# Bicyclo[4.1.0]hept-3-ene, 3,7,7-trimethyl-: Human health tier II assessment

**02 March 2018**

## CAS Number: 13466-78-9



## Preface

This assessment was carried out by staff of the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) using the Inventory Multi-tiered Assessment and Prioritisation (IMAP) framework.

The IMAP framework addresses the human health and environmental impacts of previously unassessed industrial chemicals listed on the Australian Inventory of Chemical Substances (the Inventory).

The framework was developed with significant input from stakeholders and provides a more rapid, flexible and transparent approach for the assessment of chemicals listed on the Inventory.

Stage One of the implementation of this framework, which lasted four years from 1 July 2012, examined 3000 chemicals meeting characteristics identified by stakeholders as needing priority assessment. This included chemicals for which NICNAS already held exposure information, chemicals identified as a concern or for which regulatory action had been taken overseas, and chemicals detected in international studies analysing chemicals present in babies' umbilical cord blood.

Stage Two of IMAP began in July 2016. We are continuing to assess chemicals on the Inventory, including chemicals identified as a concern for which action has been taken overseas and chemicals that can be rapidly identified and assessed by using Stage One information. We are also continuing to publish information for chemicals on the Inventory that pose a low risk to human health or the environment or both. This work provides efficiencies and enables us to identify higher risk chemicals requiring assessment.

The IMAP framework is a science and risk-based model designed to align the assessment effort with the human health and environmental impacts of chemicals. It has three tiers of assessment, with the assessment effort increasing with each tier. The Tier I assessment is a high throughput approach using tabulated electronic data. The Tier II assessment is an evaluation of risk on a substance-by-substance or chemical category-by-category basis. Tier III assessments are conducted to address specific concerns that could not be resolved during the Tier II assessment.

These assessments are carried out by staff employed by the Australian Government Department of Health and the Australian Government Department of the Environment and Energy. The human health and environment risk assessments are conducted

and published separately, using information available at the time, and may be undertaken at different tiers.

This chemical or group of chemicals are being assessed at Tier II because the Tier I assessment indicated that it needed further investigation.

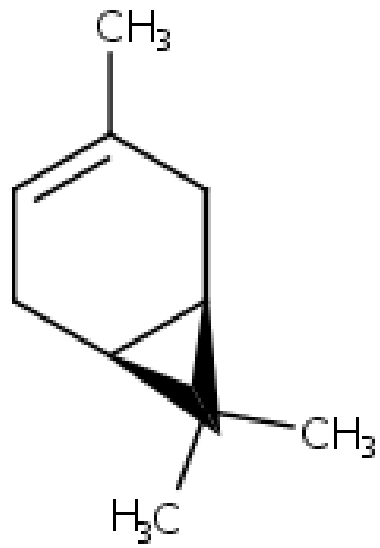
For more detail on this program please visit:www.nicnas.gov.au

**Disclaimer**



Acronyms & Abbreviations

# Chemical Identity

| | |
|---|---|
| Synonyms | 3-carene<br>(+-)-delta3-carene<br>(+-)-3-carene<br>3,7,7-trimethylbicyclo(4.1.0)hept-3-ene<br>delta-3-carene |
| Structural Formula |  |
| Molecular Formula | C10H16 |
| Molecular Weight (g/mol) | 136.2 |
| Appearance and Odour (where available) | Clear liquid with sweet citrus odour |
| SMILES | C1(C)(C)C2C1CC(C)=CC2 |

# Import, Manufacture and Use

## Australian

No specific Australian use, import, or manufacturing information has been identified.

## International

The following international uses were identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossier; Substances and Preparations in the Nordic countries (SPIN) database; United States Environmental Protection Agency (US EPA) Chemical and Product Categories (CPCat); and Cosmetic Ingredients and Substances (CosIng) database.

The chemical may have cosmetic use as a fragrance in perfumes and personal care products.

The chemical may have domestic uses in:

- car care products;
- cleaning and washing agents;
- hobby products for kids;
- laundry products;
- air fresheners; and
- polishing agents.

