculated
<b>Log Pow</b>	4.48
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Calculated Log Kow compares well with the measured value for the very closely related citronellol. Data are considered reliable.
<b>References</b>	Syracuse Research Corporation (SRC). Private communication

to FMA.

#### 1.4 Water Solubility

<b>Substance Name</b>	dl-Citronellol
<b>CAS No.</b>	106-22-9
<b>Method/guideline</b>	Calculated at log Kow=3.56 (ESPOW)
<b>Value (mg/L) at temperature</b>	211 mg/L
<b>Data Qualities Reliabilities Remarks for Data Reliability</b>	Reliability code 2. Reliable with restrictions. Comparable to guidelines/standards.
<b>References</b>	HYDROWIN

<b>Substance Name</b>	Geraniol
<b>CAS No.</b>	106-24-1
<b>Method/guideline</b>	Calculated at log Kow=3.47 (ESPKOW)
<b>Value (mg/L) at temperature</b>	256 mg/L
<b>Data Qualities Reliabilities Remarks for Data Reliability</b>	Reliability code 2. Reliable with restrictions. Comparable to guidelines/standards.
<b>References</b>	HYDROWIN

<b>Substance Name</b>	Nerol
<b>CAS No.</b>	106-25-2
<b>Method/guideline</b>	Calculated at log Kow=3.47 (ESPKOW)
<b>Value (mg/L) at temperature</b>	256 mg/L
<b>Data Qualities Reliabilities Remarks for Data Reliability</b>	Reliability code 2. Reliable with restrictions. Comparable to guidelines/standards.
<b>References</b>	HYDROWIN

<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9

<b>GLP</b>	Not given
<b>Year</b>	1990
<b>Value (mg/L) at temperature</b>	0.03% w/V (300 mg/L)
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given.
<b>References</b>	Bush Boake Allen, Inc (BBA) (1990) Biodegradability of geraniol and d,l-citronellol. Private communication to FMA.

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<b>Substance Name</b>	Geraniol
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<b>CAS</b>	106-24-1
<b>GLP</b>	Not given
<b>Year</b>	1990
<b>Value (mg/L) at temperature</b>	0.06% w/V (600 mg/L)
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given.
<b>References</b>	Bush Boake Allen, Inc (BBA) (1990) Biodegradability of geraniol and d,l-citronellol Private Communication to FMA.

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<b>Substance Name</b>	Acetylated myrcene (data for principal component geranyl acetate)
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<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	Calculated
<b>Value (mg/L) at temperature</b>	6.9 mg/L at 25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guidelines/standards.
<b>References</b>	HYDROWIN

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<b>Substance Name</b>	Acetylated myrcene (data for principal component neryl acetate)
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<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	Calculated

<b>Value (mg/L) at temperature</b>	6.9 mg/L at 25 °C
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guidelines/standards.
<b>References</b>	HYDROWIN

## 2 Environmental Fate and Pathways

### 2.1 Photodegradation

<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	Calculation using AOPWIN program
<b>Test Type</b>	AOPWIN
<b>Year</b>	2000
<b>Half life t1/2</b>	Hydroxy reaction half life: 1.3 hours
<b>Rate Constant</b>	98x10 <sup>-12</sup> cm <sup>3</sup> /molecule-sec
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	AOPWIN EPI Suite (2000) U S Environmental Protection Agency.
<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Method/guideline</b>	Calculation using AOPWIN program
<b>Test Type</b>	AOPWIN
<b>Year</b>	2000
<b>Half life t1/2</b>	Hydroxy reaction half life: 0.71 hours
<b>Rate Constant</b>	179x10 <sup>-12</sup> cm <sup>3</sup> /molecule-sec
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	AOPWIN EPI Suite (2000) U S Environmental Protection Agency.
<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2

<b>Method/guideline</b>	Calculation using AOPWIN program
<b>Test Type</b>	AOPWIN
<b>Year</b>	2000
<b>Half life t1/2</b>	Hydroxy reaction half life: 0.713 hours
<b>Rate Constant</b>	179x10 <sup>-12</sup> cm <sup>3</sup> /molecule-sec
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	AOPWIN EPI Suite (2000) U S Environmental Protection Agency.

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<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Data are for principal component geranyl acetate
<b>Method/guideline</b>	Calculation using AOPWIN program
<b>Test Type</b>	AOPWIN
<b>Year</b>	2000
<b>Half life t1/2</b>	Hydroxy reaction half life: 0.721 hours
<b>Rate Constant</b>	178x10 <sup>-12</sup> cm <sup>3</sup> /molecule-sec
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	AOPWIN EPI Suite (2000) U S Environmental Protection Agency.

## 2.2 Stability in Water

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<b>Substance Name</b>	Acetylated myrcene (acetylated myrcene is the process name for geranyl acetate. Data is for the dihydroisomer of geranyl acetate, citronellyl acetate)
<b>CAS No.</b>	68412-04-4
<b>Method/guideline</b>	Hydrolysis in simulated intestinal fluid (Longland, 1977)

<b>Test Type</b>	Ester hydrolysis in simulated intestinal fluid
<b>Year</b>	1977
<b>Duration (days)</b>	2 hours
<b>Analytical procedures</b>	Citronellyl acetate (15 uL/L) was incubated with pancreatin at a pH=7.5 in 0.5 M phosphate buffer at 37 C for 2 hours. The extent of hydrolysis was measured by gas-liquid chromatography.
<b>Temperature</b>	37 °C
<b>Nominal</b>	15 uL/L
<b>Degradation %</b>	100% hydrolysis
<b>Half-life t<sub>1/2</sub></b>	<1 hour
<b>Breakdown products</b>	Citronellol and acetic acid
<b>Conclusion remarks</b>	Citronellyl acetate was completely hydrolyzed in 2 hrs at pH7.5.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Data on citronellyl ester consistent with data for 24 other aliphatic and aromatic esters.
<b>References</b>	Grundschober F. (1977) Toxicological assessment of flavouring esters. Toxicology, 8:387-390.

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<b>Substance Name</b>	Acetylated myrcene (acetylated myrcene is the process name for geranyl acetate. Data is for the dihydroisomer of geranyl acetate, citronellyl phenylacetate)
<b>CAS No.</b>	68412-04-4
<b>Method/guideline</b>	Hydrolysis in simulated intestinal fluid (Longland, 1977)
<b>Test Type</b>	Ester hydrolysis in simulated intestinal fluid
<b>Year</b>	1977
<b>Duration (days)</b>	2 hours
<b>Analytical procedures</b>	Citronellyl phenylacetate (<18 uL/L) was incubated with pancreatin at a pH=7.5 in 0.5 M phosphate buffer at 37 C for 2 hours. The extent of hydrolysis was measured by gas-liquid chromatography.
<b>Temperature</b>	37 °C
<b>Nominal</b>	<18 uL/L
<b>Degradation %</b>	60% hydrolysis in 2 hrs.
<b>Half-life t<sub>1/2</sub></b>	<2 hours
<b>Breakdown products</b>	Citronellol and phenylacetic acid

<b>Conclusion remarks</b>	Citronellyl phenylacetate was completely hydrolyzed in 2 hours at pH 7.5.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Data on citronellyl ester consistent with data for 24 other aliphatic and aromatic esters.
<b>References</b>	Grundschober F. (1977) Toxicological assessment of flavouring esters. Toxicology 8:387-390.

<b>Substance Name</b>	Acetylated myrcene (acetylated myrcene is the process name for a mixture containing mainly nerol and geranyl acetate. Data is for geranyl acetate)
<b>CAS No.</b>	68412-04-4
<b>Method/guideline</b>	Calculation
<b>Test Type</b>	Base/Acid-Catalyzed Hydrolysis
<b>Temperature</b>	25 °C
<b>Degradation %</b>	100% hydrolysis
<b>Half-life t1/2</b>	23.14 days at pH=8: 231.4 days at pH=7
<b>Breakdown products</b>	Geraniol and acetic acid
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	AOPWIN

## 2.3 Biodegradation

<b>Substance Name</b>	dl-citronellol (greater than 95%)
<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	OECD Guideline Study
<b>Method</b>	OECD 301F
<b>Test Type</b>	Monometric respirometry test
<b>GLP</b>	No
<b>Year</b>	1986
<b>Contact time (units)</b>	28 days

<b>Innoculum</b>	Activated sludge from wastewater treatment plant
<b>Remarks for Test Conditions</b>	Substance was tested in triplicate runs at 85 mg/L. Concentration of sludge was 30 mg/L dry weight and the reference substance was aniline. Bioactivation was determined by BOD and COD measurements.
<b>Degradation % after time</b>	Greater than 60% after 10 days and 80-90% BOD/COD after 28 days.
<b>Results</b>	Substance was readily biodegradable.
<b>Time required for 10% degradation</b>	Less than 4 days
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	No
<b>Conclusion remarks</b>	Readily biodegradable.
<b>Data Qualities Reliabilities</b>	Reliability 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. Guideline study.
<b>References</b>	BASF (1986) Determination of the biodegradation of dl-citronellol in a respirometric test. Unpublished report to RIFM.

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	96.1% citronellol
<b>Method</b>	OECD 301 C
<b>Test Type</b>	Modified MITI
<b>GLP</b>	No
<b>Year</b>	1987
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Activated sludge from 2 sewage treatment plants mixed with soil from bank of Rhone river.
<b>Remarks for Test Conditions</b>	108 mg/l at 20 °C for 28 days
<b>Degradation % after time</b>	65% at 28 days
<b>Time required for 10% degradation</b>	9 days
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	No

<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Givaudan-Roure (1989) Determination of the ready biodegradability of d,l-citronellol. Unpublished report to FMA.

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<b>Substance Name</b>	dl-citronellol
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<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	96% mixture of <i>d,l</i> -citronellol
<b>Method</b>	Method F
<b>Test Type</b>	DOC - Method F from Blue book series, 1991
<b>GLP</b>	Yes
<b>Year</b>	1990
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Activated sludge from local STP
<b>Remarks for Test Conditions</b>	41.6 mg DOC/l at 20 °C for 28 days
<b>Degradation % after time</b>	100% at 15 days
<b>Results</b>	100 % biodegradation after 15 days.
<b>Time required for 10% degradation</b>	< 1 day
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Bush Boake Allen, Inc (BBA) (1990) Biodegradability of geraniol and d,l-citronellol Private communication to FMA.

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<b>Substance Name</b>	Geraniol
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<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Mixture of geraniol (50%), nerol (26%) and citronellol (18%)

<b>Method</b>	OECD 301B
<b>Test Type</b>	CO2 evolution
<b>GLP</b>	Yes
<b>Year</b>	1994
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Secondary effluent from sludge from local STP
<b>Remarks for Test Conditions</b>	10 mg/l organic carbon at 20 °C for 28 days
<b>Degradation % after time</b>	100% at 28 days
<b>Time required for 10% degradation</b>	<7 days
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Quest International Ltd. (1994) The ultimate biodegradability of citronellol in the sealed vessel test. Private communication to FMA.

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<b>Substance Name</b>	Geraniol
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<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	99% mixture of geraniol (>70%) and nerol (<30%). EOA specification 16.
<b>Method</b>	Method F
<b>Test Type</b>	DOC - Method F from Blue book series, 1991
<b>GLP</b>	No
<b>Year</b>	1990
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Activated sludge from local STP
<b>Remarks for Test Conditions</b>	42.0 mg DOC/l at 20 °C for 28 days
<b>Degradation % after time</b>	100% at 15 days
<b>Time required for 10%</b>	< 1 day

**degradation**

<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Bush Boake Allen, Inc (BBA) (1990) Biodegradability of geraniol and d,l-citronellol. Private communication to FMA.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	94% pure - 44% <i>cis</i> (neral) and 50% <i>trans</i> (geranial)
<b>Method</b>	OECD 301B
<b>Test Type</b>	CO2 evolution
<b>GLP</b>	No
<b>Year</b>	1994
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Secondary effluent from sludge from local STP
<b>Remarks for Test Conditions</b>	10 mg/l organic carbon at 20 °C for 28 days
<b>Degradation % after time</b>	92.1% at 28 days
<b>Time required for 10% degradation</b>	< 4 days
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Classification</b>	Not given
<b>Breakdown products (transient or stable?)</b>	Not given
<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Quest International Ltd. (1994) The ultimate biodegradability of citronellol in the sealed vessel test. Private communication to

FMA.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Method</b>	Method F
<b>Test Type</b>	DOC - Method F from Blue book series, 1991
<b>GLP</b>	No
<b>Year</b>	1990
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Activated sludge from local STP
<b>Remarks for Test Conditions</b>	40.3 mg DOC/l at 20 °C for 28 days
<b>Degradation % after time</b>	99.5% at 19 days
<b>Kinetic</b>	Not given
<b>Time required for 10% degradation</b>	< 1 day
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Classification</b>	Not given
<b>Breakdown products (transient or stable?)</b>	Not given
<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study
<b>References</b>	Bush Boake Allen, Inc (BBA) (1990) Biodegradability of geraniol and d,l-citronellol. Private communication to FMA.

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<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol.
<b>Method</b>	OECD 301B
<b>Test Type</b>	CO2 evolution

<b>GLP</b>	Not given
<b>Year</b>	1991
<b>Contact time (units)</b>	28 days
<b>Innoculum</b>	Secondary effluent from sludge from local STP
<b>Remarks for Test Conditions</b>	10 mg/l organic carbon at 20 °C for 28 days
<b>Degradation % after time</b>	82.2% at 28 days
<b>Results</b>	The requirements for ready and ultimate biodegradability were met.
<b>Kinetic</b>	Not given
<b>Time required for 10% degradation</b>	< 4 days
<b>10 day window criteria</b>	Yes
<b>Total degradation</b>	Yes
<b>Classification</b>	Not given
<b>Breakdown products (transient or stable?)</b>	Not given
<b>Conclusion remarks</b>	Readily biodegradable
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Birch R. R. and Fletcher R. J. (1991) The application of dissolved inorganic carbon measurements to the study of aerobic biodegradability. Chemosphere 23(4), 507-524.

## 2.4 Fugacity

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Model Conditions</b>	20 °C
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	Level III Fugacity-based Environmental Equilibrium Partitioning Model
<b>Input parameters</b>	MW, VP, log Kow, estimated MP, water solubility

<b>Year</b>	2000
<b>Media</b>	Air-Water-Soil-Sediment Partition Coefficient
<b>Model data and Results</b>	Compartment half-lives, hours: Air = 0.514; Water = 360; Soil=360; Sediment=1.44X10-3
<b>Estimated Distribution and Media Concentration</b>	Air=0.855% Water=39.8% Soil=59.6% Sediment=0.5%
<b>Conclusion Remarks</b>	Substance is predicted to persist in the environment for 288 hours. Persistence data consistent with a measured biodegradation rate of 100% within 28 days.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized fugacity calculation method. Data are considered marginally reliable because this method does not allow for biodegradation or metabolism.
<b>References</b>	Mackay D., A.DiGuardo, S.Paterson and C.E.Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Model Conditions</b>	20 °C
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	Level III Fugacity-based Environmental Equilibrium Partitioning Model
<b>Input parameters</b>	MW, VP, water solubility, estimated log Kow & MP
<b>Year</b>	2000
<b>Media</b>	Air-Water-Soil-Sediment Partition Coefficient
<b>Model Data and Results</b>	Compartment half-lives, hours: Air=0.261; Water=360;Soil=360;Sediment=1.44X10-3
<b>Estimated Distribution and Media Concentration</b>	Air=0.0429% Water=39.3% Soil=59.7%

	Sediment=0.88%
<b>Conclusion Remarks</b>	Substance is predicted to persist in the environment for 290 hours. Persistence data consistent with a measured biodegradation rate of 100% within 28 days.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized fugacity calculation method. Data are considered marginally reliable because this method does not allow for biodegradation or metabolism.
<b>References</b>	Mackay D., A.DiGuardo, S.Paterson and C.E.Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637.

