# Ethanone, 1-(3-ethyl-5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)-: Human health tier II assessment

**08 March 2019**

## CAS Number: 88-29-9



## 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.

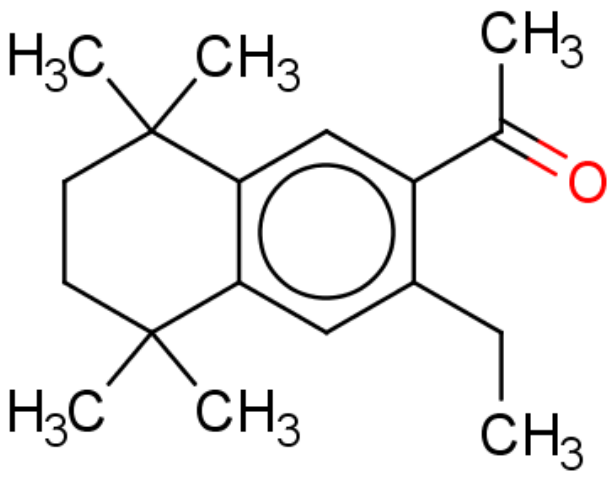
For more detail on this program please visit:www.nicnas.gov.au

**Disclaimer**



Acronyms & Abbreviations

## Chemical Identity

| | |
|---|---|
| Synonyms | 1,1,4,4-etramethyl-6-ethyl-7-acetyl-1,2,3,4-tetrahydronaphthalene<br>versalide<br>acetylethyltetramethyltetralin<br>AETT<br>Musk 36A |
| Structural Formula |  |
| Molecular Formula | C18H26O |
| Molecular Weight (g/mol) | 258.40 |
| Appearance and Odour (where available) | white powder with sweet intense musk odour |
| SMILES | C1(C)(C)c2c(C(C)(C)CC1)cc(C(C)=O)c(CC)c2 |

# Import, Manufacture and Use

## Australian

The chemical has been identified as an ingredient in three fragrance oil products sold online from an Australian website.

## International

No international uses were identified through the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers; Substances and Preparations in the Nordic countries (SPIN) database; United States (US) Environmental Protection Agency (EPA) Chemical and Product Categories (CPCat); the US Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary, the US household product data base (HPD) and Cosmetic Ingredients; Government of Canada; and Cosmetic Ingredients and Substances (CosIng) database.

The chemical is not listed on the International Fragrance Association (IFRA) transparency list (IFRA, 2017). The IFRA Transparency List is an ordered register of all fragrance ingredients used in consumer goods by the fragrance industry's customers worldwide. It represents a snapshot of all the ingredients used in active formulas at the time of publication.

The chemical is not listed as active in the US EPA non-confidential Toxic Substances Control Act (TSCA) Inventory as at April 2018 (US EPA, 2018).

# Restrictions

## Australian

No known restrictions have been identified.

## International

The chemical (CAS No. 88-29-9) is listed on the following (Galleria Chemica):

- EU Cosmetics Regulation 1223/2009 Annex II—List of substances prohibited in cosmetic products;
- New Zealand Cosmetic Products Group Standard—Schedule 4: Components cosmetic products must not contain;
- Canada Cosmetic Ingredient Hotlist — List of Ingredients that are Prohibited for Use in Cosmetic Products;
- Chile List of substances which must not form part of the composition of cosmetic products;
- China List of Banned substances for use in Cosmetics (Chinese); and
- Philippines Restricted Ingredients For Use In Cosmetics — List of Substances which must not form part of the Composition of Cosmetic Products

The chemical is listed as prohibited in the International Fragrance Association (IFRA) Standards (40th amendment) (IFRA, 2002).

# 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

No specific exposure standards are available.

## Health Hazard Information

The critical human health concern for the chemical versalide (CAS No. 88-29-9) (hereafter referred to as the chemical) and focus of this assessment relates to the potential neurotoxicity of the chemical. Limited data exists for other hazard endpoints. Available information is summarised below.

***Summary of hazard information (other than neurotoxicity)***

The chemical is rapidly distributed through tissues including the central nervous system (CNS) after intravenous (iv) or intraperitoneal (ip) administration. Excretion of the chemical is slow and mainly via faeces.

The chemical is acutely toxic by oral and dermal route with median lethal doses (LD50) of 260–316 mg/kg and 584 mg/kg, respectively and warrant hazard classification.

At low doses (below 4 %) the chemical is unlikely to cause severe skin irritation based on tests in rabbits and humans. No sensitisation reactions occurred in a maximisation test in human volunteers exposed to a solution containing 4 % of versalide.

The chemical is expected to be non-genotoxic as an Ames test was negative in 5 different bacterial strains.

The chemical is not expected to cause developmental toxicity as no developmental effects were seen in offspring from pregnant rats exposed to 5 or 30 mg/kg bw/day of the chemical once daily on days 6-16 of gestation (Butterworth, 1981; Opdyke, 1978).

### Other Health Effects

#### Neurotoxicity

Based on the available animal studies, the chemical is considered to cause serious damage to the CNS from repeated oral or dermal exposures, warranting hazard classification (see ***Recommendation*** section).

