# Waxy esters of 2-ethylhexanol: Human health tier III assessment

**8 March 2019**

| Chemical Name on the Inventory | CAS Number |
|---|---|
| **Octadecanoic acid, 2-ethylhexyl ester** | 22047-49-0 |
| **Dodecanoic acid, 2-ethylhexyl ester** | 20292-08-4 |
| **9-Octadecenoic acid, 2-ethylhexyl ester, (Z)-** | 26399-02-0 |
| **Octadecanoic acid, hydroxy-, 2-ethylhexyl ester** | 29383-26-4 |
| **Octadecanoic acid, 12-hydroxy-, 2-ethylhexyl ester** | 29710-25-6 |
| **Hexadecanoic acid, 2-ethylhexyl ester** | 29806-73-3 |
| **2-Ethylhexyl myristate** | 29806-75-5 |
| **Nonanoic acid, 2-ethylhexyl ester** | 59587-44-9 |
| **Fatty acids, tallow, 2-ethylhexyl esters** | 68648-21-5 |
| **Isononanoic acid, 2-ethylhexyl ester** | 71566-49-9 |
| **Fatty acids, C14-18, 2-ethylhexyl esters** | 91031-47-9 |
| **Fatty acids, C16-18, 2-ethylhexyl esters** | 91031-48-0 |
| **Fatty acids, coco, 2-ethylhexyl esters** | 92044-87-6 |
| **Isohexadecanoic acid, 2-ethylhexyl ester** | 93843-32-4 |
| **13-Docosenoic acid, 2-ethylhexyl ester, (Z)-** | 94094-62-9 |
| **Fatty acids, C8-C16, 2-ethyl hexyl esters** | 135800-37-2 |

# 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 III because the Tier II assessment indicated that it needed further investigation. The report should be read in conjunction with the Tier II assessment.

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

**Disclaimer**

NICNAS has made every effort to assure the quality of information available in this report. However, before relying on it for a specific purpose, users should obtain advice relevant to their particular circumstances. This report has been prepared by NICNAS

Acronyms & Abbreviations

## Synopsis

This group of 16 chemicals consists of 2-ethylhexyl esters of selected fatty acids and are widely used in cosmetics and domestic products available for consumers. In Australia, there are currently no restrictions on using these chemicals in cosmetic or domestic products.

Each chemical in this group is produced through the esterification of 2-ethylhexanol (2-EH; CAS No. 104-76-7) and its respective fatty acid; therefore, they are expected to hydrolyse to these compounds via chemical or enzymatic processes.

Quantitative risk assessments were conducted using a margin of exposure (MOE) approach to evaluate the potential health risks associated with exposure to 2-ethylhexyl esters used in cosmetic and personal care products.

This Tier III assessment indicates that there is no unacceptable risk from the use of the cosmetic products containing 2-ethylhexyl esters at likely use concentrations following dermal, oral or inhalation exposures.

The IMAP Human Health Tier II assessment for selected 2-ethylhexyl esters can be accessed online and contains detailed assessment information that remains valid (NICNAS 2013a). New or updated information is included in the Tier III human health report,  in the relevant sections. The Tier II and Tier III assessment reports should be read together.

## Rationale for Tier III Assessment

Currently, there are no restrictions in Australia on the use of these chemicals in cosmetics or domestic products.

The IMAP Human Health Tier II assessment for this group of chemicals identified the potential for  critical health effects relating to the uncertainty associated with developmental effects as a results of metabolism to 2-EH (a classified developmental toxin).

Quantitative considerations as a result of exposure related to the stronger reproductive toxin, 2-ethylhexanoic acid (2-EHA), from 2-EHA esters, led to these being controlled by scheduling in the Poisons Standard—the *Standard for the Uniform Scheduling of Medicines and Poisons* (SUSMP) (NICNAS 2013b; SUSMP, 2019). Therefore, it was recommended that similar risk calculations for 2-EH esters should be undertaken as a Tier III assessment.