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<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Model Conditions</b>	20 °C
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	Level III Fugacity-based Environmental Equilibrium Partitioning Model
<b>Input parameters</b>	MW, VP, water solubility, estimated log Kow & MP
<b>Year</b>	2000
<b>Media</b>	Air-Water-Soil-Sediment Partition Coefficient
<b>Model Data and Results</b>	Compartment half-lives, hours: Air=0.261; Water=360; Soil=360; Sediment=1.44X10 <sup>-3</sup>
<b>Estimated Distribution and Media Concentration</b>	Air=0.0529% Water=36% Soil=63.1% Sediment=0.838%
<b>Conclusion Remarks</b>	Substance is predicted to persist in the environment for 272 hours. Persistence data consistent with a measured biodegradation rate of 100% within 28 days.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized fugacity calculation method. Data are considered marginally reliable because this method does not allow for biodegradation or metabolism.
<b>References</b>	Mackay D., A.DiGuardo, S.Paterson and C.E.Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the

EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637.

<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Data are for geranyl acetate
<b>Model Conditions</b>	20 °C
<b>Test Type</b>	Environmental Equilibrium Partitioning Model
<b>Method</b>	Mackay
<b>Model Used</b>	Level III Fugacity-based Environmental Equilibrium Partitioning Model
<b>Input parameters</b>	MW, VP, BP, calc. log Kow, calc. water solubility
<b>Year</b>	2000
<b>Media</b>	Air-Water-Soil-Sediment Partition Coefficient
<b>Model Data and Results</b>	Compartment half-lives, hours: Air=0.262; Water=360; Soil=360; Sediment=1.44X10 <sup>-3</sup>
<b>Estimated Distribution and Media Concentration</b>	Air=0.0427% Water=35.9% Soil=57.5% Sediment = 0.6.51%
<b>Conclusion Remarks</b>	Substance is predicted to persist in the environment for 301 hours. Persistence data consistent with a measured biodegradation rate of 82% within 28 days.
<b>Data Qualities Reliabilities</b>	Reliability code 4. Not assignable.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized fugacity calculation method. Data are considered marginally reliable because this method does not allow for biodegradation or metabolism.
<b>References</b>	Mackay D., A.DiGuardo, S.Paterson and C.E.Cowan (1996b) Evaluating the fate of a variety of types of chemicals using the EQC model. Environmental Toxicology and Chemistry, 15(9), 1627-1637.

### 3 Ecotoxicity

#### 3.1 Acute Toxicity to Fish

<b>Substance Name</b>	Geraniol (Greater than 95% assay)
<b>CAS Numerical</b>	106-24-1
<b>Reference substances (if used)</b>	
<b>Method/guideline</b>	96-Hour semi-static toxicity test
<b>GLP</b>	Yes (Council Directive 92/69/EEC C.1 (1992))
<b>Year</b>	1993
<b>Test Type</b>	Experimental
<b>Species/Strain/Supplier</b>	Zebra fish/ <i>Brachydanio rerio</i> /Hamilton Buchanan/West Aquarium
<b>Remarks for Test Conditions</b>	Zebra fish (6-month old, length, 2.5-3.5 cm) were exposed to a series of 5 test concentrations of 0, 11, 16, 22, and 31 mg/L of geraniol for 96 hours in a semi-static test. Solutions were renewed every 24 hours. Fish were maintained on a schedule of 16 hours of light and 8 hours of darkness. Temperature, oxygen, oxygen saturation and pH measured every 24 hours were within the following limits over the course of the study; 20.8-22.5 C, 8.3-10.2 mg/L, 99.9-110%, and 7.6-8.2. Fish were observed twice daily for mortality and symptoms. GC analytical measurement of geraniol concentrations in control solutions, <1 mg/L.
<b>Conclusion Remarks</b>	The acute 96-hour LC50 for geraniol in zebra fish is 14.0 mg/L
<b>Remarks for Results</b>	The cumulative number of deaths at each 24- hour interval and the corresponding concentrations in mg geraniol/L at t=0, t=24 hours, t=48 hours are: control; 24 hours 0/<1/<1, 48 hours 0/<1/<1, 72 hours 0/<1/<1, 96 hours 0/<1/<1 11 mg/L; 24 hours 0/10.
<b>Analytical monitoring</b>	GC
<b>Unit</b>	mg/L
<b>Exposure period (unit)</b>	96 hours
<b>Nominal concentrations as mg/L</b>	0, 11, 16, 22, and 31 mg/L
<b>Measured concentrations as mg/L</b>	
<b>Endpoint value</b>	LC0=9.8, LC50=14.0 (geometric mean), and LC100=19.9 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.

**References** Caspers (1993) Acute fish toxicity of:HR91/601330 (Geraniol supra). Study No. 389A/92F. Private Communication to FFHPVC. Unpublished report.

<b>Substance Name</b>	<i>d,l</i> -Citronellol (95% assay)
<b>CAS Numerical</b>	106-22-9
<b>Reference substances (if used)</b>	Chloroacetamide
<b>Method/guideline</b>	96-Hour static toxicity test
<b>Test Type</b>	Experimental
<b>Species/Strain/Supplier</b>	Golden Orfe/Leuciscus Idus L.
<b>GLP</b>	Yes (Testverfahren mit Wasserorganism (Gruppe L) Din 38412, L15, static
<b>Year</b>	1989
<b>Remarks for Test Conditions</b>	Golden Orfe (6-month old, length, 6.0-7.2 cm) were exposed to a series of 5 test concentrations of 0, 4.64, 10, 21.5, 46.40, and 100 mg/L of dl-citronellol for 96 hours in a static test. Fish were maintained on a schedule of 16 hours of light and 8 hours of darkness. Temperature, oxygen, oxygen saturation under continuous aeration and pH measured every 24 hours were within the following limits over the course of the study; 20-21 C, 8-10 mg/L, 99.9-110%, and 7.5-8.5. Fish were observed at 1, 4, 24, 48, 72, and 96 hours for mortality and symptoms.
<b>Conclusion Remarks</b>	The acute 96-hour LC50 for <i>d,l</i> -citronellol in Golden Orfe is between 10.0 and 22 mg/L
<b>Remarks for Results</b>	The cumulative number of deaths and the corresponding concentrations in mg citronellol/L are: control and 4.64 mg/L group, no mortalities recoded; 10 mg/l, apathy up to 24 hours, but no mortalities recorded at 96 hours; at 21.5, 46.4, and 100 mg/L 100% mortality after 1 hour.
<b>Analytical monitoring</b>	GC
<b>Unit</b>	mg/L
<b>Exposure period (unit)</b>	96 hours
<b>Nominal concentrations as mg/L</b>	0, 4.64, 10, 21.5, 46.40, and 100 mg/L
<b>Endpoint value</b>	LC50 =greater than 10 but less than 22 mg/L. LC0=4.64 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restriction.
<b>Remarks for Data Reliability</b>	Code 2. Acceptable, well-documented publication/study report which meets basic scientific principles.
<b>References</b>	BASF (1989) Report on the study of the acute toxicity of dl-citronellol. Private Communication to RIFM. Unpublished report.
<b>Substance Name</b>	Acetylated myrcene (98.5% geranyl acetate)

<b>CAS Numerical</b>	68412-04-4
<b>Method/guideline</b>	96-Hour semi-static toxicity test
<b>Test Type</b>	Experimental
<b>Species/Strain/Supplier</b>	Fathead minnow/ <i>Pimephales promelas</i> /Aquatic Biosystems, Inc.
<b>GLP</b>	Yes (OECD Guidelines 203, 1992)
<b>Year</b>	2003
<b>Remarks for Test Conditions</b>	Juvenile fathead minnows (72 hours old) were maintained at the contract laboratory under static renewal conditions for 72 hours. Prior to testing the temperature and dissolved oxygen were 21.9-22.8C and 8.5 mg/L, respectively. For three days before the test were fed live <i>Artemia salina nauplii</i> . Fish were not fed during testing. Range-finding tests were performed under static conditions in sealed vessels. Survival was 100% at 1 and 5 mg/L but 0% at 10 mg/L. The definitive 96-hour test was performed under semi-static conditions with 24 hour renewal. Groups of ten fish were added to 6 nominal concentrations of geranyl acetate. A concurrent control group was also evaluated. Test solutions were maintained under 16 hours of light and 8 hours of darkness. At 24, 48, 72, and 96 hours, the number of surviving fish and sublethal observations were recorded. Test vials remained sealed during the experiment. Dissolved oxygen, pH, conductivity, and temperature were measured at 24-hour intervals. Concentrations of the test material were measured by HPLC at 0, 24 hours prior to renewal and at 24 hour intervals up to 96 hours. Standard 48, 72, and 96 hour LC50 values were calculated using probit method (Stephan, 1978). NOEC values were also noted.
<b>Conclusion Remarks</b>	The 96 hour LC50 for geranyl acetate in fathead minnows is 6.12 mg/L (95% C.I., 4.54-8.25 mg/L). 96-hour NOEC=4.54 mg/L.
<b>Remarks for Results</b>	The cumulative number of live organism in duplicate tests at each 24-hour interval and the corresponding concentrations in mg geraniol/L at t=0, t=24, 48, 72, and 96 hours are: control, 1.0 mg/L, 1.76 mg/L, 2.16 mg/L, 4.54 mg/L; 10/10 at all time intervals.
<b>Analytical monitoring</b>	GC
<b>Unit</b>	mg/L
<b>Exposure period (unit)</b>	96 hrs
<b>Nominal concentrations as mg/L</b>	0, 1.3, 2.2, 3.6, 6.0, or 10.0 mg/L
<b>Measured concentrations as mg/L</b>	0, 1.0, 1.76, 2.61, 4.54, and 8.25 mg/L
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	Code 1. OECD 203 Guideline study.

**References**

Ward T (2003a) Acute toxicity test with geranyl acetate and the fathead minnow (*Pimephales promelas*). Study Number 2454-FF. Private Communication to FFHPVC. Unpublished report.

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated based on measured Kow
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure period (unit)</b>	96 hr
<b>Conclusion remarks</b>	LC50 = 10.7 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure period (unit)</b>	96 hr
<b>Conclusion remarks</b>	LC50 = 0.57 mg/l (see Remarks for Reliability)
<b>Remarks for Data Reliability</b>	The data were obtained by a recognized SAR calculation method but are not consistent with chemical structure. Data are considered overly conservative by submitters.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish

<b>Exposure period (unit)</b>	96 hr
<b>Conclusion remarks</b>	LC50 = 0.57 mg/l (see Remarks for Reliability)
<b>Remarks for Data Reliability</b>	The data were obtained by a recognized SAR calculation method but are not consistent with chemical structure. Data are considered overly conservative by the submitters.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure period (unit)</b>	96 hr
<b>Conclusion remarks</b>	LC50 = 4.5 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method but are not consistent with chemical structure. Data are considered overly conservative by the submitters.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, geranyl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure period (unit)</b>	96 hr
<b>Conclusion remarks</b>	LC50 = 1.4 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method but are not consistent with chemical structure. Data are considered overly conservative by the submitters.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, neryl acetate)
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<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Species/Strain/Supplier</b>	Fish
<b>Exposure period (unit)</b>	96 hr
<b>Conclusion remarks</b>	LC50 = 1.4 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method but are not consistent with chemical structure. Data are considered overly conservative by the submitters.
<b>References</b>	ECOSAR

### 3.2 Acute Toxicity to Aquatic Invertebrates

<b>Substance Name</b>	Geraniol (purity: 98.8%)
<b>CAS Numerical</b>	106-24-1
<b>Method/guideline</b>	OECD Guideline 202
<b>Test Type</b>	Experimental
<b>GLP</b>	Yes
<b>Year</b>	2003
<b>Analytical procedures</b>	HPLC/UV detector
<b>Species/Strain/Supplier</b>	Daphnia magna/Aquatic Biosystems, Inc.
<b>Remarks for Test Conditions</b>	Juvenile daphnids (less than 24 hours old) produced from an in-house culture of adults were maintained at the contract laboratory under static renewal conditions for 29 days. During the 48 hours prior to testing, there was no mortality. The daphnid culture produced young before day 12 and a sub-sample of adults produced on average, more than 3 young per day during the 7 days prior to the start of the definitive test. Prior to testing the temperature and pH ranges were 19.4-20.9C and 7.0-7.2, respectively. Daphnid were fed algae and a mixture of yeast and trout chow prior to but not during the test. Range-finding tests were performed under static conditions in sealed containers without headspace. The definitive 48-hour test was performed under static conditions with 24 hour renewal. Groups of ten daphnids were added to 6 nominal concentrations of geraniol. A concurrent control group was also evaluated. Test solutions were maintained under 16 hours of light and 8 hours of darkness. At 24 and 48 hours, the number of surviving daphnids, occurrence of immobility, and sublethal effects were recorded. The presence of insoluble material was

	also noted. Test vials remained sealed during the experiment. Dissolved oxygen, pH, conductivity, and temperature were measured at 0, 24, and 48 hours. Concentrations of the test material were measured by HPIC at 0, 24 hours prior to renewal, 24 hours after renewal, and 48 hours. Standard 24- and 48 hour LC50 and EC50 values were calculated using probit method (Stephan, 1978).
<b>Nominal concentrations as mg/L</b>	0, 3.9, 6.6, 11, 18, 30, and 50 mg/L
<b>Measured concentrations as mg/L</b>	ND, 3.43, 5.90, 9.72, 16.5, 27.8, and 47.3 mg/L
<b>EC50, EL50, LC0, at 24, 48 hours</b>	24- and 48-hour EC50= 24.3 mg/L (95% CI=21.2-27.9 mg/L) and 7.75 mg/L (95% CI=6.70-8.97 mg/L), respectively. 24- and 48-Hour LC50= 35.0 mg/L (95% CI=27.8-47.3 mg/L) and 8.98 mg/L (95% CI=7.50-10.7 mg/L), respectively. The 48-hour NOEC =3.43 mg/L geraniol
<b>Unit</b>	mg/L
<b>Endpoint basis</b>	48 hr
<b>Conclusion Remarks</b>	The acute 48-hour EC50 for geraniol in Daphnid magna was 7.75 mg/L. The acute 48-hour LC50 for geraniol in Daphnid magna was 8.98 mg/L. The NOEC for geraniol in Daphnid magna is 3.43 mg/L.
<b>Remarks for Results</b>	The measured concentrations after 24 and 48 hours were 78 to 93% of the nominal concentrations, indicating the geraniol concentrations remained constant under sealed conditions. The respective ranges for conductivity, pH, dissolved oxygen, and temperature were: 580-600 umhos/cm, 7.1-7.2, 7.1-9.1 mg/L, and 19.3-20.4°C.
<b>Biological observations</b>	The number of surviving daphnids at 48 hours for duplicate runs (x/y) at each mean measured concentration was:0 mg/L, 10/10; 3.43 mg/L, 10/10; 5.90 mg/L, 7/9; 9.72 mg/L, 4/3; 16.5 mg/L, 1/1; 27.8 mg/L 1/0; 47.3 mg/L, 0/0
<b>Control response satisfactory?</b>	Yes
<b>Appropriate statistical evaluations?</b>	Probit method (Stephan, 1978)
<b>Data Qualities Reliabilities</b>	Reliability Code No. 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized guideline method and are consistent with chemical structure.
<b>References</b>	Ward T. (2003b) Acute toxicity test with geraniol and the Daphnid, <i>Daphnia magna</i> . Study No. 2452-FF. Private communication to FFHPVC. Unpublished Report.