The chemical may have commercial uses in:

- solvents for paint, varnishes, and lacquers;
- toys;
- car care products; and
- adhesives and sealants.

The chemical may have site-limited use as a starting material for synthesis of fragrances.

The chemical may have non-industrial uses in pesticides, flavouring agents and pharmaceuticals.

# Restrictions

## Australian

No restrictions for industrial use have been identified for the chemicals in Australia.

The chemical delta-3-carene has restrictions for its non-industrial use as excipient in listed medicines (TGA, 2017) at certain concentrations depending on their use as a flavour or a fragrance:

Permitted for use only in combination with other permitted ingredients as a flavour or a fragrance.

- If used in a flavour, the total flavour concentration in a medicine must be no more than 5 %.
- If used in a fragrance, the total fragrance concentration in a medicine must be no more than 1 %.

### International

The chemical is subject to the EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. Annex III: List of Substances which cosmetic products must not contain except subject to the restrictions laid down. Peroxide levels must be less than 10 mmoles/L. This limit applies to the substance and not to the finished cosmetic product (CosIng).

*Pinacea* derivatives, including delta-3-carene, are included in the International Fragrance Association (IFRA) Standards: Essential oils and isolates derived from the *Pinacea* family, should only be used when the level of peroxides is kept to the lowest practicable level, for instance by adding antioxidants at the time of production. Such products should have a peroxide value of less than 10 mM peroxide per litre (IFRA, 2009).

## Existing Work Health and Safety Controls

### Hazard Classification

The chemical is not listed on the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

### Exposure Standards

#### Australian

No specific exposure standards are available.

#### International

The following exposure standards were identified (Galleria Chemica):

The chemical delta-3-carene is covered under exposure limits for monoterpenes which are between 112–150 mg/m$^3$ (20–25 ppm) time weighted average (TWA) in different countries such as Canada, Estonia and Spain and short-term exposure limit (STEL) of 167–300 mg/m$^3$ (30–50 ppm) in Canada and Estonia.

The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a threshold limit value (TLV) of 20 ppm (112 mg/m$^3$) TWA (ACGIH, 2011).

## Health Hazard Information

The chemical is a component of turpentine and contributes to the hazard profile of turpentine (NICNASa). The amount of delta-3-carene varies with the origin of the turpentine and in general the levels are low <5 %. However, it may be a major component in turpentine from India, Finland and Sweden (NTP, 2002; Kasanen et al., 1999). Where limited data are available for the chemical, hazard information for turpentine may be used to support the assessment conclusions.

The chemical is susceptible to auto-oxidation leading to formation of hydroperoxide species. These oxidised species are thought to be responsible for sensitisation reactions elicited by the chemical, acting as haptens.

## Toxicokinetics

In a metabolic study, 8 male volunteers were exposed to 450 mg/m$^3$ (75 ppm) delta-3-carene in an exposure chamber for 2 h during light physical exercise. Approximately 65 % of the inhaled delta-3-carene was absorbed and 5 % of the uptake was detected in the expired air. Blood levels peaked 2 h after administration and the chemical was rapidly eliminated (Filipsson et al., 1996).

In a metabolic study, male albino rabbits (6/group) received a single oral dose of 400 –700 mg/kg of delta-3-carene. Over 3 days, more than 80 % of the chemical was recovered in the urine as glucuronic acid conjugates of hydroxylated terpene hydrocarbons. The main metabolite detected was m-mentha-4,6-dien-8-ol (72 %) (MAK, 2002). Similar findings were reported in humans following oral exposure. The chemical was rapidly absorbed, distributed and metabolised (Schmidt et al., 2015).

## Acute Toxicity

### Oral

The chemical is expected to have low acute toxicity based on results from animal tests following oral exposure. Observed sublethal effects included lethargy, diarrhoea and urinary incontinence.

In a non-guideline oral acute toxicity study, male Wistar rats (10/dose) were orally treated (method not specified) with 3200, 4200, 5000, 6250 and 7800 mg/kg bw of the chemical. The animals were observed for mortality or clinical signs of toxicity at 1 and 6 h after dosing and daily for 14 days. Mortalities were observed after 6-24 h at all dose levels with an oral median lethal dose (LD50) of 4800 mg/kg bw (REACH).