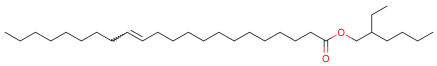
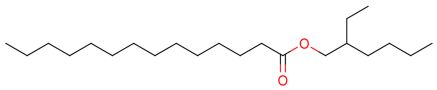
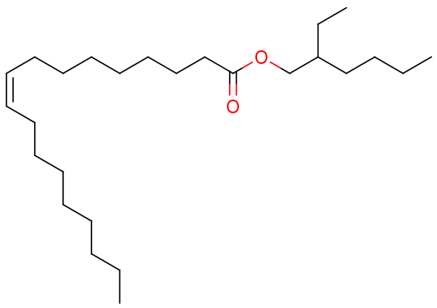
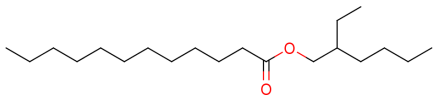
As detailed in the Tier II assessment, the majority of the chemicals in this group are reported to have cosmetic use, and it was recommended that the Tier III assessment be undertaken to examine any quantitative data to identify if an unacceptable risk of exposure exists from manufactured and/or imported cosmetic products containing these chemicals.

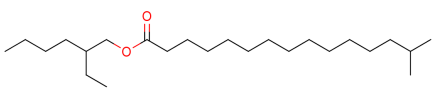
Considering that cosmetic use requires intentional application of a product, resulting in direct exposure to these chemicals, this Tier III assessment will focus on this highest use category in determining if an unacceptable risk of exposure exists.

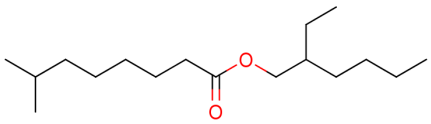
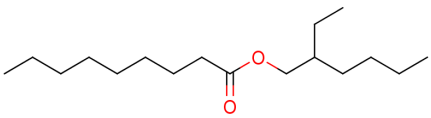
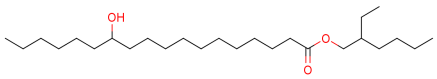
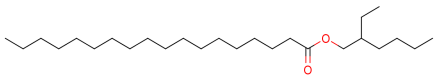
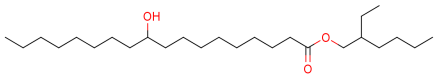
It should be noted that no significant new toxicological data have become available since the Tier II assessment and that a review of the health hazard has not been undertaken as part of this assessment.

## Chemical Identity

| Chemical name on the Inventory and Synonyms | CAS Number | Structural Formula | Molecular Formula | Molecular Weight |
|---|---|---|---|---|

| Chemical name on the Inventory and Synonyms | CAS Number | Structural Formula | Molecular Formula | Molecular Weight |
|---|---|---|---|---|
| **13-Docosenoic acid, 2-ethylhexyl ester, (Z)-**<br>erucic acid, 2-ethylhexyl ester<br>2-ethylhexyl (Z)-13-docosenoate<br>2-ethylhexyl (Z)-docos-13-enoate<br>2-octyl (Z)-13-docosenoate<br>13-docosenoic acid, 2-ethylhexyl ester, (z)- | 94094-62-9 |  | C30H58O2 | 450.79 |
| **2-Ethylhexyl myristate**<br>Bernel Ester 2014<br>octyl myristate | 29806-75-5 |  | C22H44O2 | 340.60 |
| **9-Octadecenoic acid, 2-ethylhexyl ester, (Z)-**<br>2-ethylhexyl oleate<br>oleic acid, 2-ethylhexyl ester<br>2-ethylhexyl 9-octadecenoate<br>ethylhexyl oleate | 26399-02-0 |  | C26H50O2 | 394.70 |
| **Dodecanoic acid, 2-ethylhexyl ester**<br>2-ethylhexyl laurate<br>octyl laurate<br>2-ethylhexyl dodecanoate<br>ethylhexyl laurate | 20292-08-4 |  | C20H40O2 | 312.50 |

| Chemical name on the Inventory and Synonyms | CAS Number | Structural Formula | Molecular Formula | Molecular Weight |
|---|---|---|---|---|
| **Fatty acids, C14-18, 2-ethylhexyl esters** | 91031-47-9 | No structural diagram available | Unspecified | |
| **Fatty acids, C16-18, 2-ethylhexyl esters** | 91031-48-0 | No structural diagram available | Unspecified | |
| **Fatty acids, C8-C16, 2-ethyl hexyl esters** | 135800-37-2 | No structural diagram available | Unspecified | |
| **Fatty acids, coco, 2-ethylhexyl esters**<br>coconut fatty acids, 2-ethylhexyl ester<br>2-ethylhexyl cocoate<br>octyl cocoate<br>ethylhexyl cocoate | 92044-87-6 | No structural diagram available | Unspecified | |
| **Fatty acids, tallow, 2-ethylhexyl ester**<br>tallow fatty acid, 2-ethylhexyl ester | 68648-21-5 | No structural diagram available | Unspecified | |
| **Hexadecanoic acid, 2-ethylhexyl ester**<br>2-ethylhexyl palmitate<br>octyl palmitate<br>ethylhexyl palmitate | 29806-73-3 | No structural diagram available | Unspecified | |
| **Isohexadecanoic acid, 2-ethylhexyl ester**<br>ethylhexyl isopalmitate<br>ethylhexyl isohexadecanoate | 93843-32-4 |  | C24H48O2 | 368.60 |