<b>Substance Name</b>	Acetylated myrcene (geranyl acetate) Data are for isomeric terpene ester linalyl acetate, purity: 97.1%
<b>CAS Numerical</b>	68412-04-4
<b>Method/guideline</b>	OECD Guideline 202
<b>Test Type</b>	Experimental
<b>GLP</b>	Yes

<b>Year</b>	1994
<b>Analytical procedures</b>	GC/MS
<b>Species/Strain/Supplier</b>	Daphnia magna/In house/Staus 1820.
<b>Remarks for Test Conditions</b>	Groups (20, 4 replicates of 5) of juvenile daphnids (<24 hours old) produced from an in-house culture of adults were maintained at the contract laboratory under static conditions. During the 24 hours prior to testing, there was no mortality. Prior to testing the temperature was 20.1 °C. Daphnid were fed algae and a mixture of yeast prior to but not during the test. The definitive 48-hour test was performed under static conditions for 48 hours. Groups of daphnids (20/test concentration in 4 replicates of 5) were added to 6 nominal concentrations of linalyl acetate. A concurrent control group was also evaluated. Test solutions were maintained under darkness. At 24 and 48 hours, the number of surviving daphnids, occurrence of immobility, and sublethal effects were recorded. The presence of insoluble material was also noted. Test vials remained sealed during the experiment. Dissolved oxygen, pH, and temperature were measured at 0, 24, and 48 hours. Concentrations of the test material were measured by GC/MS at 0, 24 and 48 hours. Standard 24- and 48 hour LC50 and EC50 values were calculated using statistical methods (Berkson, JASA 48, 1953).
<b>Nominal concentrations as mg/L</b>	0, 10, 18, 32, 58, and 100 mg/L
<b>Measured concentrations as mg/L</b>	ND, less than 0.2, 8.2, 15.5, 26.3, 48.7, and 87.9 mg/L
<b>EC50, EL50, LC0, at 24, 48 hours</b>	48-hour EC50 = 15 mg/L (95% CI = 12-17 mg/L) 48-Hour NOEC = 10 mg/L
<b>Unit</b>	mg/L
<b>Endpoint basis</b>	48 hr
<b>Conclusion Remarks</b>	The acute 48-hour EC50 for linalyl acetate in Daphnid magna was 15 mg/L. The NOEC in Daphnid magna is 10 mg/L.
<b>Remarks for Results</b>	The measured concentrations after 24 and 48 hours were greater than 80% of the nominal concentrations, validating the linalyl acetate concentrations under test conditions. The respective ranges for pH, % oxygen saturation, and temperature were: 7.7-8.0, 94-100% mg/L, and 21-22 °C.
<b>Biological observations</b>	The total number of immobilized daphnids at 48 hours for quadruplicate runs at each mean measured concentration was: 0 mg/L, 0/20; 10 mg/L, 0/20; 18 mg/L, 7/20; 32 mg/L, 9/20; 58 mg/L, 20/20; 100 mg/L 20/20.
<b>Control response satisfactory?</b>	Yes
<b>Appropriate statistical evaluations?</b>	Yes, Berkson, JASA 48, 1953
<b>Data Qualities Reliabilities</b>	Reliability Code No. 1. Reliable without restriction.
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized guideline method and are consistent with chemical structure.
<b>References</b>	Grade R. (1994a) Acute toxicity test of linalyl acetate one Daphnia, Daphnia magna. Study No. 928374. Ciba Geigy, Ltd.

Private communication to FFHPVC. Unpublished Report.

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated based on measured Kow
<b>Analytical procedures</b>	Daphnia
<b>Test details</b>	48 hrs
<b>EC50, EL50, LC50, at 24,48 hours</b>	LC50=12.4 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS.
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Analytical procedures</b>	Daphnia
<b>Test details</b>	48 hrs
<b>EC50, EL50, LC0, at 24,48 hours</b>	LC50=1.1 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, neryl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	ECOSAR

<b>Test Type</b>	Calculated
<b>Analytical procedures</b>	Daphnia
<b>Test details</b>	48 hrs
<b>EC50, EL50, LC0, at 24,48 hours</b>	LC50=0.86 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, geranyl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	ECOSAR
<b>Test Type</b>	Calculated
<b>Analytical procedures</b>	Daphnia
<b>Test details</b>	48 hrs
<b>EC50, EL50, LC0, at 24,48 hours</b>	LC50=0.86 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

### 3.3 Acute Toxicity To Aquatic Plants

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<b>Substance Name</b>	dl-Citronellol
<b>CAS Numerical</b>	106-22-9
<b>Method/guideline</b>	OECD 201 Guideline Study
<b>GLP</b>	Yes
<b>Year</b>	1990
<b>Test Type</b>	Experimental
<b>Species/Strain/Supplier</b>	Green algae/ <i>Selenastrum subspicatus</i> /SAG86.81

<b>Exposure period (unit)</b>	72 hrs
<b>Analytical monitoring</b>	GC
<b>Remarks for Test Conditions</b>	In a growth inhibition test green Algae/ <i>Selenastrum capricornutum</i> was exposed to seven concentrations of dl-citronellol in the range from 0.195 to 12.5 mg/L. Water and Cremophor were used as controls. Temperature was maintained at 20 °C and cell densities were measured at 0, 24, 28, and 72 hours.
<b>Nominal concentrations as mg/L</b>	0.195 to 12.5 mg/L
<b>Measured concentrations as mg/L</b>	
<b>Unit</b>	mg/L
<b>NOEC, LOEC or NOEL, LOEL</b>	72 hr EC50=2.38 based on cell density measurements (number of cells/mL)hr EC20=1.13 mg/L
<b>Biological observations</b>	
<b>Control response satisfactory?</b>	Yes
<b>Appropriate statistical evaluations?</b>	Yes
<b>Conclusion Remarks</b>	The acute toxicity of dl-citronellol measured as a 50% decrease in growth and reproduction of green algae was estimated to be 72 hr EC50=2.38 mg/L.
<b>Remarks for Data Reliabilities</b>	OECD 201 Guideline study with basic data presented.
<b>Data Qualities Reliabilities</b>	Reliability Code 2. Reliable with restrictions.
<b>References</b>	BASF (1990) The algae test on dl-citronellol. OECD 201. Private Communication to RIFM. Unpublished Report.

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	Plate Inhibition Assay [Ikawa, 1992]
<b>Test Type</b>	Algal Growth Inhibition Test
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	48 hr
<b>Analytical Monitoring</b>	Net diameter of inhibition zone= total diameter-disk diameter (5mm)
<b>Remarks for Test Conditions</b>	Three disks containing the test solution were placed on a agar plate containing Chlorella p. and then exposed to fluorescent lights for 48 hours. Zone of inhibition measured on two separate occasions.
<b>Nominal Concentration as mg/L:</b>	100, 1000, or 10,000 mg/L

<b>Unit</b>	mg/L
<b>NOEC, LOEC</b>	NOEC=100 or 1000 mg/L, LOEC=10,000 mg/L
<b>Biological Observations</b>	Complete wipe out of yellow green algal lawn at 10,000 mg/L
<b>Statistical Evaluations?</b>	None
<b>Control Response Satisfactory</b>	Yes
<b>Conclusion remarks</b>	No effects on growth of <i>Chlorella p.</i> at 1000 mg/L. Authors noted that inhibition was also observed when solution disks at concentrations of 10,000 mg/L were separated from agar medium by Teflon disks.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Data was reported in a peer-reviewed journal- <i>Journal of Chemical Ecology</i>
<b>References</b>	Ikawa M., Mosley S., and Barbero L. (1992) Inhibitory effects of terpene alcohols and aldehydes on growth of green alga <i>Chlorella pyrenoidosa</i> . <i>Journal of Chemical Ecology</i> <b>18</b> (10),1755-1760.

<b>Substance Name</b>	Geraniol (purity: 98.8%)
<b>CAS Numerical</b>	106-24-1
<b>Method/guideline</b>	OECD 201 Guideline Study
<b>GLP</b>	Yes
<b>Year</b>	2003
<b>Test Type</b>	Experimental
<b>Species/Strain/Supplier</b>	Green algae/ <i>Selenastrum capricornutum</i>
<b>Exposure period (unit)</b>	72 hrs
<b>Analytical monitoring</b>	HPLC/UV detector
<b>Remarks for Test Conditions</b>	Green Algae/ <i>Selenastrum capricornutum</i> /U. of Texas was maintained at test conditions for 14 days prior to the test. The culture was growing in at least 2 subcultures prior to the initiation of the test. In a range finding test, the number of cells/mL was at least 97% of controls after three days for test substance concentrations of 0.1, 0.5, and 1.0 mg/L and 33% of controls at 5.0 mg/L. In the definitive test, algae was treated with nominal concentrations of 0.51, 1.1, 2.0, 4.1, and 8.1 mg/L for 72 hours. pH was adjusted to 7.5 and solutions were exposed for 24 hours of light of intensity, 400-410 foot candles. The number of algal cells/mL as well as relative size, cell shapes, color, adherence and aggregation of cells was determined. At 24, 48, and 72 hours 3 treatment and 6 control

<b>Nominal concentrations as mg/L</b>	vessels were sacrificed to determine the number of algal cells/mL. Concentrations were determined by HPLC. 0, 0.51, 1.1, 2.0, 4.1, and 8.1 mg/L
<b>Measured concentrations as mg/L</b>	0, 0.467, 1.03, 1.93, 3.93, and 7.77 mg/L
<b>Unit</b>	mg/L
<b>NOEC, LOEC or NOEL, LOEL</b>	72 hr EC50=5.93 based on average specific growth rate; 72-hr EC50=3.65 mg/L calculated using the number of cells/mL; 72-hr EC50=3.32 mg/L using the area under the growth curve. The 72-hr NOEC=1.03 mg/L
<b>Biological observations</b>	At the conclusion of the test samples of test media from each test vessel with maximal growth inhibition was combined with fresh media. After 48 hours incubation the number of cells increased from 420 cells/mL to 60,000 cells/mL suggesting that the toxic effects were algistatic.
<b>Control response satisfactory?</b>	Yes
<b>Appropriate statistical evaluations?</b>	EC50 values determined by weighted least squares non-linear regression (Bruce and Versteeg, 1992)
<b>Conclusion Remarks</b>	The acute toxicity of geraniol measured as a 50% decrease in growth and reproduction of freshwater alga was estimated to be 72 hr EC50=5.93 based on average specific growth rate, 3.65 mg/L calculated using the number of cells/mL, and 3.32 mg/L using the area under the growth curve. The 72-hr NOEC was determined to be 1.03 mg/L.
<b>Remarks for Data Reliabilities</b>	OECD 201 Guideline study with basic data presented.
<b>Data Qualities Reliabilities</b>	Reliability Code 1. Reliable without restrictions.
<b>References</b>	Ward T. (2003c) The growth and reproduction toxicity test with geraniol and freshwater alga, <i>Selenastrum capricornutum</i> . OECD 201. Study No. 2453-FF. Private Communication to FFHPVC. Unpublished Report.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Method/guideline</b>	Plate Inhibition Assay [Ikawa, 1992]
<b>Test Type</b>	Algal Growth Inhibition Test
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	48 hr
<b>Analytical Monitoring</b>	Net diameter of inhibition zone= total diameter-disk diameter (5mm)
<b>Remarks for Test Conditions</b>	Three disks containing the test solution were placed on an agar plate containing Chlorella p. and then exposed to fluorescent lights for 48 hours. Zone of inhibition measured on two separate occasions.

<b>Nominal Concentration as mg/L:</b>	100, 1000, or 10,000 mg/L
<b>Unit</b>	mg/L
<b>NOEC, LOEC</b>	NOEC=100 mg/L, LOEC=1000 mg/L
<b>Biological Observations</b>	Lightening of lawn color at 1000 mg/L. Complete wipe out of yellow green algal lawn at 10,000 mg/L
<b>Statistical Evaluations?</b>	None
<b>Control Response Satisfactory</b>	Yes
<b>Conclusion remarks</b>	No effects on growth of <i>Chlorella p.</i> at 100 mg/L. Authors noted that inhibition was also observed when solution disks at concentrations of 1000 or 10,000 mg/L were separated from agar medium by Teflon disks.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Data was reported in a peer-reviewed journal- <i>Journal of Chemical Ecology</i>
<b>References</b>	Ikawa M., Mosley S., and Barbero L. (1992) Inhibitory effects of terpene alcohols and aldehydes on growth of green alga <i>Chlorella pyrenoidosa</i> . <i>Journal of Chemical Ecology</i> <b>18</b> (10),1755-1760.

<b>Substance Name</b>	Acetylated myrcene (geranyl acetate). Data for isomeric ester linalyl acetate:97.1%
<b>CAS Numerical</b>	68412-04-4
<b>Method/guideline</b>	OECD 201 Guideline Study
<b>GLP</b>	Yes
<b>Year</b>	1994
<b>Test Type</b>	Experimental
<b>Species/Strain/Supplier</b>	Green algae/ <i>Selenastrum subspicatus</i> /University of Gottingen
<b>Exposure period (unit)</b>	72 hrs
<b>Analytical monitoring</b>	GC/MS
<b>Remarks for Test Conditions</b>	Green Algae/ <i>Selenastrum subspicatus</i> was maintained at test conditions for 3 days prior to the test. pH was adjusted to 7.9 and solutions were exposed for 72 hours to light of intensity, 119 uE/m <sup>2</sup> . Cell densities were measured at 24, 48, and 72 hours for 3
<b>Nominal concentrations as mg/L</b>	0, 4.4, 9.6, 21, 46, and 100 mg/L
<b>Measured concentrations as mg/L</b>	At t=0, 2.3, 4.7, 11.6, 15.9, 75.5 mg/L

<b>Unit</b>	mg/L
<b>NOEC, LOEC or NOEL, LOEL</b>	72-hr EC50=62 mg/L calculated using the cell densities (number of cells/mL); 72-hr EC50=16 mg/L using the area under the growth curve. The 72-hr NOEC=9.6 and less than 4.4 mg/L based on growth rate and area growth curve, respectively.
<b>Biological observations</b>	At t=0 test concentrations were 49 to 76% of nominal concentrations. At 72hr, all test concentrations were less than 0.2 mg/L. Test substance was reported to be unstable to light conditions of the experiment. The test substance was homogeneously distributed in the 4.4 and 9.6 mg/L test vessel sat t=0 and at 72 hours. At higher concentrations droplets were observed on the solution surface at 72 hours.
<b>Control response satisfactory?</b>	Yes
<b>Appropriate statistical evaluations?</b>	EC50 values determined by maximum likelihood method (McCullagh and Nelder, 1983)
<b>Conclusion Remarks</b>	The acute toxicity of linalyl acetate measured as a 50% decrease in growth and reproduction of freshwater alga was estimated to be 72 hr EC50=62 mg/L based on cell density measurements and 16 mg/L using the area under the growth curve. The 72-hr NOEC was determined to be 9.6 (cell density) and less than 4.4 mg/L (area under the growth curve)
<b>Remarks for Data Reliabilities</b>	OECD 201 Guideline study with basic data presented.
<b>Data Qualities Reliabilities</b>	Reliability Code 1. Reliable without restrictions.
<b>References</b>	Grade R. (1994b) Report on the growth inhibition test of linalyl acetate to green algae, <i>Selenastrum subspicatus</i> . OECD 201. Study No. 938273. Private Communication to FFHPVC. Unpublished Report.