In a 14-week dermal toxicity study, female rats (20/dose; strain not specified) received topical applications of the chemical at 50, 100, 200 or 400 mg/kg bw/day [10 % (w/v) in ethanol] once daily seven days per week for up to 14 weeks followed by a recovery phase of approximately 20 weeks. Autopsy was performed on animals at weeks 2, 4, 6, 9, 11, 14 of the study or 20 weeks after the end of the treatment. Clinical signs of toxicity included hyperexcitability, motor incoordination, blue skin, hunched back, weight loss, tremors and wobbly gait. All animals of the two highest dose groups (200 or 400 mg/kg bw/day) were euthanised in a moribund state within 14 and 3 days, respectively. Most animals receiving 50 or 100 mg/kg bw/day survived to end of the study but showed serious impairment of motor function. All treated animals had blue coloured internal organs. The treated animals showed time and dose-dependent vacuolisation and focal swelling of the brain, demyelinisation of nerve tracts

and spongy degeneration of white matter. Animals in the 20-week recovery group displayed similar neuropathological changes, although with some degree of reversibility (Opdyke, 1978).

In a 26-week dermal toxicity study, male and female rats (strain not specified) received topical applications of the chemical at 0.6, 3 or 18 mg/kg bw/day in ethanol (males and females), 1.8 or 17.1 mg/kg bw/day in a wax-based vehicle (females), 0.9 or 9.1 mg/kg bw/day in a creamy vehicle (females) or 0.2 or 2.2 mg/kg bw/day in a liquid cream vehicle (females) once daily 5 days a week for up to 26 weeks. A group of animals were kept without treatment up to 12 weeks after the end of the treatment. All animals survived the study. Hyperexcitability and blue-coloured skin were observed at all doses but more pronounced at the higher doses (9.1, 17.1 and 19 mg/kg bw/day). After 26 weeks of treatment, autopsy revealed focal vacuolisation of the brain and spinal cord in rats receiving 17.1 or 18 mg/kg bw/day. These effects were still apparent 4 and 12 weeks after the end of the treatment (Opdyke, 1978).

Clear signs of neurotoxicity and neuropathological changes were seen in another dermal study at 13 and 26 weeks in female Sprague Dawley (SD) rats after topical applications of the chemical at doses ≥9 mg/kg bw/day in ethanol. A no observed adverse effect level (NOAEL) of 3 mg/kg bw/day was reported. Limited details are available for this study (Opdyke, 1978).

In an oral study, male SD rats (4/dose) received 25 or 50 mg/kg bw/day via the diet for 20 weeks. One animal from each dose group was allowed to recover for 7 weeks after the end of the treatment. Behavioural changes such as aggressiveness were noted during the first 2–3 weeks of treatment. All rats receiving the high dose developed abnormal arching of the back, gait difficulties and limb weakness. The neurological symptoms became less severe during the treatment free recovery period after the end of the treatment. The treated animals showed darkening of the eyes, ears and feet. Structural damage (de-myelination) involving grey and white matter in the brain and the peripheral nervous system was apparent upon necropsy. Structures similar to those observed in human motor neuron disease were observed in the neurons of treated animals (Spencer, 1979).

In three separate 13-week oral studies, rats (further details not available) were fed up to 1.04 ppm (~0.104 mg/kg bw day) of the chemical in diet for 13 weeks. The chemical was introduced into the diet through detergent containing a small amount of the chemical. No treatment related effects were noted in these studies (Opdyke, 1978).

Signs of neurotoxicity including hyperactivity followed by depression and tremors were also observed in oral and dermal acute toxicity studies (Opdyke, 1978).

# Risk Characterisation

## Critical Health Effects

The critical health effect for risk characterisation is the systemic long-term effect of neurotoxicity.

## Public Risk Characterisation

The public could be exposed to the chemical if it is used in cosmetic and/or domestic products in Australia.

While the extent of current use of the chemical in cosmetic or domestic products in Australia is unknown, the chemical is listed as an ingredient in fragrance oil sold in Australia. Therefore, the public may be exposed to the chemical (see ***Use*** section).

Widespread use of the chemical is unlikely due to international prohibitions (see ***Restrictions*** section). However, any public exposure to this chemical would be considered to give rise to unreasonable risk due to its high level of neurotoxicity. The Scientific Committee on Cosmetic and non-food products intended for Consumers (SCCNFP) concluded that the chemical constitutes a hazard for the CNS after dermal exposure and is of the opinion that the chemical must not be used in cosmetic products (SCCNFP, 1998).

Currently, there are no restrictions in Australia on using this chemical in cosmetics or domestic products.

## Occupational Risk Characterisation

During product formulation, dermal 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 the chemical. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic long-term health effects, the chemical could pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure are implemented. The chemical should be appropriately classified and labelled to ensure that a person conducting a business or undertaking (PCBU) 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 Hazardous Chemical Information System (HCIS) (Safe Work Australia) (see ***Recommendation*** section).