| Chemical name on the Inventory and Synonyms | CAS Number | Structural Formula | Molecular Formula | Molecular Weight |
|---|---|---|---|---|
| **Isononanoic acid, 2-ethylhexyl ester**<br>ethylhexyl isononanoate<br>2-ethylhexyl isononanoate | 71566-49-9 |  | C24H48O2 | 368.60 |
| **Nonanoic acid, 2-ethylhexyl ester**<br>2-ethylhexyl pelargonate<br>octyl pelargonate<br>2-ethylhexyl nonanoate | 59587-44-9 |  | C17H34O2 | 270.50 |
| **Octadecanoic acid, 12-hydroxy-, 2-ethylhexyl ester**<br>2-ethylhexyl 12-hydroxystearate<br>ethylhexyl hydroxystearate | 29710-25-6 |  | C26H52O3 | 412.70 |
| **Octadecanoic acid, 2-ethylhexyl ester**<br>octyl stearate<br>2-ethylhexyl octadecanoate<br>2-ethylhexyl stearate<br>ethylhexyl stearate | 22047-49-0 |  | C26H52O2 | 396.70 |
| **Octadecanoic acid, hydroxy-, 2-ethylhexyl ester**<br>2-ethylhexyl hydroxystearate<br>octyl hydroxystearate<br>ethylhexyl hydroxystearate | 29383-26-4 |  | C26H52O3 | 412.70 |

## Exposure from cosmetic and personal care products

The chemicals in this group are predominantly reported to be used in leave-on cosmetic products. Available information on types of leave-on cosmetic products containing the chemicals are provided in Table 1. This information is more detailed than what is available in the Tier II assessment of these chemicals, and has been obtained from online searches and databases, including the European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers, the European Commission Cosmetic Ingredients and Substances (CosIng) database, the US Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary, the US Department of Health and Human Services Household Products Database (HPD) and the Substances and Preparations in Nordic countries (SPIN) database. For information on other reported categories of use for these chemicals, please refer to the Tier II assessment.

**Table 1.** Leave-on cosmetic (skin and hair care) products containing 2-ethylhexyl esters of selected fatty acids, identified as available to consumers in Australia (AUS) or internationally (INT).

| CAS Registry Number and Chemical name on the Inventory | Common name listed as product ingredient | Body Lotion | Face Cream | Hand Cream | Hair Styling | Other/ Notes |
|---|---|---|---|---|---|---|
| 71566-49-9<br>**Isononanoic acid, 2-ethylhexyl ester** | Ethylhexyl isononoate | AUS; INT | AUS; INT | - | INT | Makeup fixing spray or mist (AUS; INT)[1] |
| 29806-73-3<br>**Hexadecanoic acid, 2-ethylhexyl ester** | Ethylhexyl palmitate | AUS; INT (1-5%) | AUS; INT | AUS; INT | AUS; INT | Baby lotion;<br>Spray lotion |
| 22047-49-0<br>**Octadecanoic acid, 2-ethylhexyl ester** | Ethylhexyl stearate | - | AUS; INT | - | - | - |
| 29383-26-4<br>**Octadecanoic acid, hydroxy-, 2-ethylhexyl ester** | Ethylhexyl hydroxystearate[2] | - | AUS; INT (5-10%) | - | - | Mostly lipstick |
| 92044-87-6<br>**Fatty acids, coco, 2-ethylhexyl esters** | Ethylhexyl cocoate | INT | - | - | - | Pregnancy and after birth lotion |

*1) Inhalation exposure is also likely in the case of this product.*

*2) Although the products list this common name in reference to CAS No. 29383-26-4, it is more likely that CAS No. 29710-25-6 (the 12-hydroxy) is the ingredient used in these products.*

The only available information on concentrations of the chemicals used in these products is for 2-ethylhexyl hydroxystearate (CAS No. 29383-26-4) reported at 5-10 % in face cream and/or moisturising products, and 2-ethylhexyl palmitate (CAS No. 29806-73-3) reported at 1-5 % in body lotion and/or moisturising products (HPD).