The chemical or mixtures containing the chemical could have the potential to cause chemical pneumonitis if aspirated. This would be dependent on the viscosity of the chemical as introduced (NICNASa). The threshold viscosity value for classification as an aspiration hazard is 20.5 mm$^2$/s at 40 °C (Safe Work Australia).

### Dermal

The chemical is expected to have low acute dermal toxicity based on results from animal tests following dermal exposure.

In a non-guideline dermal acute toxicity study, 10 New Zealand White (NZW) rabbits (sex not reported) were treated with a single dermal application of 5000 mg/kg bw of the chemical for 24 h under occlusion. The animals were observed for mortality and clinical signs of toxicity for 7 days. No mortalities or clinical signs of toxicity were observed during the study. No signs of toxicity were seen at necropsy (REACH).

### Inhalation

No acute inhalation toxicity data are available for the chemical. However, turpentine (containing a mix of monoterpenes including the chemical) is known to be harmful via acute inhalation exposure with a median lethal concentration (LC50) of 13.7 mg/L (NICNASa). Therefore the chemical may have moderate acute inhalation toxicity.

## Corrosion / Irritation

### Respiratory Irritation

Studies in mice suggest that turpentine is a sensory irritant. Sensory irritation is the result of the chemical stimulating the trigeminal nerve endings in the cornea and nasal mucosa, which evokes a stinging or burning sensation in the eyes and upper respiratory tract (nose and throat). This is a receptor mediated mode of action and occurs at relatively low concentrations. Sensory irritation is different to eye and skin irritation used for hazard classification and also different from the irritation leading to cytotoxicity. This latter example is a result of physical damage to the cells, whereas sensory irritation is a nerve response (NICNASc). While there is clear evidence of irritation, sensory irritation is not considered to be specific target organ toxicity (STOT) under GHS.

The concentration that causes a 50 % respiratory rate decrease (RD50) was determined in a mouse bioassay measuring a decrease in breathing rate due to stimulation of the trigeminal nerve endings in the nasal mucosa. In the study, 56 Oncin France 1 (OF1) mice were exposed to delta-3-carene, in a glass tube attached to an exposure chamber (head only exposure). The concentration in the chamber was regulated by airflow and the actual concentration in the chamber was continuously monitored by infrared spectroscopy. Control mice (n=8) were exposed to room air only. The maximum response generally occurred after 30 min. At higher concentrations, body movements slowed down and at exposures above 1400 ppm (7.8 mg/L) slight sedation or drowsiness was observed. Recovery was rapid and no macroscopic effects were seen 1 h or 7 days after the end of the exposure. An RD50 of 1345 ppm (7.5 mg/L) was reported for the chemical (Kasanen et al., 1999). Similar effects were observed in OF1 mice exposed to turpentine containing 53 % of the chemical as well as beta-pinene (15 %), alpha-pinene (14 %) and limonene (2 %). The reported RD50 for turpentine was 1173 ppm (6.5 mg/L) (NICNASa).

### Skin Irritation

Based on the available data in vitro and in humans (refer to ***Observation in Humans*** section) the chemical is a potential skin irritant, warranting hazard classification (refer to ***Recommendation*** section).

In an in vitro study similar to the Economic Co-operation and Development (OECD Test Guideline (TG) 439, 10 µL of the chemical was applied to reconstructed human epidermis for 15 min. The mean tissue viability was 29.8 %. Substances that reduce viability to less than 50 % are classified as irritants. Therefore the chemical can be considered a skin irritant (REACH).

### Eye Irritation

The chemical is reported to be a slight eye irritant in animal studies. The effects are not sufficient to warrant a hazard classification.