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<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Method/guideline</b>	Plate Inhibition Assay [Ikawa, 1992]
<b>Test Type</b>	Algal Growth Inhibition Test
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	48 hr
<b>Analytical Monitoring</b>	Net diameter of inhibition zone= total diameter-disk diameter (5mm)
<b>Remarks for Test Conditions</b>	Three disks containing the test solution were placed on a agar plate containing Chlorella p. and then exposed to fluorescent lights for 48 hours. Zone of inhibition measured on two separate occasions.
<b>Nominal Concentration as mg/L:</b>	100, 1000, or 10,000 mg/L
<b>Unit</b>	mg/L

<b>NOEC, LOEC</b>	NOEC=100 mg/L, LOEC=1000 mg/L
<b>Biological Observations</b>	Lightening of lawn color at 1000 mg/L. Complete wipe out of yellow green algal lawn at 10,000 mg/L
<b>Statistical Evaluations?</b>	None
<b>Control Response Satisfactory</b>	Yes
<b>Conclusion remarks</b>	No effects on growth of <i>Chlorella p.</i> at 100 mg/L. Authors noted that inhibition was also observed when solution disks at concentrations of 1000 or 10,000 mg/L were separated from agar medium by Teflon disks.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Data was reported in a peer-reviewed journal- <i>Journal of Chemical Ecology</i>
<b>References</b>	Ikawa M., Mosley S., and Barbero L. (1992) Inhibitory effects of terpene alcohols and aldehydes on growth of green alga <i>Chlorella pyrenoidosa</i> . <i>Journal of Chemical Ecology</i> <b>18</b> (10),1755-1760.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Method/guideline</b>	Plate Inhibition Assay [Ikawa, 1992]
<b>Test Type</b>	Algal Growth Inhibition Test
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	48 hr
<b>Analytical Monitoring</b>	Net diameter of inhibition zone= total diameter-disk diameter (5mm)
<b>Remarks for Test Conditions</b>	Three disks containing the test solution were placed on a agar plate containing <i>Chlorella p.</i> and then exposed to fluorescent lights for 48 hours. Zone of inhibition measured on two separate occasions.
<b>Nominal Concentration as mg/L:</b>	100, 1000, or 10,000 mg/L
<b>Unit</b>	mg/L
<b>NOEC, LOEC</b>	NOEC=100 mg/L, LOEC=1000 mg/L
<b>Biological Observations</b>	Complete wipe out of yellow green algal lawn at 1000 and 10,000 mg/L
<b>Statistical Evaluations?</b>	None

<b>Control Response Satisfactory</b>	Yes
<b>Conclusion remarks</b>	No effects on growth of <i>Chlorella p.</i> at 100 mg/L. Authors noted that inhibition was also observed when solution disks at concentrations of 1000 or 10,000 mg/L were separated from agar medium by Teflon disks.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Data was reported in a peer-reviewed journal.
<b>References</b>	Ikawa M., Mosley S., and Barbero L. (1992) Inhibitory effects of terpene alcohols and aldehydes on growth of green alga <i>Chlorella pyrenoidosa</i> . <i>J. of Chem. Ecology</i> <b>18</b> (10),1755-1760.

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	Calculated
<b>Test Type</b>	ECOSAR
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	96 hr
<b>Conclusion remarks</b>	EC50 = 8.2 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS.
<b>Method/guideline</b>	Calculated
<b>Test Type</b>	ECOSAR
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	96 hr
<b>Conclusion remarks</b>	EC50 = 3.9 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.

References ECOSAR

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, neryl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	Calculated
<b>Test Type</b>	ECOSAR
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	96 hr
<b>Conclusion remarks</b>	EC50 = 0.12 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

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<b>Substance Name</b>	Acetylated myrcene (data given for major component, geranyl acetate)
<b>CAS</b>	68412-04-4
<b>Method/guideline</b>	Calculated
<b>Test Type</b>	ECOSAR
<b>Species/Strain/Supplier</b>	Green algae
<b>Exposure period (duration)</b>	96 hr
<b>Conclusion remarks</b>	EC50 = 0.12 mg/l
<b>Remarks for Data Reliability</b>	The data are obtained by a recognized SAR calculation method and are consistent with chemical structure. Data are considered reliable.
<b>References</b>	ECOSAR

## 4 Human Health Data

### 4.1 Acute Toxicity

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	Purity undetermined.
<b>Method/guideline</b>	NG
<b>Test Type</b>	Acute ED25
<b>GLP</b>	Not reported
<b>Year</b>	1977
<b>Species/Strain</b>	Mouse/CD-1
<b>Sex</b>	Female
<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	None
<b>Route of administration</b>	Inhalation
<b>Remarks for test conditions</b>	The respiratory irritation potential of fragrance raw materials was assessed in CD-1 females by recording respiratory rate using a whole body plethysmograph. Mice, weighing between 23-28 grams were exposed to test materials for 1 minute using a nebulizer for aerosolization in a 2600 ml chamber. Materials shown to be sensory irritants were further tested in mice cannulated via the trachea & compared to an intact mouse breathing through its nose. Comparisons made were between the pre-exposure & exposure rate values for each material at each dose level. Materials were of undetermined purity.
<b>Value LD50 or LC50 with confidence limits</b>	ED25=990 micrograms/L
<b>Remarks for results</b>	Slight respiratory depression. Lower tract exposures not performed
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Troy, W.R. (1977) Doctoral Dissertation: The comparative respiratory irritation potential of fourteen fragrance raw materials. Unpublished report to RIFM.

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<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	Not reported
<b>Method/guideline</b>	NG
<b>Test Type</b>	Acute dermal LD50
<b>GLP</b>	Not reported
<b>Year</b>	1973
<b>Species/Strain</b>	Rabbits/New Zealand White
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	None
<b>Route of administration</b>	Dermal
<b>Remarks for test conditions</b>	Five rabbits per dose were administered 0, 1.25, 2.5 or 5.0 g/kg bw citronellol. Animals were observed for toxic signs and death.
<b>Value LD50 or LC50 with confidence limits</b>	2.65 g/kg (95% C.L. 1.78-3.52 g/kg)
<b>Number of deaths at each dose level</b>	1.25 g/kg 0/5 deaths; 2.5 g/kg 2/5 deaths; 5 g/kg 5/5 deaths
<b>Remarks for results</b>	The LD50 was calculated to be 2.65 g/kg calculated LD50, 95% limits=1.78-3.52 gm/kg. Toxic signs were ataxia and papillary dilation.
<b>Conclusion remarks</b>	The LD50 was reported to be 2.65 g/kg bw (2650 mg/kg bw)
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Moreno O. M. (1973) Acute oral toxicity studies on rats and rabbits. Unpublished report to RIFM.

<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	Not reported
<b>Method/guideline</b>	NG
<b>Test Type</b>	Oral LD50

<b>GLP</b>	Not reported
<b>Year</b>	1973
<b>Species/Strain</b>	Rat
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	10
<b>Vehicle</b>	None reported
<b>Route of administration</b>	Oral
<b>Remarks for test conditions</b>	Ten rats per dose level were administered 2050, 2560, 3200, 4000, or 5000 mg/kg bw citronellol and observed for fourteen days.
<b>Value LD50 or LC50 with confidence limits</b>	3450 mg/kg bw (95% C.L. 3210-3690 mg/kg bw)
<b>Number of deaths at each dose level</b>	2050 mg/kg 1/10 deaths; 2560 mg/kg 0/10 deaths; 3200 mg/kg 7/10 deaths; 4000 mg/kg 6/10 deaths; 5000 mg/kg 8/10 deaths
<b>Remarks for results</b>	Spontaneous activity reduced 20 min after administration. 2000 mg/kg bw spontaneous activity reduced. All animals affected 10-30 min after administration, peaked at 4-6 hr & returned to normal at 48 hr.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Moreno O. M. (1973) Acute oral toxicity studies on rats and rabbits. Unpublished report to RIFM.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Purity undetermined
<b>Method/guideline</b>	Not given
<b>Test Type</b>	Acute ED25
<b>GLP</b>	Not reported
<b>Year</b>	1977
<b>Species/Strain</b>	Mouse/CD-1
<b>Sex</b>	Female
<b># of animals per sex per dose</b>	5

<b>Vehicle</b>	None
<b>Route of administration</b>	Inhalation
<b>Remarks for test conditions</b>	The respiratory irritation potential of fragrance raw materials was assessed in CD-1 females by recording respiratory rate using a whole body plethysmograph. Mice were exposed to test materials for 1 min using a nebulizer for aerosolization in a 2600 ml chamber. Materials shown to be sensory irritants were further tested in mice cannulated via the trachea & compared to an intact mouse breathing through its nose. Comparisons made were between the pre-exposure & exposure rate values for each material at each dose level. Materials were of undetermined purity.
<b>Value LD50 or LC50 with confidence limits</b>	ED25=570 micrograms/L
<b>Remarks for results</b>	Mild moderate respiratory depression. No effects when inhaled through tracheal cannula.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Troy W.R. (1977) Doctoral Dissertation: The comparative respiratory irritation potential of fourteen fragrance raw materials. Unpublished report to RIFM.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Not reported
<b>Method/guideline</b>	Litchfield-Wilcoxon, 1949 (FDA study)
<b>Test Type</b>	Oral LD50
<b>GLP</b>	Not reported
<b>Year</b>	1964
<b>Species/Strain</b>	Rat/Osborne-Mendel
<b>Sex</b>	Male and Female
<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	None
<b>Route of administration</b>	Intubation
<b>Remarks for test conditions</b>	5 male and 5 female young adult Osborne-Mendel rats were fasted for 18 hrs prior to treatment. Animals were observed for toxic signs and death. The observation period was 2 wks.

<b>Value LD50 or LC50 with confidence limits</b>	3600 mg/kg bw (95% C.L. 2840-4570)
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for results</b>	Slope function: 1.7 (95% C.L. 1.3-2.2). Toxic signs were depression, coma, and wet fur. Times of deaths were between 4-18 hours.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study
<b>References</b>	Jenner P.M., Hagan E.C., Taylor J.M., Cook E.L., Fitzhugh O.G. (1964) Food flavorings and compounds of related structure I. Acute Oral Toxicity. <i>Fd. Cosmet. Toxicol.</i> 2, 327-343.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Not reported
<b>Method/guideline</b>	Litchfield and Wilcoxon, 1949
<b>Test Type</b>	Oral LD50
<b>GLP</b>	Not reported
<b>Year</b>	1962
<b>Species/Strain</b>	Mixed strains rat
<b>Sex</b>	Not reported
<b>Vehicle</b>	Propylene glycol
<b>Route of administration</b>	Gavage
<b>Remarks for test conditions</b>	Groups of 8 mixed breed rats weighing approximately 150 g were given geraniol at the following doses, 1, 5, 10, 100, 1000, 2000, 5000 mg/kg bw in propylene glycol by stomach tube & observed for 48 hr. A vehicle control was also administered.
<b>Value LD50 or LC50 with confidence limits</b>	4800 mg/kg bw (95% C.I. 2900-5900 mg/kg bw)
<b>Number of deaths at each dose level</b>	5000 mg/kg bw 3/5 deaths
<b>Remarks for results</b>	The LD50 reported was 4800 mg/kg bw.
<b>Conclusion remarks</b>	The LD50 reported was 4800 mg/kg bw.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.

**Remarks for Data Reliability** Basic data given and comparable to guidelines/standards.

**References** Yamawaki T. (1962). Pharmacological effects of geraniol. Nippon Yakurigaku Zasshi, 58, 394-400.

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<b>Substance Name</b>	Nerol
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<b>CAS</b>	106-25-2
<b>Remarks for Substance</b>	Purity undetermined.
<b>Method/guideline</b>	NG
<b>Test Type</b>	Acute ED25
<b>GLP</b>	Not reported
<b>Year</b>	1977
<b>Species/Strain</b>	Mouse/CD-1
<b>Sex</b>	Female
<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	None
<b>Route of administration</b>	Inhalation
<b>Remarks for test conditions</b>	The respiratory irritation potential of fragrance raw materials was assessed in CD-1 females by recording respiratory rate using a whole body plethysmograph. Mice were exposed to test materials for 1 min using a nebulizer for aerosolization in a 2600 ml chamber. Materials shown to be sensory irritants were further tested in mice cannulated via the trachea & compared to an intact mouse breathing through its nose. Comparisons were between the preexposure & exposure rate values for each material at each dose level. Materials were of undetermined purity.
<b>Value LD50 or LC50 with confidence limits</b>	ED25=590 micrograms/L
<b>Remarks for results</b>	Mild moderate respiratory depression. Lower tract exposures not performed.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Troy W.R. (1977) Doctoral Dissertation: The comparative respiratory irritation potential of fourteen fragrance raw materials. Unpublished report to RIFM.

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<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Remarks for Substance</b>	Not reported
<b>Method/guideline</b>	NG
<b>Test Type</b>	Acute dermal LD50
<b>GLP</b>	Not reported
<b>Year</b>	1972
<b>Species/Strain</b>	Rabbit/New Zealand White
<b>Sex</b>	Not reported
<b># of animals per sex per dose</b>	10
<b>Vehicle</b>	None
<b>Route of administration</b>	Dermal
<b>Remarks for test conditions</b>	A single 24 hr application was made to the clipped abraded abdominal skin of ten rabbits weighing 1.9 to 2.2 kg. Observations were made for mortality and toxic effects for a period of seven days. Gross necropsies were performed on all animals at the termination of the study.
<b>Value LD50 or LC50 with confidence limits</b>	>5000 mg/kg bw
<b>Number of deaths at each dose level</b>	1 at 5000 mg/kg bw
<b>Remarks for results</b>	The LD50 was reported to be >5000 mg/kg bw.
<b>Conclusion remarks</b>	The LD50 was reported to be >5000 mg/kg bw.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Moreno O. M. (1972) Acute oral toxicity of nerol in rats and rabbits. Unpublished report to RIFM.

<b>Substance Name</b>	Nerol
<b>CAS</b>	106-25-2
<b>Remarks for Substance</b>	Clear liquid
<b>Method/guideline</b>	NG
<b>Test Type</b>	Oral LD50

<b>GLP</b>	Not reported
<b>Year</b>	1972
<b>Species/Strain</b>	Rat/Wistar
<b>Sex</b>	Male
<b># of animals per sex per dose</b>	10
<b>Vehicle</b>	None
<b>Route of administration</b>	Oral
<b>Remarks for test conditions</b>	Ten rats per dose level were administered 2560, 4000, 6250 or 9800 mg/kg bw nerol and observed for fourteen days. Gross necropsies performed on all survivors.
<b>Value LD50 or LC50 with confidence limits</b>	4500 mg/kg bw (95% C.L. 3400-5600 mg/kg bw)
<b>Number of deaths at each dose level</b>	2560 mg/kg bw 1/10 deaths; 4000 mg/kg bw 4/10 deaths; 6250 mg/kg bw 7/10 deaths; 9800 mg/kg bw 10/10 deaths
<b>Remarks for results</b>	The animals experienced axophthalmia, hyperreflexiveness, restlessness, lethargy and the loss of the righting reflex. Deaths occurred overnight to two days following administration of the test substance.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Moreno O. M. (1972) Acute oral toxicity of nerol in rats and rabbits. Unpublished report to RIFM.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS.
<b>Method/guideline</b>	Litchfield-Wilcoxon, 1949
<b>Test Type</b>	Oral LD50
<b>GLP</b>	Not reported
<b>Year</b>	1964
<b>Species/Strain</b>	Rat/Osborne-Mendel
<b>Sex</b>	Male and Female
<b># of animals per sex per dose</b>	5

<b>Vehicle</b>	None
<b>Route of administration</b>	Intubation
<b>Remarks for test conditions</b>	5 male and 5 female young adult Osborne-Mendel rats were fasted for 18 hours prior to treatment. Animals were observed for toxic signs and death. The observation period was 2 wks.
<b>Value LD50 or LC50 with confidence limits</b>	4960 mg/kg bw (95% C.L. 3940-6240)
<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for results</b>	Slope function: 1.5 (95% C.L. 1.2-2.0). Toxic signs were depression. Times of deaths were between 4-96 hours.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Jenner P.M., Hagan E.C., Taylor J.M., Cook E.L., Fitzhugh O.G. (1964) Food flavorings and compounds of related structure I. Acute Oral Toxicity. <i>Fd. Cosmet. Toxicol.</i> 2, 327-343.