## Relative 2-EH exposure

The esters in this group all share a common hydrolysis product, that being 2-EH, with exposure to the each of the esters resulting in exposure to 2-EH. The differing molecular weights across the 2-ethylhexyl esters are due to their respective fatty acid components, with hydrolysis resulting in differing proportions of 2-EH formed for each of the esters.

The values provided in Table 2 represent the proportion of 2-EH formed on hydrolysis of each of the esters (ranging from the smallest, being 2-ethylhexyl nonoanoate, to the largest, being 2-ethylhexyl (Z)-13-docosenoate) in this group, at ester use concentrations of 1, 2, 3, 5, 10 and 15 %.

**Table 2.** Proportion (%) of 2-EH formed on hydrolysis of 2-ethylhexyl esters.

| Ester Concentration (%) | Concentration of 2-EH formed on hydrolysis [a] (%) |
|---|---|
| **15** | 4.3 – 7.2 |
| **10** | 2.9 – 4.8 |
| **5** | 1.4 – 2.4 |
| **3** | 0.9 – 1.4 |
| **2** | 0.6 – 1.0 |
| **1** | 0.3 – 0.5 |

***a*** *Represents 2-ethylhexyl esters with specifiable molecular weight, ranging from the largest, being 2-ethylhexyl (Z)-13-docosenoate to the smallest, being 2-ethylhexyl nonoanoate.*

## Routes of exposure

Considering the range of identified cosmetic and personal care products reported to contain these chemicals, the main route of exposure is expected to be through the skin. There is also concern regarding oral exposure from cosmetic products such as

lipsticks which may inadvertently be ingested, and incidental inhalation exposure from products containing these chemicals which are applied as sprays (refer to Table 1).

## Estimates of dermal exposure to 2-EH in adults

Dermal exposure to these chemicals are calculated as an internal dose which is proportional to the use volumes, product retention factors (reflecting proportions of product remaining on the skin during normal use), and concentration of the particular chemical per product type. The dermal bioavailability of the chemical, or alternatively, the rate of dermal absorption of the chemical, is also required in the calculations.

Based on the available information for the chemicals in this group, including the relatively high molecular weights, wax-like physical appearance, and the expectation that they will have similar physico-chemical properties, this group of esters are expected to have very low dermal absorption potential (OECD, 2014; also refer to Chemical Identity section). While metabolism of the chemicals by skin esterases will produce 2-EH as a hydrolysis product, with 2-EH expected to have higher dermal absorption than the parent esters, the reported dermal absorption for 2-EH is low at five to seven percent (Government of Canada, 2018; REACH). Taking this information into consideration, and assuming 100 % hydrolysis, an assumption of 10 % dermal absorption is used in calculating the exposure estimates.

While no relevant data on Australian use patterns (for example, typical amount used each application, frequency of use and exposure duration) are available for cosmetics or personal care products, data collected overseas (mainly Europe) are available on typical use patterns of some classes of products, including leave-on cosmetic products, as provided in the Technical Guidance Document on risk assessment (TGD) of the European Chemicals Bureau (ECB, 2003) and the Scientific Committee on Consumer Safety's (SCCS) 'Notes of guidance for the testing of cosmetic substances and their safety evaluation' (SCCS, 2018).

For the purposes of this assessment, Australian use patterns are considered similar to those in Europe and, as such, this data has been used in determining Australian exposures for leave-on cosmetic products containing these chemicals.

Estimates of the internal dose of 2-EH arising from dermal exposure to cosmetic and personal care products containing 2-ethylhexyl esters were calculated using Equation 1, below.

**Equation 1**

$$D_{int,derm} = \frac{A_{prod} \times n \times \frac{C}{100} \times \frac{B_{derm}}{100} \times RF \times CF}{BW}$$

Where:

| | | |
|---|---|---|
| $D_{int,derm}$ | = | Internal dose via the dermal route (µg/kg bw/day) |
| $A_{prod}$ | = | Amount of cosmetic/personal care product applied to skin (mg/event) |
| n | = | Frequency of product application (event/day) |
| C | = | Concentration of 2-EH available on hydrolysis of the ester (% w/w) (refer to Table 2) |
| $B_{derm}$ | = | Bioavailability via the dermal route ( %) |
| RF | = | Retention factor |
| CF | = | Conversion factor (1000 µg/mg) |
| BW | = | Adult bodyweight (70 kg) |

The other exposure parameters used and the calculated internal dose of 2-EH from dermal exposure ($D_{int,derm}$) from different leave-on product types are shown below in Table 3.