In an OECD TG 405 eye irritation study, 0.1 mL of undiluted delta-3-carene was applied to one eye of 3 NZW rabbits while the other eye served as the control. The eyes were examined for irritation scores at 1 h and 1, 2, 3, 4, 7 and 8 days after application. Moderate redness of the conjunctivae was observed 1 h after the treatment. The average scores at 24, 48 and 72 h after exposure for the 3 rabbits were 0, 0, 0 for the cornea; 0, 0, 0 for the iris; 2, 1.33, 1.33 for the conjunctivae and 2, 1.33, 1 for chemosis. After 8 days the irritation had completely resolved (REACH).

### Observation in humans

In patch tests in 30 patients that were not allergic to turpentine, freshly distilled delta-3-carene (non-oxidised) was irritating to the skin at high concentrations (70–80 %) but not at lower concentrations (20–35 %). However, oxidised delta-3-carene (>2 % hydroperoxide) caused irritation in almost all patients (MAK, 2002).

In an inhalation study, 8 male volunteers reported an unpleasant feeling in the throat and airways after exposure to the chemical at 450 mg/m$^3$ for 2 h (Falk et al., 1991; MAK, 2002).

Eye, nose and throat irritation was also reported in human volunteers exposed to turpentine 75–81 ppm (NICNASa).

## Sensitisation

### Skin Sensitisation

Based on the weight of evidence from the available animal studies, in silico and human data (refer to ***Observation in humans*** section), the chemical is a potential skin sensitiser and warrants hazard classification (refer to ***Recommendation*** section). Hydroperoxide species originating from auto-oxidation are thought to be the major contributors.

In a cumulative contact enhancement test in female Dunkin Hartley guinea pigs (10–12/group), the chemical (50 % v/v) was applied to the scapular region for 24 h under occlusion. Four induction applications were made at the same site followed by a challenge dose at a different site at 10, 3, and 1 % (v/v) of the chemical. The experiment was performed twice; in the first 8/12 and in the second experiment 7/10 guinea pigs displayed erythema and were considered positive for sensitisation (REACH).

In a study in domestic pigs, repeated applications of the chemical containing approximately 5 % hydroperoxides for one week induced skin sensitisation. The contact allergy could be transferred passively to the healthy animals with spleen and thymus cells from the sensitised animals. No further data are available (MAK, 1996).

The profiling functionality of the OECD Quantitative Structure Activity Relationship (QSAR) Toolbox v3.4 was used to determine the presence of potential structural alerts for skin sensitisation. While the unmetabolised chemical did not display any mechanistic alerts for skin sensitisation, several auto-oxidation products displayed alerts for protein binding via nucleophilic additions and free radical formation.

The knowledge based expert system Deductive Estimation of Risk from Existing Knowledge (DEREK) Nexus version 6.0.0 was utilised to estimate the sensitisation potential of delta-3-carene. The chemical was predicted to be a moderate skin sensitiser with a predicted concentration of 9.7 % delta-3-carene producing a three-fold increase in lymphocyte proliferation (EC3) in local lymph node assay (LLNA). The confidence level of the prediction was equivocal. The prediction was supported by the mechanistic alert '712 terpenoid'.

Skin sensitisation was predicted using Laboratory of Mathematical Chemistry OASIS–TIMES (tissue metabolism simulator) software (version 2.27.19). The chemical was predicted to be a non-sensitiser (90 % in domain). Several auto-oxidised metabolites of the chemical were predicted to be weak sensitisers which were supported by mechanistic alerts for hydroperoxide free radical decomposition and nucleophilic addition to ketones.

### Observation in humans

In a maximisation test in 25 volunteers, a 10 % concentration of the chemical did not produce skin reactions (Opdyke, 1973). No further data are available.

Turpentines containing high levels of delta-3-carene were more potent sensitisers than turpentines with low delta-3-carene levels (MAK, 1996). No further data are available.

Oxidised delta-3-carene is considered a contributor of the sensitising properties of turpentine. As little as 20 µg of the oxidised delta-3-carene was sufficient to elicit positive results in epicutaneous tests (species unknown but most likely human) and physicochemical studies have demonstrated that delta-3-carene is oxidised more rapidly than other turpentine components (MAK, 1996).

## Repeated Dose Toxicity

### Oral

No data are available.

### Dermal

No data are available.

