

Hexanoic acid, 2-ethyl-, 2-ethylhexyl ester: Human health tier II assessment

12 September 2013

CAS Number: 7425-14-1



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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.

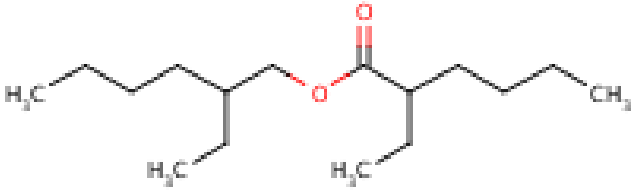
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Acronyms & Abbreviations

Chemical Identity

Synonyms	2-Ethylhexyl 2-ethylhexanoate Ethylhexyl ethylhexanoate Octyl octanoate 2-Ethylhexanoic acid, 2-ethylhexyl ester
Structural Formula	
Molecular Formula	C ₁₆ H ₃₂ O ₂
Molecular Weight (g/mol)	256.42
SMILES	<chem>C(=O)(C(CCCC)CC)OCC(CCCC)CC</chem>

Import, Manufacture and Use

Australian

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

International

The following international uses have been identified through the Substances and Preparations in the Nordic countries (SPIN) database, the European Commission Cosmetic Ingredients and Substances (CosIng) database, and through eChemPortal sources including the US National Library of Medicine's Hazardous Substances Data Bank (HSDB).

Reported cosmetic use:

- as an emollient.

Reported domestic use including:

- in cleaning/washing agents.

Reported commercial use including:

- in lubricants and additives;
- in reprographic agents; and
- as a solvent.

Restrictions

Australian

No known restrictions have been identified.

International

No known restrictions have been identified.

Existing Work Health and Safety Controls

Hazard Classification

The chemical is classified as hazardous, with the following risk phrases for human health in the Hazardous Substances Information System (HSIS) (Safe Work Australia):

Repr. Cat 3; R63 (Reproductive toxicity)

Exposure Standards

Australian

No specific exposure standards are available.

International

No specific exposure standards are available.

Health Hazard Information

Toxicokinetics

The chemical is an alkyl ethylhexanoate produced through the esterification of 2-ethylhexanoic acid (CAS No. 149-57-5) and 2-ethylhexanol (CAS No. 104-76-7). It is expected to hydrolyse to these compounds via chemical or enzymatic processes (CIR, 2013). 2-Ethylhexanoic acid is also the major metabolite of 2-ethylhexanol (NICNAS a).

Acute Toxicity

Oral

The chemical is of low acute toxicity in rats following oral exposure. The median lethal dose (LD50) was reported to be >2000 mg/kg bw. No documented signs of toxicity are available.

Dermal

The chemical is of low dermal toxicity in rabbits. The LD50 was reported to be >2000 mg/kg bw. No documented signs of toxicity are available.

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

While no specific data are available for this chemical, a Cosmetic Ingredient Review (CIR) of 16 alkyl ethylhexanoates, including this chemical, concluded that there is concern regarding potential irritancy of these chemicals (CIR, 2013). This conclusion was based on a number of experimental studies and observations in humans demonstrating that cetyl ethylhexanoate is irritating to the skin.

Eye Irritation

No data are available.

Sensitisation

Skin Sensitisation

No specific data are available for this chemical. The CIR assessment of alkyl ethylhexanoates did not come to a conclusion regarding potential skin sensitisation, although it was noted that cetearyl ethylhexanoate was reported to not cause skin sensitisation in humans based on a patch test study using 103 volunteers (CIR, 2013).

The chemical does not contain any functional groups associated with skin sensitisation, which is consistent with the observation that the two hydrolysis products of the chemical are non-sensitising (NICNAS a; NICNAS b).

Repeated Dose Toxicity

Oral

No specific data are available for this chemical.

While there are experimental data available for two hydrolysis products of the chemical, 2-ethylhexanoate (NICNAS a) and 2-ethylhexanoic acid (NICNAS b), the data are limited and insufficient to extrapolate the conclusions to this chemical.