<b>Substance Name</b>	Acetylated myrcene (data given for major component, geranyl acetate)
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Principal component of acetylated myrcene
<b>Method/guideline</b>	Litchfield-Wilcoxon, 1949
<b>Test Type</b>	Oral LD50
<b>GLP</b>	Not reported
<b>Year</b>	1964
<b>Species/Strain</b>	Rat/Osborne-Mendel
<b>Sex</b>	Male and Female
<b># of animals per sex per dose</b>	5
<b>Vehicle</b>	None
<b>Route of administration</b>	Intubation
<b>Remarks for test conditions</b>	5 male and 5 female young adult Osborne-Mendel rats were fasted for 18 hours prior to treatment. Animals were observed for toxic signs and death. The observation period was 2 weeks.
<b>Value LD50 or LC50 with confidence limits</b>	6330 mg/kg bw (95% C.L. 5450-7340)

<b>Number of deaths at each dose level</b>	Not reported
<b>Remarks for results</b>	Slope function: 1.3 (95% C.L. 1.2-1.4). Toxic signs were depression. Times of deaths were between 4-96 hours.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study.
<b>References</b>	Jenner P.M., Hagan E.C., Taylor J.M., Cook E.L., Fitzhugh O.G. (1964) Food flavorings and compounds of related structure I. Acute Oral Toxicity. <i>Fd. Cosmet. Toxicol.</i> 2, 327-343.

## 4.2 *In Vitro* Genotoxicity

<b>Substance Name</b>	dl-citronellol
<b>CAS</b>	106-22-9
<b>Method/guideline</b>	Ames
<b>Test Type</b>	Reverse mutation
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1979
<b>Species/Strain</b>	Salmonella typhimurium/TA 100 and TA98
<b>Metabolic Activation</b>	Rat liver microsome fraction S9 from Aroclor induced rats
<b>Doses/concentration levels</b>	0.05 - 100 microliters per plate
<b>Statistical Methods</b>	NG
<b>Remarks for test conditions</b>	After 48-hour incubation at 37 °C, each assay plate was counted. Routine positive control plates were prepared: sodium azide & picolonic acid were used as positive controls for TA100 and TA98. Plates with aflatoxin B1 were positive controls for experiments performed with activation by S9
<b>Result</b>	No mutagenic effects
<b>Cytotoxic concentration</b>	NG
<b>Genotoxic effects</b>	None
<b>Statistical evaluations</b>	NG
<b>Conclusion remarks</b>	No evidence of mutagenicity
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.

<b>Remarks for Data Reliability</b>	Comparable to guideline study with acceptable restrictions. Data were acquired prior to GLP or OECD guidelines but were obtained by standard methodology and published in a peer-reviewed journal.
<b>References</b>	Rockwell P. and Raw I. (1979) A mutagenic screening of various herbs, spices, and food additives. Nutrition and Cancer, 1(4), 10-15.

<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	99.4% purity
<b>Method/guideline</b>	Chromosomal Aberration test
<b>Test Type</b>	Non-bacterial
<b>System of Testing</b>	Chinese hamster fibroblast
<b>GLP</b>	No
<b>Year</b>	1984
<b>Species/Strain</b>	Chinese hamster fibroblast
<b>Metabolic Activation</b>	None
<b>Doses/concentration levels</b>	3 doses at different concentrations. The maximum dose was 125 ug/plate
<b>Statistical Methods</b>	None performed
<b>Remarks for test conditions</b>	Replicates performed if no dose response was observed. Intervals for testing were 24 and 48 hrs. The solvent used was DMSO. Untreated cells and solvent treated cells were negative controls. The incidence of chromosomal aberrations for negative controls was usually less than 3.0%. 100 metaphases were examined for incidence of aberrations and considered negative <4.9%, equivocal 5.0-9.9%, positive. >10.0%. If no reasonable dose-response relationships were found, additional experiments were conducted at similar dose levels.
<b>Result</b>	Equivocal. Polyploidization effects were observed. The incidence of polyploid cells at 48 hours after treatment was 8.0%. The incidence of chromosomal aberrations at 48 hours was 4.0% at 48 hours.
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	Polyploidization effects were observed.
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	The result was considered equivocal presumably based on the

polyploidization effects observed. The incidence of chromosomal aberrations at 48 hours was in the range considered negative by the authors.

**Data Qualities Reliabilities** Reliability code 3. Invalid.

**Remarks for Data Reliability** Test was conducted by standard methodology and published in a peer-reviewed journal. This study closely followed OECD guideline 473, except for metabolic activation and the lack of positive controls.

**References** Ishidate M., Sofuni T., Yoshikawa K., Hayashi M., Nohmi T., Sawada M., Matsuoka A. (1984) Primary Mutagenicity Screening of Food Additives Currently Used in Japan. Food Chemical Toxicology. 22, 623-636.

<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	99.4% purity
<b>Method/guideline</b>	Ames
<b>Test Type</b>	Reverse mutation
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1984
<b>Species/Strain</b>	Salmonella typhimurium/TA 92, TA1535, TA100, TA1537, TA94, TA98
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 from PCB-induced Fisher rats
<b>Doses/concentration levels</b>	6 different concentrations, maximum tested 500 ug/plate
<b>Statistical Methods</b>	Not given
<b>Remarks for test conditions</b>	DMSO was used as the solvent. Results were considered positive if number of colonies found was at least twice the number found in the control.
<b>Result</b>	Negative
<b>Cytotoxic concentration</b>	Not specified
<b>Genotoxic effects</b>	Negative
<b>Statistical evaluations</b>	Not given
<b>Conclusion remarks</b>	No mutagenic effects
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.

**Remarks for Data Reliability** Basic data given and comparable to guidelines/standards.

**References** Ishidate M., Sofuni T., Yoshikawa K., Hayashi M., Nohmi T., Sawada M., Matsuoka A. (1984) Primary Mutagenicity Screening of Food Additives Currently Used in Japan. Food Chemical Toxicology. 22, 623-636.

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<b>Substance Name</b>	Geraniol
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<b>CAS</b>	106-24-1
<b>Method/guideline</b>	Ames
<b>Test Type</b>	Reverse mutation
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1980
<b>Species/Strain</b>	Salmonella typhimurium/TA 98, TA 100, TA 1535 and TA 1537
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 from Aroclor-induced rats
<b>Doses/concentration levels</b>	3 micromol/plate (462 ug/plate)
<b>Statistical Methods</b>	Not given
<b>Remarks for test conditions</b>	The solvent used was ethanol. Only one replicate was performed for the substances, which tested negative.
<b>Result</b>	No mutagenic effects.
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	None
<b>Statistical evaluations</b>	Not given
<b>Conclusion remarks</b>	No mutagenic activity.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Not reliable.
<b>Remarks for Data Reliability</b>	Does not meet important criteria of today's standard methods.
<b>References</b>	Florin I., Rutberg L., Curvall M., and Enzell C.R. (1980) Screening of tobacco smoke constituents for mutagenicity using the Ames test. Toxicology, 18, 219-232.

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<b>Substance Name</b>	Geraniol
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<b>CAS</b>	106-24-1
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<b>Remarks for Substance</b>	99% purity
<b>Method/guideline</b>	Ames
<b>Test Type</b>	Reverse mutation
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No
<b>Year</b>	1980
<b>Species/Strain</b>	Salmonella typhimurium/TA100
<b>Metabolic Activation</b>	With and without rat liver microsome fraction S9 from Aroclor induced rats
<b>Doses/concentration levels</b>	0.01-1 microliter per 2ml DMSO
<b>Statistical Methods</b>	Not given
<b>Remarks for test conditions</b>	Values are average of two experiments. Positive controls were 6.5 µg sodium azide per 2 ml incubation volume w/out activation and 25 µg 2-aminoanthracene per 2 ml incubation volume with activation. Dose = 0.01 - 1 ul per 2 ml incubation volume in DMSO.
<b>Result</b>	No mutagenic effects
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	None
<b>Statistical evaluations</b>	Not given
<b>Conclusion remark</b>	No mutagenic activity
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Basic data given and comparable to guidelines/standards.
<b>References</b>	Eder E., Nedecker T., Lutz D., Henschler D. (1980) Mutagenic potential of allyl and allylic compounds. Biochemical Pharmacology 29, 993-998.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Volunteered under SIDS program. 98.2% purity.
<b>Method/guideline</b>	Chromosomal Aberration test
<b>Test Type</b>	Non-bacterial
<b>System of Testing</b>	Chinese hamster fibroblast cell line

<b>GLP</b>	No
<b>Year</b>	1984
<b>Species/Strain</b>	Chinese hamster fibroblast
<b>Metabolic Activation</b>	None
<b>Doses/concentration levels</b>	3 doses at different concentrations. The maximum dose was 30 ug/plate
<b>Statistical Methods</b>	None performed
<b>Remarks for test conditions</b>	Replicates performed if no dose response was observed. Intervals for testing were 24 and 48 hrs. The solvent used was DMSO. Untreated cells and solvent treated cells were negative controls. The incidence of chromosomal aberrations for negative controls was usually less than 3.0%. 100 metaphases were examined for incidence of aberrations and considered negative. <4.9%, equivocal 5.0-9.9%, positive. >10.0%. If no reasonable dose-response relationships were found, additional experiments were conducted at similar dose levels.
<b>Result</b>	Negative. The incidence of polyploid cells at 48 hours after treatment was 4.0%. The incidence of chromosomal aberrations at 48 hours was 2.0%.
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	Negative
<b>Statistical evaluations</b>	Not given
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Test was conducted by standard methodology and published in a peer-reviewed journal. This study closely followed OECD guideline 473, except for metabolic activation and the lack of positive controls.
<b>References</b>	Ishidate M., Sofuni T., Yoshikawa K., Hayashi M., Nohmi T., Sawada M., Matsuoka A. (1984) Primary Mutagenicity Screening of Food Additives Currently Used in Japan. Food Chemical Toxicology. 22, 623-636.

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<b>Substance Name</b>	Acetylated myrcene
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<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. Purity of test substance for this assay was 69.6%.
<b>Method/guideline</b>	Ames
<b>Test Type</b>	Reverse mutation

<b>System of Testing</b>	Bacterial
<b>GLP</b>	Not given
<b>Year</b>	1986
<b>Species/Strain</b>	Salmonella typhimurium/TA1535, TA1537, TA97, TA98, TA100
<b>Metabolic Activation</b>	With and without rat and hamster liver microsome fraction S9 from Aroclor-induced rats and hamsters, respectively.
<b>Doses/concentration levels</b>	1-3333 micrograms/plate
<b>Statistical Methods</b>	None employed
<b>Remarks for test conditions</b>	Positive controls included the following: sodium azide for TA1535 and TA100; 4-nitro-o-phenylenediamine for TA98; 9-aminoacridine for TA97 and TA1537; 2-aminoanthracene for all strains with hamster and rat liver metabolic activation. At least 5 dose levels were tested, with 3 plates per dose level. All assays were repeated at least one week following initial assay.
<b>Result</b>	No mutagenic effects.
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	None
<b>Statistical evaluations</b>	Not given
<b>Conclusion remarks</b>	No evidence of mutagenicity.
<b>Data Qualities Reliabilities</b>	Reliability code 3. Invalid.
<b>Remarks for Data Reliability</b>	Guideline study. Test was conducted by laboratory under contract with the National Toxicology Program.
<b>References</b>	Mortelmans, K., Haworth, S., Lawlor, T., Speck, W., Tainer, B., and Zeiger, E. (1986). Salmonella mutagenicity tests: II. Results from the testing of 270 chemicals. Environmental Mutagenesis 8(7), 1-119.

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<b>Substance Name</b>	Acetylated myrcene
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<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol.
<b>Method/guideline</b>	Ames
<b>Test Type</b>	Reverse mutation
<b>System of Testing</b>	Bacterial
<b>GLP</b>	No

<b>Year</b>	1989
<b>Species/Strain</b>	Salmonella typhimurium/TA1535, TA1537, TA1538, TA98, TA100
<b>Metabolic Activation</b>	Rat liver microsome fraction S9 from Aroclor-induced rats
<b>Doses/concentration levels</b>	20000 ug/plate
<b>Statistical Methods</b>	Not given
<b>Remarks for test conditions</b>	After two days incubation at 37 °C, revertant colonies were counted.
<b>Result</b>	No mutagenic effects.
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	None
<b>Statistical evaluations</b>	Not given
<b>Conclusion remarks</b>	No evidence of mutagenicity
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study.
<b>References</b>	Heck, J. D., Vollmuth, T. A., Cifone, M. A., Jagannath, D. R., Myhr B., and R.D. Curren (1989). An evaluation of food flavoring ingredients in a genetic toxicity screening battery The Toxicologist, 9(1), 257.

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<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol.
<b>Method/guideline</b>	Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells In Vitro Unscheduled DNA Synthesis
<b>Test Type</b>	Unscheduled DNA Synthesis (Butterworth, 1987)
<b>System of Testing</b>	F344 rat hepatocytes
<b>GLP</b>	No
<b>Year</b>	1989
<b>Species/Strain</b>	Rat/ Adult male Fisher 344
<b>Metabolic Activation</b>	None
<b>Doses/concentration levels</b>	100 nanoliters/millilitre (nl/ml)

<b>Statistical Methods</b>	Not given
<b>Remarks for test conditions</b>	Cultures of freshly prepared hepatocytes were incubated with the test article for 18-20 hours. Cell survival was measured by concurrent cell counting and measurement of LDH release from cells. UDS was measured by counting nuclear grains and subtracting average grain counts in three adjacent nuclear-sized cytoplasmic areas. This was designated the net nuclear grain count (NNG). An NNG in excess of 6 grains was considered a positive response.
<b>Result</b>	No unscheduled DNA synthesis observed.
<b>Cytotoxic concentration</b>	Not given
<b>Genotoxic effects</b>	None
<b>Statistical evaluations</b>	Not given
<b>Conclusion remarks</b>	No evidence of genotoxicity
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study.
<b>References</b>	Heck, J. D., Vollmuth, T. A., Cifone, M. A., Jagannath, D. R., Myhr B., and R.D. Curren (1989). An evaluation of food flavoring ingredients in a genetic toxicity screening battery <i>The Toxicologist</i> , 9(1), 257.

### 4.3 *In Vivo* Genotoxicity

<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. The test substance in this study was geranyl acetate (CAS 105-87-3) obtained from the National Toxicology Program Repository. Purity tests revealed the test substance; acetylated myrcene consisted of 79% geranyl acetate and 21% citronellyl acetate. Remaining impurities accounted for less than 0.37%.
<b>Method/guideline</b>	Mouse bone marrow micronucleus assay
<b>Test Type</b>	Micronucleus
<b>GLP</b>	NG
<b>Year</b>	1993
<b>Species/Strain</b>	Mouse/ B6C3F1
<b>Sex</b>	Male
<b>Route of Administration</b>	Intraperitoneal injection

**Doses/concentration** 0, 450, 900, or 1800

**Exposure period** 3 days

**Remarks for test conditions** Groups of five to six mice each were administered 0, 450, 900 or 1800 mg/kg bw by intraperitoneal injection for three consecutive days. Positive and negative controls were also maintained. Positive controls were either DMBA (7,12-dimethylbenzanthracene) in corn oil or MMC (mitomycin C) in PBS. 48 hr after the last treatment the mice were euthanized. Bone marrow and peripheral blood smears were obtained by a direct technique

<b>Effect on mitotic index or PCE/NCE ratio by dose level and sex</b>	Dose	MN-PCE/1000	# Animals	Pairwise Comparison	Survival	PCE
	0	2.20 +/-0.26	5		5/5	65.0
	450	2.50 +/-0.42	5	0.3307	5/5	62.1
	900	3.30+/-1.06	5	0.0687	5/5	66.3
	1800	2.83+/-0.56	6	0.1766	6/6	67.3

**Genotoxic effects** Negative

**NOEL (C)/ LOEL (C)** NOEL=1800 mg/kg bw

**Statistical evaluations** Yes, trend test and pairwise comparison alpha=0.05

**Remarks for results** The initial test was negative to the high dose and was not repeated.

**Conclusion** The test was negative.

**Data Qualities Reliabilities** Reliability code 2. Reliable with restrictions.

**Remarks for Data Reliability** Basic data given and comparable to guidelines/standards.

**References** Shelby M.D., Erexson G.L., Hook G.J., and Tice R.R. (1993) Evaluation of a Three-Exposure Mouse Bone Marrow Micronucleus Protocol; Results with 49 Chemicals. Environmental and Molecular Mutagenesis, 21: 160-179.