### Inhalation

No repeated dose toxicity data are available for the chemical or for turpentine.

In general, terpenes can cause adverse health effects following repeated inhalation exposure (refer to ***Observation in humans*** section). This is supported by toxicity following prolonged inhalation exposure to other terpenes in experimental animals and in humans (NICNASa; NICNASb).

### Observation in humans

Fumes in sawmills contain a mix of volatile terpenes including beta-pinene, alpha-pinene and delta-3-carene. Respiratory symptoms have been reported in 48 sawmill workers exposed to 100–550 mg/m$^3$ of a-pinene and delta-3-carene in a ratio of 3:1 or 2:1 (MAK, 2002).

In another study, 24 non-smoking sawmill workers reported symptoms in the mouth and throat, constriction in the chest and coughing more often than 30 non-exposed workers. Sawmill employees that had been exposed to terpenes for up to 37 years (average 7.6 years) had reduced lung function. Employees exposed to high concentrations reported coughing or chronic bronchitis and irritation in the throat more often than persons exposed to concentrations below 25 mg/m$^3$ (MAK, 2002). Information on confounding factors such as wood dust exposure is not available for the study.

## Genotoxicity

Based on the available in vitro data, the chemical is not considered to be genotoxic.

The chemical was negative in several in vitro assays (REACH):

- in vitro point mutation studies in *Salmonella typhimurium* strains TA1535, TA1537, TA98, TA100 and *E. coli* WP2 at concentrations up to 500 µg/plate, with or without metabolic activation.
- in vitro point mutation studies in *S. typhimurium* strains A1535, TA1537, TA98, TA100 and TA102 at concentrations up to 5000 µg/plate, with or without metabolic activation.
- gene mutation in Chinese hamster ovary cells exposed to 21 to 130 µg/mL of the chemical and with metabolic activation and 6.5 to 40 µg/mL without metabolic activation.
- micronucleus test in human lymphocytes exposed to up to 680 µg/mL of the chemical.

## Carcinogenicity

Data from long-term animal carcinogenicity studies are not available.

One epidemiological study in Finnish woodworkers found a weak association between exposure to terpenes (primarily alpha-pinene and delta-3-carene) lasting longer than 1 month, and the incidence of respiratory cancers (NTP, 2016).

## Reproductive and Developmental Toxicity

No data are available.

# Risk Characterisation

### Critical Health Effects

The critical health effects for risk characterisation are local effects including sensory irritation, skin irritation and skin sensitisation. The local effects are expected to be mainly caused by the oxidised chemical. The chemical or mixtures containing the chemical could have the potential to cause chemical pneumonitis if aspirated depending on the viscosity as introduced.

### Public Risk Characterisation

Based on international uses identified, the chemical may be used in cosmetic and domestic products in Australia. The general public could be exposed to the chemical when using cosmetics or domestic products containing the chemical.

In Europe, the chemical is restricted in cosmetics and can only be used if the peroxide levels are below 10mM (CosIng). The distribution of the chemical for fragrance purposes is expected to be controlled by members of IFRA. The restriction of the chemical under the IFRA Standard is expected to sufficiently address the public risks associated with chemical exposure through fragrances (e.g. concentration limits of peroxide levels in the product of 10mM) (IFRA, 2009).

Consumer products containing the chemical could oxidise over time; however, the concentration of the chemical in domestic and cosmetic products is expected to be low, hence peroxide levels are expected to very low. The risk to public health is not considered to be unreasonable and further risk management is not considered necessary for public safety.

### Occupational Risk Characterisation

The main occupational exposure to delta-3-carene is expected to occur during wood processing activities. Exposure may also occur during product formulation, dermal and inhalation exposure might occur, particularly where manual or open processes are used. These could include transfer and blending activities, quality control analysis, and cleaning and maintaining equipment. Worker exposure to the chemical at lower concentrations could also occur while using formulated products containing these chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical local health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to dermal exposure is implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking at a workplace (such as an employer) has adequate information to determine the appropriate controls.

The data available support an amendment to the hazard classification in the HCIS (Safe Work Australia) (refer to ***Recommendation*** section).