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

While no specific data are available for this chemical, it is not expected to be genotoxic.

The chemical's two hydrolysis products, 2-ethylhexanoate and 2-ethylhexanoic acid, have both been assessed by NICNAS and are not considered to be genotoxic based on both in vitro and in vivo studies (NICNAS a; NICNAS b).

Carcinogenicity

While no specific data are available for the chemical, one of its hydrolysis products, 2-ethylhexanol (CAS No. 104-76-7), was reported to not be carcinogenic in a two-year oral gavage study in rats (NICNAS a). As 2-ethylhexanol is metabolised to form 2-ethylhexanoic acid, exposure to both hydrolysis products of the chemical were tested in this study.

Reproductive and Developmental Toxicity

The chemical is classified as hazardous, as a Category 3 reproductive toxin, with the risk phrase 'Possible risk of harm to the unborn child' (Xn; R63) in HSIS (Safe Work Australia). While there are no data available for this specific chemical, experimental data available for its two hydrolysis products support this classification.

2-Ethylhexanoic acid (CAS No. 149-57-5) is classified as hazardous, as a Category 3 reproductive toxin, with the risk phrase 'Possible risk of harm to the unborn child' (Xn; R63) in HSIS (Safe Work Australia). Developmental toxic effects were reported in several studies in rats following treatment via the oral route (NICNAS b). These effects were noted in the absence of signs of

maternal toxicity. The lowest observed adverse effect level (LOAEL) for developmental toxicity was reported to be 100 mg/kg bw/day. Effects on fertility were also reported, with evidence being sufficient to warrant classification as potentially toxic to fertility.

2-Ethylhexanol (CAS No. 104-76-7) was reported to cause developmental toxicity, but not teratogenicity, in rats following treatment via the oral route (NICNAS a). These effects were noted in the absence of signs of marked maternal toxicity. The no observed adverse effect level (NOAEL) for developmental toxicity was reported to be 130 mg/kg bw/day.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include the systemic long-term effect of developmental toxicity. The chemical may also cause skin irritation.

Public Risk Characterisation

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

Although use in cosmetic/domestic products in Australia is not known, the chemical is reported to be used overseas at concentrations up to 8.3 % in leave-on moisturising products (CIR, 2013).

The chemical readily hydrolyses to form 2-ethylhexanoic acid (CAS No. 149-57-7) and 2-ethylhexanol (CAS No. 104-76-7), therefore exposure to the chemical in a leave-on moisturiser will result in exposure to both hydrolysis products. The concentrations of each of these hydrolysis products available from a 8.3% solution of the chemical are calculated to be 4.7% and 4.2%, respectively.

As product application levels for leave-on moisturisers have been estimated at 1540 mg/day (SCCS, 2012), a cumulative calculation can be used to assess the margin of exposure (MOE) for the two hydrolysis products of the chemical (NICNAS, 2012).

Comparing the levels at which adverse reproductive/developmental effect were observed for the two hydrolysis products (LOAEL of 100 mg/kg bw/day for 2-ethylhexanoic acid, and NOAEL of 130 mg/kg bw/day for 2-ethylhexanol), with their respective estimated exposure levels (based on a 70 kg adult) of 1027 µg/kg bw/day for 2-ethylhexanoic acid, and 927 µg/kg bw/day for 2-ethylhexanol, results in a cumulative MOE for the chemical of 26. An MOE of less than 100 indicates a risk of adverse health effects due to the use of the chemical at 8.3 % in leave-on moisturisers.

As no data are available on the absorption potential of the chemical, an assumption of 100 % dermal absorption is used in calculating the cumulative MOE, in addition to an uncertainty factor of three for the comparative use of a LOAEL and NOAEL value (ExxonMobil, 2010).

While use of the chemical in domestic products in Australia is not known, it is reported to be used overseas in products that are potentially available for domestic use (cleaning/washing products). However, the chemical is not listed as used in domestic products on the US National Library of Medicine's Household Products Database. Considering the limited information, in addition to no reported domestic use of the chemical in Australia, the likelihood of public exposure to domestic products containing the chemical is low.