**Table 3.** Calculated ranges for estimated daily internal dose of 2-EH from dermal exposure ($D_{int,derm}$) to various reported leave-on cosmetic products in adults for which reported 2-ethylhexyl ester use concentrations are available.

| Product type | $A_{prod}$—n [a] (mg/day) | Ester use concentration [b] | $D_{int,derm}$ [c] of 2-EH (mg/kg bw/day) |
|---|---|---|---|

| Product type | $A_{prod}$—n [a] (mg/day) | Ester use concentration [b] | $D_{int,derm}$ [c] of 2-EH (mg/kg bw/day) |
|---|---|---|---|
| **Body Lotion** | 7820 | 1 – 5 % | 39 – 197 |
| **Face Cream** | 1540 | 5 – 10 % | 35 – 69 |

***a*** *Typical values for use parameters are derived from SCCS (2018). Aprod = Amount of product applied daily (mg/event) and n = frequency of product application (event/day) are presented here as a product of the two parameters.*

***b*** *Refer to Table 1*

***c*** *A retention factor (RF) value of 1 for leave-on cosmetic products was used in these calculations (SCCS, 2018), in addition to the bioavailability assumption of 10 %.*

## Estimates of dermal exposure to 2-EH in children

There are no available data on cosmetic product usage in children by age, or of differences in skin permeability between children and adults.

Using the model developed by NICNAS (NICNAS 2010), the quantity of whole body product applied to a child or infant can be estimated from the child or infant's ratio of body surface area compared with the adult. The systemic dose depends on the body weight of the child or infant; and therefore, the systemic dose for any product used similarly in children and adults will vary according to the ratio of surface area to body weight, if the skin permeability is the same in adults and children. An estimate of the magnitude of the difference between adults and children can be made using data issued by the SCCS on the Margin of Safety calculation for children (SCCS, 2018). For children aged 0–10 years, the difference between the surface area to bodyweight (SA/BW) ratio compared with adults is as follows: 2.3-fold at birth, 1.8-fold at six months, 1.6-fold at 12 months, 1.5-fold at five years and 1.3-fold at 10 years.

One type of cosmetic product used on infants or children, is body lotions or creams. The maximum reported concentration for 2-ethylhexyl esters in lotions and creams is 5 % (2-ethylhexyl palmitate was the specific ester reported; see Table 1). The internal dose of 2-EH for children up to 12 months using these products is calculated using the correction for the SA/BW ratio (SCCS 2018). These calculations and assumptions were previously used by NICNAS (NICNAS, 2013c; 2010; 2011). Estimated internal doses of 2-EH for infants by age can be calculated as shown in Table 4.

**Table 4.** Calculated daily internal dose of 2-EH for infants from dermal exposure ($D_{int,derm}$) to baby lotions containing 2-ethylhexyl palmitate.

| Infant age | Adult $D_{int,derm}$ (mg/kg bw/day) | SA/BW ratio | $D_{int,derm}$ (mg/kg bw/day) |
|---|---|---|---|
| **Newborn** | 197 | 2.3 | 454 |
| **6 months** | 197 | 1.8 | 355 |
| **12 months** | 197 | 1.6 | 316 |

## Estimates of oral exposure to 2-EH

At least one of the chemicals in this group is reported to be used in cosmetic lipstick or lip gloss products. For these products, exposure through the oral route is likely. A conservative assumption of 100 % ingestion rate is used for calculation purposes, in addition to a typical use value of 57 mg/day for lipstick or lip gloss (SCCS, 2018). This typical use value is a product of $A_{prod}$ (mg/event) and the frequency of product application (event/day). A retention factor (RF) value of 1 for leave-on cosmetic products was also used in the calculations (SCCS, 2018).

Calculated estimates of the daily internal dose of 2-EH from exposure to lipstick or lip gloss products containing 2-ethylhexyl esters (2-ethylhexyl hydroxystearate was the specific ester reported; see Table 1) are determined to be 12.6, 25.2 and 50.3 µg/kg bw/day for use concentrations of 5, 10 and 20 %, respectively. No information is available on the actual use concentration of the chemicals in lipstick or lip gloss products.