Sensory irritation and respiratory symptoms are reported in humans following exposure to mixed monoterpenes. Exposure standards to minimise the potential for these effects have been established overseas. An exposure standard encompassing the total level of monoterpenes may be beneficial to mitigate the risk of adverse effects.

## NICNAS Recommendation

Assessment of the chemical is considered to be sufficient, provided that the recommended classification is adopted, and labelling and all other requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

It is recommended that Safe Work Australia consider whether introduction of controls are required to adequately minimise the risk to workers. A Tier III assessment may be necessary to provide further information about whether exposure controls are needed to offer adequate protection to workers.

### Regulatory Control

### Public Health

Products containing the chemical should be labelled in accordance with state and territory legislation (SUSMP, 2018).

### Work Health and Safety

The chemical is recommended for classification and labelling aligned with the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as below. This does not consider classification of physical hazards and environmental hazards.

For mixtures containing the chemical the aspiration hazard classification should only be applied if the kinematic viscosity criteria for aspiration classification in the GHS is met.

From 1 January 2017, under the model Work Health and Safety Regulations, chemicals are no longer to be classified under the Approved Criteria for Classifying Hazardous Substances system.

| Hazard | Approved Criteria (HSIS)[a] | GHS Classification (HCIS)[b] |
|---|---|---|
| Acute Toxicity | Not Applicable | May be fatal if swallowed and enters airways - Aspi. Cat. 1 (H304) |
| Irritation / Corrosivity | Not Applicable | Causes skin irritation - Cat. 2 (H315) |
| Sensitisation | Not Applicable | May cause an allergic skin reaction - Cat. 1 (H317) |

[a] Approved Criteria for Classifying Hazardous Substances [NOHSC:1008(2004)].

[b] Globally Harmonized System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third Edition.

[*] Existing Hazard Classification. No change recommended to this classification

## Advice for consumers

Products containing the chemical should be used according to the instructions on the label.

## Advice for industry

***Control measures***

Control measures to minimise the risk from dermal and inhalation exposure to the chemical should be implemented in accordance with the hierarchy of controls. Approaches to minimise risk include substitution, isolation and engineering controls. Measures required to eliminate, or minimise risk arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used. Examples of control measures that could minimise the risk include, but are not limited to:

- using local exhaust ventilation to prevent the chemical from entering the breathing zone of any worker;
- health monitoring for any worker who is at risk of exposure to the chemical, if valid techniques are available to monitor the effect on the worker’s health;

- air monitoring to ensure control measures in place are working effectively and continue to do so;
- minimising manual processes and work tasks through automating processes;
- work procedures that minimise splashes and spills;
- regularly cleaning equipment and work areas; and
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Guidance on managing risks from hazardous chemicals are provided in the Managing risks of hazardous chemicals in the workplace—Code of practice available on the Safe Work Australia website.

Personal protective equipment should not solely be relied upon to control risk and should only be used when all other reasonably practicable control measures do not eliminate or sufficiently minimise risk. Guidance in selecting personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

## References

American Conference of Governmental Industrial Hygienists (ACGIH). Turpentine and selected monterpenes. Documentation of the Threshold Limit Values for Chemical Substances. ACGIH Signature Publications, 7th Edition, 2011.

Cosmetic Ingredients& Substances (CosIng) Database. European Commission. Accessed December 2017 at http://ec.europa.eu/consumers/cosmetics/cosing/

DEREK Nexus: 5.0.1 Lhasa Limited (2017) [Computer software]. Accessed May 2017 https://www.lhasalimited.org/

Falk A, Löf, A., Hagberg, M, Hjelm EW& Wang Z 1991. Human exposure to 3-carene by inhalation: toxicokinetics, effects on pulmonary function and occurrence of irritative and CNS symptoms. Toxicology and applied pharmacology, 110(2) pp. 198-205.

Filipsson AF 1996. Short term inhalation exposure to turpentine: toxicokinetics and acute effects in men. Occupational and environmental medicine 53(2) pp.100-105.