Occupational Risk Characterisation

Given the critical health effects, the chemical may pose an unreasonable risk to workers unless adequate control measures to minimise exposure to the chemical 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 appropriate controls.

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 cosmetics and/or domestic products be managed through changes to poisons scheduling, 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

Given the risk characterisation, it is recommended that the concentration of the chemical in cosmetic products be restricted. Consideration should be given to the following:

- use of the chemical in a range of cosmetic products potentially available in Australia;
- reported use overseas at concentrations up to 8.3 % in leave-on moisturising products;
- the chemical readily hydrolyses to form 2-ethylhexanoic acid and 2-ethylhexanol, both of which are developmental/reproductive toxins; and
- a cumulative MOE of less than 100 is derived for a leave-on moisturiser containing 8.3 % of the chemical.

Work Health and Safety

The chemical is recommended for classification and labelling under the current Approved Criteria and adopted GHS as below. This assessment does not consider classification of physical hazards and environmental hazards.

Hazard	Approved Criteria (HSIS) ^a	GHS Classification (HCIS) ^b
Reproductive and Developmental Toxicity	Repro. Cat 3 - Possible risk of harm to the unborn child (Xn; R63)*	Suspected of damaging the unborn child - Cat. 2 (H361d)

^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 label instructions.

Advice for industry

Control measures

Control measures to minimise the risk from 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 which may minimise the risk include, but are not limited to:

- using closed systems or isolating operations;
- 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;
- 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 assist with meeting 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

Cosmetic Ingredient Review (CIR) 2013. Amended Safety Assessment of Alkyl Ethylhexanoates as Used in Cosmetics. Accessed August 2013 at <http://www.cir-safety.org/supplementaldoc/safety-assessment-alkyl-ethylhexanoates-used-cosmetics>

eChemPortal. Accessed August 2013 at <http://www.echemportal.org/echemportal/substancesearch/substancesearchlink.action>.

European Commission Cosmetic Substances and Ingredients (CosIng) database. Accessed August 2013 at <http://ec.europa.eu/consumers/cosmetics/cosing/>

ExxonMobil 2010. Proposed Approach to Conducting a Cumulative Risk Assessment for 6 Phthalates (DINP, DIDP, DnOP, DEHP, DBP, and BBP). Submitted to the US Chronic Hazard Advisory Panel (CHAP) on Phthalates, July 2010 meeting.

Accessed August 2013 at <http://www.cpsc.gov/en/Regulations-Laws--Standards/CPSIA/Phthalates/Chronic-Hazard-Advisory-Panel-CHAP-on-Phthalates/July-2010-Meeting/>

Household Products Database: Health& Safety Information on Household Products from the US National Library of Medicine (NLM). Accessed August 2013 at <http://householdproducts.nlm.nih.gov/>

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (NICNAS a). Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for 1-Hexanol, 2-ethyl- (104-76-7). Available at <http://www.nicnas.gov.au>

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (NICNAS b). Inventory Multi-tiered Assessment and Prioritisation (IMAP) Human Health Tier II Assessment for Hexanoic acid, 2-ethyl- (149-57-5). Available at <http://www.nicnas.gov.au>

NICNAS 2012. Priority Existing Chemical Assessment Report No. 35: Diisononyl phthalate (DINP). National Industrial Chemicals Notification and Assessment Scheme, Commonwealth of Australia. Available at <http://www.nicnas.gov.au>

Safe Work Australia (SWA). Hazardous Substances Information System (HSIS). Accessed August 2013 at <http://hsis.safeworkaustralia.gov.au/HazardousSubstance>

Scientific Committee on Consumer Safety (SCCS) 2012. Notes of Guidance for Testing of Cosmetic Ingredients and Their Safety Evaluation by the SCCS. 8th revision. Adopted during the 17th SCCS plenary meeting of 11 December 2012. Accessed August 2013 at http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_006.pdf

Substances in Preparations in Nordic Countries (SPIN). Accessed August 2013 at <http://188.183.47.4/dotnetnuke/Home/tabid/58/Default.aspx>

Last update 12 September 2013

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