<b>Substance</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol.
<b>Method/guideline</b>	Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells In Vivo
<b>Test Type</b>	Unscheduled DNA
<b>GLP</b>	NG
<b>Year</b>	1983

<b>Species/Strain</b>	Rat/Fischer 344
<b>Sex</b>	Male
<b>Route of Administration</b>	Gavage
<b>Genotoxic effects</b>	No genotoxic effects.
<b>Conclusion</b>	No evidence of genotoxicity.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study. Data considered reliable and followed OECD guideline 486. Test was conducted by laboratory under contract with the National Toxicology Program.
<b>References</b>	Mirsalis, J., Tyson, K., Beck, J., Loh, E., Steinmetz, K., Contreras, C., Austere, L., Martin, S., and J. Spalding (1983). Induction of unscheduled DNA synthesis (UDS) in hepatocytes following in vitro and in vivo treatment. Environmental Mutagenesis 5(3), 482.

#### 4.4 Repeat Dose Toxicity

<b>Substance Name</b>	Citronellol
<b>CAS</b>	106-22-9
<b>Remarks for Substance</b>	Mixture of citronellol (50%) and linalool (50%)
<b>Method/guideline</b>	The test mixture was incorporated in the ration at a level designed to provide daily in the food 100 mg of the flavor blend per kg of body wt. The un-supplemented diet was fed to the controls. The rats were fed for 12 weeks
<b>GLP</b>	Pre-GLP
<b>Year</b>	1958
<b>Species/Strain</b>	Unspecified strain rat
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Diet
<b>Doses/concentration levels</b>	100 mg/kg of mixture per day
<b>Exposure period</b>	12 weeks
<b>Frequency of treatment</b>	Continuously in diet
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	NG

<b>Remarks for test conditions</b>	After 12 weeks on test, the urine of 3 rats of each sex per group was examined for the presence of sugar and albumin, blood hemoglobin levels were determined and autopsies were performed on all animals.
<b>NOAEL(NOEL)</b>	100 mg/kg bw/day ppm
<b>LOAEL(LOEL)</b>	No adverse effects at highest dose
<b>Actual dose received by dose level and sex</b>	Not given
<b>Toxic response/effects by dose level</b>	No adverse effects on efficiency of food utilization or other observable physiological criteria were noted.
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	The depression in the growth and food intake of the male rats was attributed to impalatability of the test material at the level administered.
<b>Conclusion remarks</b>	Feeding tests with a mixture of equal parts of citronellol and linalool fed at a level 100 times the estimated use level in the diet disclosed no adverse effect on efficiency of food utilization or other observable criteria..
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>References</b>	Oser, B. (1958) Toxicological Screening of Components of Food Flavors Class VI. Citronellol and Linalool. Food and Drug Research Laboratories.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Data are for mixture of geranial and neral.
<b>Method/guideline</b>	National Toxicology Program 2-yr Bioassay
<b>Year</b>	2001
<b>Species/Strain</b>	Rat/F344/N
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Oral-dietary
<b>Doses/concentration levels</b>	1,000, 2,000, or 4,000 ppm citral (geranial and neral) microencapsulated for 104 to 105 weeks
<b>Exposure period</b>	104 - 105 weeks
<b>Frequency of treatment</b>	Continuous
<b>Control Group</b>	Basal diet

<b>Remarks for test conditions</b>	A carcinogenicity study was conducted in which groups of 50 F344/N rats of each sex were maintained on diets containing 0 (untreated control), 0 (vehicle control containing placebo microcapsules), 1,000, 2,000, or 4,000 ppm citral microencapsulated for 104 to 105 weeks. The dietary concentrations were calculated to provide an average daily intake of 50, 100, or 210 mg/kg bw per day of citral. Feed analysis for citral concentrations are as specified in the study with mice (see above). Female rats were housed five per cage, while male rats were housed two or three per cage. Feed and water were provided ad libitum. Clinical findings and body weights were monitored on days 0 (body weights only), 8, and 33 and then every four weeks until the end of the study. Seven (7)-day feed consumption was measured every 4 weeks during the study. Gross and histopathological examinations were performed on all animals at termination of the study.
<b>NOAEL(NOEL)</b>	4000 ppm
<b>Toxic response/effects by dose level</b>	Mean body weights of high-dose females and males (4,000 ppm) were less than those of the vehicle control after weeks 25 and 49, respectively. There was no difference in feed consumption between treated and vehicle control groups. Survival of all treated groups of male rats was greater than that for the vehicle control group. No neoplastic or non-neoplastic lesions were observed that could be associated with the administration of diets containing 1,000, 2,000, or 4,000 ppm of citral. There was, however, a significant decrease in the incidence of clitoral gland hyperplasia, adenoma, and carcinomas in female rats maintained on diets containing 4,000 ppm citral. There also was a dose-related decrease in the incidence of mammary gland fibroadenomas in female rats at 4,000 ppm. The authors hypothesized that these decreases may be related to the antiestrogenic effects of citral (Geldof et al., 1992). A dose-dependent increase in the incidence of kidney mineralization was observed in males; however, this also was observed in the vehicle control group, and consequently, citral was deemed only to exacerbate these otherwise spontaneously occurring lesions. Furthermore, similar effects were not observed in the 14-week rat study (NTP draft, 2001).
<b>Statistical evaluations</b>	Yes
<b>Remarks for results</b>	Based on the above observations, the NTP concluded "under the conditions of these 2-year feed studies there was no evidence of carcinogenic activity of citral in male or female rats exposed to 1,000, 2,000, or 4,000 ppm.
<b>Conclusion remarks</b>	The results of the NTP study in both sexes of F344 rats and B6C3F1 mice indicate that under conditions of the 2-year feed studies, citral shows no evidence of carcinogenic potential in rodents.
<b>Data Qualities Reliabilities</b>	Reliability Code 1. Reliable without restriction.

**References**

NTP (2001) National Toxicology Program. Toxicology and carcinogenesis studies of citral (microencapsulated) (CAS No. 5392-40-5) in F344/N rats and B6C3F1 Mice. (Feed studies) Technical Report Series 505 NIH Publication No. 01-4439. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health.

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<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Data are for mixture of geranial and neral.
<b>Method/guideline</b>	National Toxicology Program 2-yr Bioassay
<b>Year</b>	2001
<b>Species/Strain</b>	Mice/B6C3F1
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Oral-dietary
<b>Doses/concentration levels</b>	0, 500, 1,000, or 2,000 ppm microencapsulated citral (geranial and neral) in the diet
<b>Exposure period</b>	104 - 105 weeks
<b>Frequency of treatment</b>	Continuous
<b>Control Group</b>	Basal diet
<b>Remarks for test conditions</b>	<p>A carcinogenicity study was conducted in which groups of 50 B6C3F1 mice of each sex were maintained on diets containing 0 (untreated control), 0 (vehicle control containing placebo microcapsules), 500, 1,000, or 2,000 ppm microencapsulated citral for 104 to 105 weeks. The dietary concentrations were calculated based on food consumption to provide an average daily intake of 0, 60, 120, or 260 mg citral/kg bw. The microencapsulate particles were composed of a sugar and starch mixture 50 to 100 µm in size. The concentration of citral in the microencapsules was measured by HPLC to be 32.3%, with a geranial (trans isomer) to neral (cis isomer) ratio of approximately 2:1. The diets (NTP-2000) used in the study contained less protein and more fiber and fat than diets (NIH-07) previously used in NTP 2-year studies.</p> <p>Female mice were housed five per cage while male mice were housed individually. Feed and water were provided ad libitum. Clinical findings and body weights were monitored on days 0 (body weights only), 8, and 36 and then every four weeks until the end of the study. Seven-day feed consumption was measured every 4 weeks during the study. Gross and histopathological examinations were performed on all animals at termination of the study.</p>

<b>NOAEL(NOEL)</b>	2000 ppm
<b>Toxic response/effects by dose level</b>	<p>Mean body weights of both sexes were generally (statistical significance not specified) lower than mean body weights of the vehicle control groups of mice in the high-dose group (2,000 ppm) throughout the study, and during the second year in mid-dose (1,000 ppm) males and from week 14 in mid-dose (1,000 ppm) females. At the low dose (500 ppm), female mice exhibited lower mean body weights after week 30. No clinical signs of toxicity attributable to citral exposure were observed. There was no difference in feed consumption between treated and vehicle control groups. Survival of the treated groups of male and female mice was similar to that of the vehicle control group. The increased incidence of malignant lymphoma in female mice [untreated control 4/50, (8%); vehicle control 3/49, (6%); 500 ppm 5/50, (10%); 1,000 ppm 9/50, (18%); 2,000 ppm 12/50, (24%)] predominantly affecting the spleen, mesenteric lymph nodes, thymus and to a lesser extent the ovaries, was statistically significant (<math>p=0.011</math>) in high-dose (2,000 ppm) female mice compared to the incidence in vehicle control animals. There was no difference in the incidence of malignant lymphoma between treated and vehicle control male mice. The authors noted that the incidence of lymphoma in the high-dose female mice was within the historical control range for control female mice given the NTP 200 diet or feed controls maintained on the NIH-07 diet. Although a significant positive trend was identified in the incidence of hepatocellular adenoma in females, it was not statistically significant upon pairwise comparison with vehicle controls and therefore presumed to be unrelated to treatment.</p>
<b>Statistical evaluations</b>	Yes
<b>Remarks for results</b>	<p>The neoplastic response reported in the NTP study was a dose-related increase in the incidence of lymphoma that was statistically significant only in the high dose in B6C3F1 female mice (<math>p=0.011</math> by Fisher exact test; 12/50 (24%) at 2000 ppm versus 3/49 (6%) in vehicle controls}. There was no evidence of increased incidence of malignant lymphoma in either sex of F344/N rats, in male B6C3F1 mice and the incidence in female B6C3F1 mice maintained on diets containing 500 or 1,000 ppm of citral was not statistically significant.</p> <p>The background incidence of malignant lymphoma in control female B6C3F1 mice maintained on a NTP-2000 diet is high (98/659), with a historical incidence of 14.0% (standard deviation <math>\pm 7.1\%</math>), and a range of 6 to 30% (NTP draft, 2001). The historical incidence in controls maintained on the NIH-07 diet at the same contract laboratory performing the citral study was also high (167/953) with a historical incidence of 17.5% (standard deviation 7.7%) and a range of 6 to 30%.</p> <p>Therefore, these tumours occur at a high and variable rate in control animals. It is recommended (Haseman et al., 1986) that a compound is anticipated to exhibit a carcinogenic potential if the highest dose is associated with an increased incidence of a</p>

common tumour that is significant at the 1% (p less than 0.01) level, or an increased incidence in a rare tumour at the 5% (p less than 0.05) level. Therefore, statistical analysis should apply a significance level of 1% (p less than 0.01) to account for the high background incidence of a commonly observed tumour (lymphomas) in female B6C3F1 mice. Based on pair-wise comparisons of the incidence of malignant lymphoma in the NTP study by a Fisher exact test, the incidence of this neoplasm is not considered to be statistically significant (p=0.011) for female mice at the 1% level.

Decreased body weights in female mice exposed to 500 (after week 30), 1,000 or 2,000 ppm citral also confounded the interpretation of the neoplastic response in female mice. The lack of any significant decrease in feed consumption in these groups supports the conclusion that the dose-dependent decrease in body weights is evidence of toxicity.

Based upon the high frequency of this neoplastic response in historical controls in NTP studies, the fact that toxicity was observed at all dose levels in female B6C3F1 mice, and the observation that the incidences of lymphoma reported in the NTP study were not significant at the 1% level (p less than 0.01) (Haseman et al., 1986), the Committee concludes that the results of the NTP bioassay in female mice are not relevant to the safety assessment of citral. The results of the NTP study in both sexes of F344 rats and B6C3F1 mice indicate that under conditions of the 2-year feed studies, citral shows no evidence of carcinogenic potential in rodents.

**Conclusion remarks**

The results of the NTP study in both sexes of F344 rats and B6C3F1 mice indicate that under conditions of the 2-year feed studies, citral shows no evidence of carcinogenic potential in rodents.

**Data Qualities Reliabilities**

Reliability Code 1. Reliable without restriction.

**References**

NTP (2001) National Toxicology Program. Toxicology and carcinogenesis studies of citral (microencapsulated) (CAS No. 5392-40-5) in F344/N rats and B6C3F1 Mice. (Feed studies) Technical Report Series 505 NIH Publication No. 01-4439. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health.

<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	Mixture of 3,7-dimethyl-2,6-octadienol (geraniol) and 3,7-dimethyl-6-octenol (citronellol)
<b>Method/guideline</b>	Screening method used by U.S. Food and Drug Administration
<b>GLP</b>	No
<b>Year</b>	1967

<b>Species/Strain</b>	Osborne-Mendel rats
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Diet
<b>Doses/concentration levels</b>	1000 or 10000 ppm
<b>Exposure period</b>	112 days at 10,000 ppm, 189-196 days at 1000 ppm
<b>Frequency of treatment</b>	Continuously in diet
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	NG
<b>Remarks for test conditions</b>	Groups of five male and five female Osborne-Mendel rats were provided geraniol in the diet at concentrations of 0, 1000 or 10,000 ppm for 16 and 27-28 weeks, respectively. No vehicle was used. The diet was prepared and analyzed weekly. Measurements of body weight, food intake and general condition were recorded weekly. Hematological examinations (white cell counts, red cell counts, hemoglobins and hematocrits) were performed at the termination 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 animals (evenly divided by sex) from both doses and the control dose group.
<b>NOAEL(NOEL)</b>	10000 ppm
<b>LOAEL(LOEL)</b>	No adverse effects at highest dose
<b>Actual dose received by dose level and sex</b>	Not given
<b>Toxic response/effects by dose level</b>	None
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	Measurements of body weight, food intake and general condition recorded weekly showed no significant differences between test and control animals at any intake level. At termination, hematological examinations revealed no difference from controls. At necropsy, no differences were reported between major organ weights of test and control animals. Gross examination of tissue of all animals was unremarkable and histopathological examination revealed no treatment-related lesions.
<b>Conclusion remarks</b>	This study demonstrates a NOAEL in rats of at least 500 mg/kg/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study. This study was performed by

the FDA prior to the establishment of GLP and OECD.

**References**

Hagan E.C., Hansen W.H., Fitzhugh O.G., Jenner P.M., Jones W.I., Taylor J.M., Long E.L., Nelson A.A., and Brouwer J.B. (1967) Food Flavourings and Compounds of Related Structure. II. Subacute and Chronic Toxicity. Food Cosmetic Toxicology 5, 141-157.