Galleria Chemica. Accessed January 2018 at https://jr.chemwatch.net/galleria/

Globally Harmonised System of Classification and Labelling of Chemicals (GHS) United Nations, 2009. Third edition. Accessed January 2018 at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

International Fragrance Association (IFRA) Standards 2009: (Pinacea derivatives). Accessed January 2018 at http://www.ifraorg.org/

Kasanen KP, Pasanen AL, Pasanen P, Liesivuori J, Kosma VM & Alarie Y 1999. Evaluation of sensory irritation of 3-carene and turpentine, and acceptable levels of monoterpenes in occupational and indoor environment. Journal of Toxicology and Environmental Health Part A 57(2) pp 89-114.

National Industrial Chemicals Notification and Assessment Scheme (NICNASa). Human health Tier II assessment for turpentine (CAS Nos 8006-64-2, 9005-90-7, 8052-14-0) Australian Government Department of Health. Accessed December 2017 at https://www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNASb). Human health Tier II assessment for alpha-pinene (CAS No 80-56-8) Australian Government Department of Health. Accessed December 2017 at https://www.nicnas.gov.au

National Industrial Chemicals Notification and Assessment Scheme (NICNASc) 2006. Formaldehyde (CAS No. 50-00-0). Priority Existing Chemical Secondary Notification Assessment Report No. 28. Accessed January 2018 at http://www.nicnas.gov.au/__data/assets/pdf_file/0006/4389/PEC_28_Formaldehyde_Full_Report_PDF.pdf

National Toxicology Program (NTP) Review of Toxicological Literature Turpentine (Turpentine Oil, Wood Turpentine, Sulfate Turpentine, Sulfite Turpentine) 2002. Accessed December 2017 at

https://ntp.niehs.nih.gov/ntp/htdocs/chem_background/exsumpdf/turpentine_508.pdf

Opdyke DL. Monographs on fragrance raw materials. Food Cosmet Toxicol. 1973 pp. 1053-1054

Optimised Approach based on Structural Indices Set–TIssue MEtabolism Simulator (OASIS–TIMES) Version 2.27.19. Accessed December 2017 at http://superhosting.oasis-lmc.org/downloads.aspx

Organisation for Economic Co-operation and Development (OECD) Quantitative Structure-Activity Relationship (QSAR) Toolbox Version 3.4. Accessed December 2017

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Dossier. delta-3-carene (CAS No 13466-78-9 ). Accessed December 2017 at https://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

Safe Work Australia. Hazardous Chemicals Information System (HCIS). Accessed January 2018 at http://hcis.safeworkaustralia.gov.au/HazardousChemical

Schmidt L, Belov VN,& Göen T 2015. Human metabolism of ?3-carene and renal elimination of ?3-caren-10-carboxylic acid (chaminic acid) after oral administration. Archives of toxicology, 89(3) pp. 381-392.

Substances in Preparations in Nordic Countries (SPIN) Database. Accessed December 2017 at http://www.spin2000.net/spinmyphp/

The Poisons Standard, February 2018. The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No. 19. Accessed at https://www.legislation.gov.au/Details/F2017L01285

Therapeutic Goods (Permissible Ingredients) Determination No. 3 of 2017. Australian Government Department of Health. Accessed January 2018 at https://www.legislation.gov.au/Details/F2017L00926

Turpentine [MAK Value Documentation, 1996]. 2012 The MAK Collection for Occupational Health and Safety: Wiley-VCH Verlag GmbH& Co. KGaA. Accessed December 2017 at http://onlinelibrary.wiley.com/doi/10.1002/3527600418.mb800664e0017/abstract

Turpentine [MAK Value Documentation, 2000]. 2012 The MAK Collection for Occupational Health and Safety: Wiley-VCH Verlag GmbH& Co. KGaA. Accessed December 2017 at http://onlinelibrary.wiley.com/doi/10.1002/3527600418.mb800664e0017/abstract

United States Environmental Protection Agency (US EPA) Chemical and Product Categories (CPCat) database. Accessed December 2017 at https://www.epa.gov/chemical-research/chemical-and-product-categories-cpcat

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