# NICNAS Recommendation

Further risk management is required. Sufficient information is available to recommend that risks to public health and safety from the potential use of the chemical in cosmetic and domestic products be managed through changes to the Poisons Standard, and risks for workplace health and safety be managed through changes to classification and labelling.

Assessment of the chemical is considered to be sufficient provided that risk management recommendations are implemented and all requirements are met under workplace health and safety and poisons legislation as adopted by the relevant state or territory.

## Regulatory Control

### Public Health

Due to the toxicity profile at low concentrations that could potentially be used in cosmetic products, the chemical is recommended for scheduling in schedule 10 of the Poisons Standard, the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) to prohibit the sale, supply and use in cosmetic products. Matters to be taken into consideration include:

- the known uses of the chemical, with indication that the chemical may be currently used in cosmetic products in Australia;
- the chemical is neurotoxic following dermal exposure at low doses; and
- the chemical is prohibited for domestic/cosmetic use overseas (see ***Restrictions*** section).

### 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.

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 | Toxic if swallowed - Cat. 3 (H301) Toxic in contact with skin - Cat. 3 (H311) |

| Hazard | Approved Criteria (HSIS)[a] | GHS Classification (HCIS)[b] |
|---|---|---|
| Repeat Dose Toxicity | Not Applicable | Causes damage to nervous system through prolonged or repeated exposure - Cat. 1 (H372) |

[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 oral/dermal/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 closed systems or isolating operations;
- 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[s], if valid techniques are available to monitor the effect on the worker's health;
- 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.

***Obligations under workplace health and safety legislation***

Information in this report should be taken into account to help meet obligations under workplace health and safety legislation as adopted by the relevant state or territory. This includes, but is not limited to:

- ensuring that hazardous chemicals are correctly classified and labelled;

- ensuring that (material) safety data sheets ((M)SDS) containing accurate information about the hazards (relating to both health hazards and physicochemical (physical) hazards) of the chemical are prepared; and
- managing risks arising from storing, handling and using a hazardous chemical.

Your work health and safety regulator should be contacted for information on the work health and safety laws in your jurisdiction.

Information on how to prepare an (M)SDS and how to label containers of hazardous chemicals are provided in relevant codes of practice such as the *Preparation of safety data sheets for hazardous chemicals—Code of practice* and *Labelling of workplace hazardous chemicals—Code of practice*, respectively. These codes of practice are available from the Safe Work Australia website.

A review of the physical hazards of the chemical has not been undertaken as part of this assessment.

## References

Butterworth KR & Mason PL 1981. Acute toxicity of thioguaiacol and of versalide in rodents. Food and cosmetics toxicology 19 pp. 753-755.

CosIng. Cosmetic Ingredients and Substances. Accessed October 2018 at http://ec.europa.eu/growth/tools-databases/cosing/

Galleria Chemica. Accessed November 2018 at http://jr.chemwatch.net/galleria/

Globally Harmonized System of Classification and Labelling of Chemicals (GHS) 2009. United Nations. 3rd edition. Accessed October 2018 at http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html

International Fragrance Association (IFRA) 2002. The 40th Amendment of the IFRA Standard – Acetyl ethyl tetramethyl tetralin Accessed December 2018 at http://www.ifraorg.org/en-us/standards

International Fragrance Association (IFRA) 2017 Transparency List. Accessed November 2018 at http://www.ifraorg.org/en/ingredients

Opdyke DLJ 1979. Monographs on fragrance raw materials AETT. Food and cosmetics toxicology 17(5) pp. 357-390.

Personal Care Product Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary. Accessed November 2018 at http://www.ctfa-gov.org/jsp/gov/GovHomePage.jsp

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH). Accessed November 2018 at https://echa.europa.eu/search-for-chemicals

Rietschel L and Fowler F 2008. Fisher's Contact Dermatitis. BC Decker, Ontario, Canada.

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

Scientific Committee on Cosmetic Products and Non-Food Products (SCCNPF) 1998. Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers Concerning 7-Acetyl-6-Ethyl-1,1,4,4-Tetramethyl-1,2,3,4-Tetrahydronaphtalen (AETT). Accessed Febryary 2018 at http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions

Spencer, P.S., Sterman, A.B., Horoupian, D.S. and Foulds, M.M., 1979. Neurotoxic fragrance produces ceroid and myelin disease. Science, 204(4393), pp.633-635.

Substances in Preparations in Nordic countries (SPIN) database. Accessed November 2018 at http://www.spin2000.net/spinmyphp/

The Poisons Standard October 2018. The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No. 22. Accessed November 2018 at https://www.tga.gov.au/publication/poisons-standard-susmp

United States Environmental Protection Agency (US EPA) Chemical and Product Categories database (CPCat). Accessed November 2018 at https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat

United States Environmental Protection Agency (US EPA) TSCA Chemical Substance Inventory Interim List of Active Substances. Accessed December 2018 at www.epa.gov.

US Department of Health and Human Services, Household Products Database (HPD). Accessed December 2018 at https://hpd.nlm.nih.gov/advancedsearch.htm

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