<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS.
<b>Method/guideline</b>	Screening method used by U.S. Food and Drug Administration.
<b>GLP</b>	No
<b>Year</b>	1967
<b>Species/Strain</b>	Osborne-Mendel rats
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Diet
<b>Doses/concentration levels</b>	1000, 2500 or 10000 ppm
<b>Exposure period</b>	91 days
<b>Frequency of treatment</b>	Continuously in diet
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	Not given
<b>Remarks for test conditions</b>	Groups of ten male and ten female Osborne-Mendel rats were provided citral in the diet at concentrations of 0, 1000, 2500 or 10,000 ppm for 13 weeks. No vehicle was used. The diet was prepared and analyzed weekly. Measurements of body weight, food intake and general condition were recorded weekly. Hematological examinations (white cell counts, red cell counts, hemoglobins and hematocrits) were performed at the termination 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 animals (evenly divided by sex) from the high dose and control dose groups.
<b>NOAEL(NOEL)</b>	10000 ppm
<b>LOAEL(LOEL)</b>	No adverse effects at highest dose
<b>Actual dose received by dose level and sex</b>	Not given

<b>Toxic response/effects by dose level</b>	None.
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	Determination of the dietary concentration of citral revealed a weekly loss of 58% therefore the average daily dose received is estimated to be about 200 mg/kg based on an assumed daily intake of food of 50g/kg. Measurements of body weight, food intake and general condition recorded weekly showed no significant differences between test and control animals at any intake level. At termination, hematological examinations revealed no difference from controls. At necropsy, no differences were reported between major organ weights of test and control animals. Gross examination of tissue of all animals was unremarkable and histopathological examination revealed no treatment-related lesions.
<b>Conclusion remarks</b>	This study demonstrates a NOAEL in rats of at least 200 mg/kg/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study. This study was performed by the FDA prior to the establishment of GLP and OECD.
<b>References</b>	Hagan E.C., Hansen W.H., Fitzhugh O.G., Jenner P.M., Jones W.I., Taylor J.M., Long E.L., Nelson A.A., and Brouwer J.B. (1967) Food Flavourings and Compounds of Related Structure. II. Subacute and Chronic Toxicity. Food Cosmetic Toxicology 5, 141-157.

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<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. The test substance under study is geranyl acetate (CAS 105-87-3).
<b>Method/guideline</b>	Screening method used by U.S. Food and Drug Administration
<b>GLP</b>	Not given
<b>Year</b>	1967
<b>Species/Strain</b>	Osborne-Mendel rats
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Diet
<b>Doses/concentration levels</b>	1000, 2500 or 10000 ppm
<b>Exposure period</b>	118 days
<b>Frequency of treatment</b>	Continuously in diet

<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	Not given
<b>Remarks for test conditions</b>	Groups of ten male and ten female Osborne-Mendel rats were provided geranyl acetate in the diet at concentrations of 0, 1000, 2500 or 10,000 ppm for 17 weeks. No vehicle was used. The diet was prepared and analyzed weekly. Measurements of body weight, food intake and general condition were recorded weekly. Hematological examinations (white cell counts, red cell counts, hemoglobins and hematocrits) were performed at the termination 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 animals (evenly divided by sex) from the high dose and control dose groups.
<b>NOAEL(NOEL)</b>	10000 ppm
<b>LOAEL(LOEL)</b>	No adverse effects at highest dose
<b>Actual dose received by dose level and sex</b>	Not given
<b>Toxic response/effects by dose level</b>	None.
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	Determination of the dietary concentration of geranyl acetate revealed a weekly loss of 4%. The average daily dose received is estimated to be about 500 mg/kg based on an assumed daily intake of food of 50g/kg. Measurements of body weight, food intake and general condition recorded weekly showed no significant differences between test and control animals at any intake level. At termination, hematological examinations revealed no difference from controls. At necropsy, no differences were reported between major organ weights of test and control animals. Gross examination of tissue of all animals was unremarkable and histopathological examination revealed no treatment-related lesions.
<b>Conclusion remarks</b>	This study demonstrates a NOAEL in rats of at least 500 mg/kg/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study. This study was performed by the FDA prior to the establishment of GLP and OECD.
<b>References</b>	Hagan E.C., Hansen W.H., Fitzhugh O.G., Jenner P.M., Jones W.I., Taylor J.M., Long E.L., Nelson A.A., and Brouwer J.B. (1967) Food Flavourings and Compounds of Related Structure. II. Subacute and Chronic Toxicity. Food Cosmetic Toxicology 5, 141-157.

<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. The test substance was food grade geranyl acetate (CAS 105-87-3). Purity tests revealed the test substance consisted of 79% geranyl acetate and 29% citronellyl acetate. Remaining impurities accounted for less than 0.37%.
<b>Method/guideline</b>	National Toxicology Program Carcinogenesis study (NIH Publication No. 88-2508) or (NTP TR 252).
<b>GLP</b>	Yes
<b>Year</b>	1987
<b>Species/Strain</b>	F344/N rats
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Gavage
<b>Doses/concentration levels</b>	1000 or 2000 mg/kg bw/d
<b>Exposure period</b>	103 weeks
<b>Frequency of treatment</b>	Daily (5 days/week)
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	Not given
<b>Remarks for test conditions</b>	A carcinogenicity study was conducted in which groups of 50 F344/N rats of each sex were administered 0, 1000, or 2000 mg/kg bw of a mixture of geranyl acetate (79%) and citronellyl acetate (29%) in corn oil by gavage daily, 5 days/week for 103 weeks. Body weights were recorded weekly for the first 12 weeks and monthly thereafter. Necropsies were performed on all animals surviving until the end of the study and on all animals found dead during the study. Histopathological examination was conducted on the following: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, thymus, larynx, trachea, lungs, and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, pituitary, and spinal cord.
<b>NOAEL(NOEL)</b>	2000 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	Not applicable

**Toxic response/effects by dose level**

A statistically significant decrease in mean body weights was reported for high-dose male rats throughout the study and dosed female rats after week 40. Reduced mean body weight gains were dose related. Survival of the high-dose group (18/50) of male rats was significantly less than the controls (34/50;  $p=0.001$ ) and the low-dose group (29/50;  $p=0.003$ ). There was no other significant difference in survival between any groups of either sex. There was a statistically significant ( $p<0.05$ ) increase in the incidence of squamous cell neoplasms (combined papillomas and carcinomas) in low-dose male rats, but not in the high-dose group (controls, 0/50; low dose, 5/50; high dose, 1/50) or any group of female rats. A positive trend (controls, 6/50: low dose, 8/50; high dose, 9/50) in the incidence of adrenal pheochromocytomas in male rats was not statistically significant. Two (2) low-dose male rats had tubular cell adenomas, but none were observed in the controls or the high-dose group. There was no significant increase in the incidence of any neoplasms in high-dose male or female rats compared to the control groups. The incidence of mammary gland fibroadenomas in high-dose female rats was significantly less (pairwise comparisons,  $p<0.002$ ) than those in the control group (controls, 12/50; high dose, 1/50). Based on pair-wise comparisons between high-dose and control groups of male rats, there was a significant decrease ( $p<0.02$ , Fisher) in the incidence of pituitary adenomas in high-dose males (controls, 10/50; high dose, 2/50). Based on life table analysis of male rats, the incidence of adenomas was not significantly different between control and high-dose groups. A negative trend (controls, 4/49: low dose, 3/48; high dose, 0/50) was observed in the incidence of pancreatic islet-cell adenomas and carcinomas in male rats, but was not statistically significant based on pairwise comparisons between control and dosed groups.

**Statistical evaluations**

Not given

**Remarks for results**

A statistically significant decrease in mean body weights was reported for high-dose male rats throughout the study and dosed female rats after week 40. Reduced mean body weight gains were dose related. Survival of the high-dose group (18/50) of male rats was significantly less than the controls (34/50;  $p=0.001$ ) and the low-dose group (29/50;  $p=0.003$ ). There was no other significant difference in survival between any groups of either sex. There was a statistically significant ( $p<0.05$ ) increase in the incidence of squamous cell neoplasms (combined papillomas and carcinomas) in low-dose male rats, but not in the high-dose group (controls, 0/50; low dose, 5/50; high dose, 1/50) or any group of female rats. A positive trend (controls, 6/50: low dose, 8/50; high dose, 9/50) in the incidence of adrenal pheochromocytomas in male rats was not statistically significant. Two (2) low-dose male rats had tubular cell adenomas, but none were observed in the controls or the high-dose group. There was no significant increase in the incidence of any neoplasms in high-dose male or female rats compared to the control groups. The incidence of mammary gland fibroadenomas in high-dose female rats was significantly

less (pairwise comparisons,  $p < 0.002$ ) than those in the control group (controls, 12/50; high dose, 1/50). Based on pair-wise comparisons between high-dose and control groups of male rats, there was a significant decrease ( $p < 0.02$ , Fisher) in the incidence of pituitary adenomas in high-dose males (controls, 10/50; high dose, 2/50). Based on life table analysis of male rats, the incidence of adenomas was not significantly different between control and high-dose groups. A negative trend (controls, 4/49; low dose, 3/48; high dose, 0/50) was observed in the incidence of pancreatic islet-cell adenomas and carcinomas in male rats, but was not statistically significant based on pairwise comparisons between control and dosed groups [NTP, 1987]. The increases in the incidence of squamous cell papillomas and carcinomas, adrenal pheochromocytomas, and renal tubular adenomas in male rats were not dose related. These types of tumors occur commonly in male F344 rats. The overall incidence of these commonly observed adrenal pheochromocytomas and squamous cell tumors in paired control groups of male rats have been reported to be 25.1% and 3.7%, respectively [Haseman et al., 1986]. Under conditions of this study, geranyl acetate was not carcinogenic for either sex of F344/N rats [NTP, 1987]. In summary, no significant toxic or carcinogenic effects were reported when a mixture of geranyl acetate and citronellyl acetate was administered at dose levels up to 2000 mg/kg bw/d to rats, which correspond to estimated dose levels of 1420 mg geranyl acetate/kg bw/d and 580 mg citronellyl acetate/kg bw/d (the estimated dose levels correspond to 71% and 29% of the administered dose which are the fractions of geranyl acetate and citronellyl acetate contained in the mixture).

**Conclusion remarks**

Under conditions of this study, the mixture of geranyl acetate and citronellyl acetate was not carcinogenic for either sex of B6C3F1 mice.

**Data Qualities Reliabilities**

Reliability code 1. Reliable without restrictions.

**Remarks for Data Reliability**

Guideline study. This study was performed by the NTP.

**References**

National Toxicology Program (NTP) (1987) Carcinogenesis studies of food grade geranyl acetate (71%) and citronellyl acetate (29%). NTP-TR-252. National Technical Information Services. PB-88-2508.

<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. The test substance in this study was food grade geranyl acetate (CAS 105-87-3). Purity tests revealed the test substance consisted of 79% geranyl acetate and 29% citronellyl acetate. Remaining impurities accounted for less than 0.37%.
<b>Method/guideline</b>	National Toxicology Program Carcinogenesis study (NIH Publication No. 88-2508) or (NTP TR 252).

<b>GLP</b>	Yes
<b>Year</b>	1987
<b>Species/Strain</b>	Mouse/B6C3F1
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Gavage
<b>Doses/concentration levels</b>	500 or 1000 mg/kg bw/d
<b>Exposure period</b>	103 weeks
<b>Frequency of treatment</b>	Daily (5 days/week)
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	Not given
<b>Remarks for test conditions</b>	A carcinogenicity study was conducted in which groups of 50 B6C3F1 mice of each sex were administered 0, 500, or 1000 mg/kg bw of a mixture of geranyl acetate (79%) and citronellyl acetate (29%) in corn oil by gavage daily, 5 days/week for 103 weeks. Body weights were recorded weekly for the first 12 weeks and monthly thereafter. Necropsies were performed on all animals surviving until the end of the study and on all animals found dead during the study. Histopathological examination was conducted on the following: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, thymus, larynx, trachea, lungs, and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, pituitary, and spinal cord.
<b>NOAEL(NOEL)</b>	1000 mg/kg bw/d
<b>LOAEL(LOEL)</b>	>1000 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	Not applicable
<b>Toxic response/effects by dose level</b>	Mean body weights of high-dose male and female mice were lower than those of control groups after week 18 of the study. Survival of male mice in the high-dose group was significantly reduced (controls, 31/50; high dose, 0/50). Survival of the high- and low-dose groups of female mice was significantly less ( $p < 0.001$ ; low dose, 0.020) than that of the control group (controls, 28/50; low dose, 15/50; high dose, 0/50). Inflammation of the vagina, uterus, ovaries, or multiple organs occurred in 18 control, 14 low-dose, and 2 high-dose female mice. The incidence of malignant lymphoma in high-dose male mice was significantly less ( $p < 0.044$ ) than in the control group (controls, 7/50; high dose, 1/50). There was a significant ( $p = 0.030$ , Fisher) decrease in the incidence of thyroid follicular-

	cell adenoma in high dose female mice (controls, 7/50; high dose, 1/50). The incidence of non-neoplastic lesions was significantly increased in high-dose male and female mice only; an increased incidence of cytoplasmic vacuolization of the liver in male (control, 1/50; low dose, 7/50; high dose, 47/50) and female mice (control, 1/50; low dose, 27/50; high dose, 46/50) and the kidney or kidney tubule in male (control, 0/50; low dose, 0/50; high dose, 41/50) and female mice (control, 0/50; low dose, 24/49; high dose, 37/50).
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	The probable cause of death of many females was a genital tract infection. Inflammation of the vagina, uterus, ovaries, or multiple organs occurred in 18 control, 14 low-dose, and 2 high-dose female mice. Although the etiologic agent was not isolated, <i>Klebsiella pneumoniae</i> were isolated from similarly affected mice at this laboratory in subsequent chronic studies. Surviving male (36) and female (11) mice in the high-dose groups were killed in a moribund condition at week 91 after an inadvertent overdose of the test substance. Eleven other animals (3 control males, 3 low-dose males, 3 low-dose females and 2 high-dose females) were killed by gavage accidents during the course of the study. There was no increase in the incidence of neoplastic lesions associated with administration of the test substance. The incidence of non-neoplastic lesions was significantly increased in high-dose male and female mice only; an increased incidence of cytoplasmic vacuolization of the liver in male (control, 1/50; low dose, 7/50; high dose, 47/50) and female mice (control, 1/50; low dose, 27/50; high dose, 46/50) and the kidney or kidney tubule in male (control, 0/50; low dose, 0/50; high dose, 41/50) and female mice (control, 0/50; low dose, 24/49; high dose, 37/50).
<b>Conclusion remarks</b>	Under conditions of this study, the mixture of geranyl acetate and citronellyl acetate was not carcinogenic for either sex of B6C3F1 mice.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study. This study was performed by the NTP.
<b>References</b>	National Toxicology Program (NTP) (1987) Carcinogenesis studies of food grade geranyl acetate (71%) and citronellyl acetate (29%). NTP-TR-252. National Technical Information Services. PB-88-2508.

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<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. The test substance in this study was food grade geranyl acetate (CAS 105-87-3). Purity tests revealed the test substance consisted of 79% geranyl acetate and 29% citronellyl acetate. Remaining impurities accounted for less than 0.37%.

<b>Method/guideline</b>	National Toxicology Program Carcinogenesis study (NIH Publication No. 88-2508) or (NTP TR 252).
<b>GLP</b>	Yes
<b>Year</b>	1987
<b>Species/Strain</b>	B6C3F1 mice
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Gavage
<b>Doses/concentration levels</b>	125, 250, 500, 1000, or 2000 mg/kg bw/d
<b>Exposure period</b>	13 weeks
<b>Frequency of treatment</b>	Daily (5 days/week)
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	Not given
<b>Remarks for test conditions</b>	In a 13-week study, a mixture of geranyl acetate (71%) and citronellyl acetate (29%) was administered by gavage in corn oil to six groups of B6C3F1 mice (10/sex/group) at dose levels of 0, 125, 250, 500, 1000, or 2000 mg/kg bw daily 5 days/week. Animals were checked twice daily for mortality and signs of morbidity. Body weight data were collected weekly. Necropsies were performed on all animals surviving until the end of the study and on all animals found dead during the study. Histopathologic examination was conducted on the following organs for the 2000 mg/kg bw/d dose group and the control groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, thymus, larynx, trachea, lungs, and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, pituitary, and spinal cord.
<b>NOAEL(NOEL)</b>	1000 mg/kg bw/d
<b>LOAEL(LOEL)</b>	2000 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	NA
<b>Toxic response/effects by dose level</b>	Seven (7) of 10 males and 9/10 females receiving 2000 mg/kg bw/d died during the study. Male and female mice in the 2000 mg/kg bw/d dose groups exhibited cytoplasmic vacuolization of the liver, kidney and myocardium.
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	Gavage errors resulted in the death of three females at lower dose levels. Mean body weights were comparable for dosed

<b>Conclusion remarks</b>	and control animals. Male and female mice in the 2000 mg/kg bw/d dose groups exhibited cytoplasmic vacuolization of the liver, kidney and myocardium. Vacuolization was the result of lipid droplets that were present throughout the liver lobule, particularly in the periportal region. No treatment-related histopathological lesions or other effects were observed in the 1000 mg/kg bw/d group. This study demonstrates a NOAEL in mice of 1000 mg/kg bw/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study. This study was performed by the NTP.
<b>References</b>	National Toxicology Program (NTP) (1987) Carcinogenesis studies of food grade geranyl acetate (71%) and citronellyl acetate (29%). NTP-TR-252. National Technical Information Services. PB-88-2508.

<b>Substance Name</b>	Acetylated myrcene
<b>CAS</b>	68412-04-4
<b>Remarks for Substance</b>	Acetylated myrcene is a mixture that is primarily (62%) acetate esters of nerol and geraniol. The test substance in this study was food grade geranyl acetate (CAS 105-87-3). Purity tests revealed the test substance consisted of 79% geranyl acetate and 29% citronellyl acetate. Remaining impurities accounted for less than 0.37%.
<b>Method/guideline</b>	National Toxicology Program Carcinogenesis study (NIH Publication No. 88-2508) or (NTP TR 252).
<b>GLP</b>	Yes
<b>Year</b>	1987
<b>Species/Strain</b>	Rat/F344/N
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Gavage
<b>Doses/concentration levels</b>	250, 500, 1000, 2000 or 4000 mg/kg bw/d
<b>Exposure period</b>	13 weeks
<b>Frequency of treatment</b>	Daily (5 days/week)
<b>Control Group</b>	Yes
<b>Post exposure observation period</b>	NG
<b>Remarks for test conditions</b>	In a 13-week study, a mixture of geranyl acetate (71%) and citronellyl acetate (29%) was administered by gavage in corn oil to six groups of F344/N rats (10/sex/group) at dose levels of 0, 125, 250, 500, 1000, or 2000 mg/kg bw daily 5 days/week.

Animals were checked twice daily for mortality and signs of morbidity. Body weight data were collected weekly. Necropsies were performed on all animals surviving until the end of the study and on all animals found dead during the study. Histopathologic examination was conducted on the following organs for the 2000 mg/kg bw/d dose group and the control groups: gross lesions, tissue masses, abnormal lymph nodes, skin, mandibular lymph nodes, mammary gland, salivary gland, thigh muscle, sciatic nerve, bone marrow, thymus, larynx, trachea, lungs, and bronchi, heart, thyroid, parathyroid, esophagus, stomach, duodenum, jejunum, ileum, colon, mesenteric lymph nodes, liver, pancreas, spleen, kidneys, adrenals, urinary bladder, seminal vesicles/prostate/testes or ovaries/uterus, brain, pituitary, and spinal cord.

<b>NOAEL(NOEL)</b>	2000 mg/kg bw/d
<b>LOAEL(LOEL)</b>	4000 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	NA
<b>Toxic response/effects by dose level</b>	Two of ten males and 1/10 females receiving 4000 mg/kg bw/d died. A decrease in mean body weight gain in males and females (19 % and 8% relative to controls, respectively) was reported at the 4000 mg/kg bw/d dose level.
<b>Statistical evaluations</b>	Not given
<b>Remarks for results</b>	Mean body weights were comparable for dosed and control animals, except for a decrease in mean body weight gain in males and females (19 % and 8% relative to controls, respectively) at the 4000 mg/kg bw/d dose level. No treatment-related histopathologic effects were observed at necropsy.
<b>Conclusion remarks</b>	This demonstrates a NOAEL in rats of 2000 mg/kg bw/day.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Guideline study. This study was performed by the NTP.
<b>References</b>	National Toxicology Program (NTP) (1987) Carcinogenesis studies of food grade geranyl acetate (71%) and citronellyl acetate (29%). NTP-TR-252. National Technical Information Services. PB-88-2508.

#### 4.5 Reproductive Toxicity

<b>Substance Name</b>	Citral (Mixture of geranial and neral)
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Volunteered under SIDS program.
<b>Method/guideline</b>	Not given
<b>Test Type</b>	Two generation

<b>GLP</b>	Not given
<b>Year</b>	1989
<b>Species/Strain</b>	Rat/ CR Sprague Dawley
<b>Sex</b>	Female
<b>Route of administration</b>	Oral
<b>Duration of test</b>	14 days prior to cohabitation; days 0 through 25 of presumed gestation; days 1-21 of lactation
<b>Doses/concentration levels</b>	50, 160, 500 mg/kg bw/d
<b>Premating Exposure period for males</b>	Not available
<b>Premating Exposure period for females</b>	14 days
<b>Frequency of treatment</b>	Continuous
<b>Control Group and treatment</b>	Yes
<b>Remarks for test conditions</b>	Thirty Sprague/Dawley/Charles River females rats were administered citral at dose levels of 0, 50, 160, and 500 mg/kg bw/d for 14 days prior to cohabitation, days 0-25 of presumed gestation and days 1-21 of lactation. Per group, fifteen rats were assigned to caesarean sectioning while the other fifteen were assigned natural delivery. Parameters evaluated for the adult female rats included clinical observation, estrous cycle, body weight and body weight change, feed consumption, mating and fertility, duration of gestation, delivery and maternal behavior, reproductive indices, and gross necropsy. Fetuses were evaluated for fetal wastage, body weight, sex and gross external examination. Pups were evaluated for clinical observations, body weight and gross necropsy.
<b>NOAEL(NOEL)</b>	50 mg/kg bw/d
<b>LOAEL(LOEL)</b>	160 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	Not available
<b>Parental data and F1 as appropriate</b>	At the 160 and 500 mg/kg bw/d dose levels, increased mortality (1/30 and 7/30, respectively), clinical signs of toxicity, significant decreases in body weight gain during gestation, and significant increases in feed consumption during lactation. No adverse effects were reported on estrous cycling, mating, fertility, duration of gestation, numbers of corpora lutea, number of implantations, live litter sizes, resorption of male/female ratio at dosages as high as 500 mg/kg bw/d.
<b>Offspring toxicity F1 and F2</b>	Decreases in fetal body weight (not statistically significant) were reported for fetuses delivered by Caesarean delivery, and

significantly decreased pup body weight for delivered pups were reported at the 500 mg/kg bw/d level. No other effects were reported in the offspring.

<b>Statistical evaluations</b>	Yes, ANOVA F test
<b>Remarks for results</b>	The maternal NOAEL is 50 mg/kg bw/d and the fetal/pup NOAEL is 160 mg/kg bw/d.
<b>Conclusion remarks</b>	Citral did not affect the reproductive performance or the pre-weaning development of offspring in female Sprague/Dawley Charles River female rats.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study.
<b>References</b>	Hoberman, A.M., Christian, M.S., Bennett, M.B. and Vollmuth, T.A. (1989). Abstract. Oral general reproduction study of citral in female rats. The Toxicologist 9, 271.

#### 4.6 Developmental/Teratogenicity Toxicity

<b>Substance Name</b>	Geraniol
<b>CAS</b>	106-24-1
<b>Remarks for Substance</b>	The test substance was citral diethyl acetal, the diethyl acetal of geraniol.
<b>Method/guideline</b>	<i>In vivo</i> Reproductive and Developmental Tox. Screening Test
<b>Test Type</b>	<i>In vivo</i> mammalian test system
<b>GLP</b>	No
<b>Year</b>	1997
<b>Species/Strain</b>	Rat/Sprague Dawley
<b>Sex</b>	Female
<b>Route of administration</b>	Oral
<b>Duration of test</b>	39 days
<b>Doses/concentration levels</b>	0, 125, 250, 500 mg/kg bw/d
<b>Exposure period</b>	14 days
<b>Frequency of treatment</b>	Daily
<b>Control Group and treatment</b>	Vehicle alone
<b>Remarks for test conditions</b>	The test substance was administered orally by gavage at the dose levels specified or the vehicle alone for seven days prior to cohabitation and then through cohabitation, gestation, delivery and a 4-day lactation/postparturition period. The

vehicle was either corn oil or methylcellulose. Body weights, food consumption and clinical signs were recorded throughout the observation period. All dams were necropsied and examined for gross lesions on Day 25 of presumed gestation for rats not delivering a litter and four days postpartum for rats delivering a litter. Pups delivered were sacrificed on day 4 postpartum, any pups dying during the lactation period were necropsied.

<b>NOAEL(NOEL) maternal</b>	125 mg/kg bw/d
<b>LOAEL(LOEL) maternal</b>	250 mg/kg bw/d
<b>NOAEL (NOEL) developmental</b>	250 mg/kg bw/d
<b>LOAEL (LOEL) developmental</b>	500 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	Not given
<b>Maternal data with dose level</b>	125 mg/kg bw/d- no effects; 250 mg/kg bw/d-clinical observations, body weight decrease compared to control, reduced body weight gain compared to control; 500 mg/kg bw/d-clinical observations, body weight decrease compared to control, reduced body weight gain compared to control
<b>Fetal data with dose level</b>	125 mg/kg bw/d-no effects; 250 mg/kg bw/d-no effects; 500 mg/kg bw/d-body weight decrease compared to control
<b>Statistical evaluations</b>	Bartlett's test of homogeneity, ANOVA (F-test); alpha= 0.05
<b>Conclusion remarks</b>	The NOAEL for maternal toxicity was reported to be 125 mg/kg bw/d, and the NOAEL for offspring toxicity was 250 mg/kg bw/d.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Acceptable, well documented publication, which meets basic scientific principles. Study duration shorter than guideline studies and less animals used.
<b>References</b>	Vollmuth T.A., Bennett, M.B., Hoberman, A.M. and Christian, M.S. (1995) An Evaluation of Food Flavoring Ingredients Using an In Vivo Reproductive and Developmental Toxicity Screening Test. Teratology 41(5): 597.

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<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS. 95% pure
<b>Test Type</b>	Embryo-feto toxicity
<b>GLP</b>	NG
<b>Year</b>	1995

<b>Species/Strain</b>	Wistar rats
<b>Sex</b>	Male and Female
<b>Route of administration</b>	Oral
<b>Duration of test</b>	21 days
<b>Doses/concentration levels</b>	0, 60, 125, 250, 500, and 1000 mg/kg bw in corn oil
<b>Exposure period</b>	Once a day for days 6-15 of pregnancy
<b>Frequency of treatment</b>	Daily
<b>Control Group and treatment</b>	Yes, the control group received only corn oil.
<b>Remarks for test conditions</b>	Citral was administered orally at the dose levels specified to female Wistar rats on days 6-15 of pregnancy. Caesarean sections were performed on day 21. Numbers of resorption and implantation sites were recorded. Fetuses were weighed and examined for gross malformations, visceral and skeletal malformations. Exposure to citral was limited to the main period of organogenesis.
<b>NOAEL(NOEL) maternal</b>	<60 mg/kg bw/d
<b>LOAEL(LOEL) maternal</b>	60 mg/kg bw/d
<b>NOAEL (NOEL) developmental</b>	<60 mg/kg bw/d
<b>LOAEL (LOEL) developmental</b>	60 mg/kg bw/d
<b>Actual dose received by dose level and sex</b>	NG
<b>Maternal data with dose level</b>	Statistically significant reductions in pregnancy weight gain (minus uterus weight) were reported for the two highest dose levels (500 and 1000 mg/kg bw/d) administered.
<b>Fetal data with dose level</b>	Statistically significant reductions in fetal body weight were reported for dose levels at 125, 250, and 500 mg/kg bw/d. Increases in the frequency of delayed ossifications were reported for the 125 and 250 mg/kg bw/d and were statistically significant. The incidence of hematomas was significantly increased in animals receiving 250, 500 or 1000 mg/kg bw/d. The only fetal organ with treatment related reductions in weight were spleens at doses of 250 mg/kg bw/d or higher. Statistically significant increases in the number of fetuses showing skeletal abnormalities was reported for the 125, 250 and 1000 mg/kg bw/d dose levels. No treatment related effects were reported on the occurrence of gross structural abnormalities, or visceral malformations.
<b>Statistical evaluations</b>	One way ANOVA (F-test), or the Kruskal- Alpha value of 0.05.
<b>Remarks for results</b>	The authors hypothesized the later start day for treatment administration may have reduced in the induction of metabolic

enzymes responsible for detoxification of citral.

<b>Conclusion remarks</b>	The NOAEL for developmental toxicity for citral is reported to be less than 60 mg/kg bw/d.
<b>Data Qualities Reliabilities</b>	Reliability code 2. Reliable with restrictions.
<b>Remarks for Data Reliability</b>	Acceptable, well documented publication, which meets basic scientific principles. Exposure to test material limited to main period of organogenesis.
<b>References</b>	Cristina A., Nogueira A.M., Carvalho R., Souza A., Chahoud I., Paumgarten F. (1995) Study on the embryofeto-toxicity of citral in the rat. Toxicology, 96, 105-113.

<b>Substance Name</b>	Citral
<b>CAS</b>	5392-40-5
<b>Remarks for Substance</b>	Substance supported under SIDS. Commercially available citral. Purity > 90%. Isomeric distribution of approximately 35% neral and 55% geranial.
<b>Method/guideline</b>	Not given
<b>GLP</b>	No
<b>Year</b>	1989
<b>Species/Strain</b>	Rat/Sprague-Dawley
<b>Sex</b>	Female
<b>Route of administration</b>	Inhalation
<b>Duration of test</b>	20 days
<b>Doses/concentration levels</b>	0, 10, 35 ppm as vapor or 85 ppm as aerosol/vapor
<b>Exposure period</b>	6 hr/day on gestational days 6-15
<b>Frequency of treatment</b>	Daily
<b>Control Group and treatment</b>	Yes
<b>Remarks for test conditions</b>	Pregnant Sprague Dawley rats were exposed via inhalation to 0, 10, 35, or 85 ppm citral for six hours a day on gestational days 6-15. Dams were sacrificed on day 20. Fetuses were examined for gross, visceral and skeletal malformations.
<b>NOAEL(NOEL) maternal</b>	35 ppm
<b>LOAEL(LOEL) maternal</b>	85 ppm
<b>NOAEL (NOEL) developmental toxicity</b>	85 ppm

<b>LOAEL (LOEL) developmental toxicity</b>	None reported
<b>Actual dose received by dose level and sex</b>	10.2 +/- 0.9 ppm, 34.4 +/- 4.1 ppm, 68 ppm (30.7 +/-4.2 ppm citral aerosol and 37.0 +/-14.1 ppm citral vapor)
<b>Maternal data with dose level</b>	At the 85 ppm dose level, a statistically significant ( $p < 0.05$ ) difference in maternal weight gain for the dosed compared to the controls was reported. Additional signs of clinical toxicity were also reported. No toxicity was reported for the animals receiving 10 or 35 ppm citral.
<b>Fetal data with dose level</b>	No exposure related effects were reported on corpus lutea, implantations or resorptions, or for fetal viability, litter size, sex ratio and body weight. No exposure related malformations were reported. The incidence of hypoplastic bones (lumbar and pubis) was increased slightly compared to the controls at the highest maternal dose level.
<b>Statistical evaluations</b>	Yes, ANOVA (F-test) and Fischers exact
<b>Remarks for results</b>	Citral administered via inhalation produced no teratogenic effects in rats at the dose levels tested.
<b>Conclusion remarks</b>	Citral administered via inhalation produced no teratogenic effects in rats at the dose levels tested.
<b>Data Qualities Reliabilities</b>	Reliability code 1. Reliable without restrictions.
<b>Remarks for Data Reliability</b>	Comparable to guideline study.
<b>References</b>	Gaworski C.L., Vollmuth, T.A., York R.G., Heck J.D., Arany C. (1992) Developmental toxicity evaluation of inhaled citral in rats. Food Chemical Toxicology, 30 269-275.