## Estimates of inhalation exposure to 2-EH

Inhalation exposure to chemicals in cosmetic and personal care products commonly occur through the use of spray products. In the case of the chemicals in this group, two spray product types have been identified, one being a makeup setting spray which is applied directly to the face, and the other being a body lotion spray.

In order to estimate the internal dose of 2-EH from the use of these products, the following parameters and assumptions were used:

- an adult inhalation rate is 20 $m^3$/day (enHealth, 2012);
- as no data are available on the inhalation absorption potential of the chemicals, an assumption of 100 % bioavailability was used;
- the average body weight is 70 kg (enHealth, 2012);
- the exposure duration estimate is 5 min (RIVM, 2006); and
- a room volume of 2 $m^3$ to represent the volume of air immediately surrounding the user, except for the makeup setting spray, for which a volume 1 $m^3$ is considered appropriate, as it is expected to occur close to the face (RIVM, 2006 – refer to nail polish scenario).

Additionally, while no data are available on the amount of product sprayed during typical use, instruction on use of these products are available (LOREAL; BEAUTYHQ). Based on the available information, it is considered reasonable to use a face cream or face moisturiser $A_{prod}$ value for the makeup setting spray and a body lotion $A_{prod}$ value for the body lotion spray (SCCS, 2018).

Therefore, under these assumptions, estimates of the daily internal dose of 2-EH from inhalation exposure to a these cosmetic products can be calculated using Equation 2, below.

**Equation 2**

$$D_{int,inh} = \frac{A_{prod} \times n \times \frac{C}{100} \times \frac{B_{inh}}{100} \times t \times IR_{air} \times CF_1 \times CF_2}{BW \times V_{room}}$$

Where:

| | | |
|---|---|---|
| $D_{int,inh}$ | = | Internal dose via the inhalation route (µg/kg bw/day) |
| $A_{prod}$ | = | Amount of product spray (mg/event) |
| n | = | Frequency of spray application (event/day) |
| C | = | Concentration of 2-EH available on of the ester (% w/w) (refer to Table 2) |
| $B_{inh}$ | = | Bioavailability via the inhalation route (%) |
| t | = | Time of contact, i.e. spray and exposure duration (minute) |
| $IR_{air}$ | = | Inhalation rate of person ($m^3$/day) |
| $CF_1$ | = | Conversion factor for time (1 day/1440 minutes) |
| $CF_2$ | = | Conversion factor for amount (1000 µg/mg) |
| V | = | Room volume ($m^{3)}$ |
| BW | = | Adult body weight (kg) |

The exposure parameters used and the calculated internal doses from inhalation exposure ($D_{int,inh}$) from the two identified product types are shown below in Table 5.

**Table 5.** Calculated estimate daily internal dose of 2-EH for adults from inhalation exposure ($D_{int,inh}$) to the reported cosmetic spray product types.

| Product type | $A_{prod}$—n [a] (mg/day) | $V_{room}$ (m3) | C[b] (% w/w) | $D_{int,inh}$ [c] of 2-EH (mg/kg bw/day) |
|---|---|---|---|---|
| **Body lotion spray** | 7820 | 2 | 1 – 5 % | 13.7 – 68.5 |
| **Makeup setting spray** | 1540 | 1 | 5 – 10 % | 36.8 – 73.6 |

***a*** *Typical values for use parameters are derived from SCCS (2018). Aprod = Amount of product applied daily (mg/event) and n = frequency of product application (event/day) are presented here as a product of the two parameters.*

***b*** *As no information are available on actual use concentrations of the chemicals in these products. Reported concentration values for face creams and body lotions (see Table 1) were used in calculating dose estimates for makeup setting sprays and body lotion sprays, respectively.*

***c*** *A retention factor (RF) value of 1 for leave-on cosmetic products was used in these calculations (SCCS, 2018), in addition to the bioavailability assumption of 100 %.*

## Risk Characterisation

A margin-of-exposure (MOE) methodology is commonly used to characterise risks to human health associated with exposure to chemicals (ECB, 2003). The risk characterisation is conducted by comparing quantitative exposure information with a no observed adverse effect level (NOAEL) and/or a no observed adverse effect concentration (NOAEC) from appropriate animal studies and deriving an MOE as follows:

1. Identification of critical health effect(s).

2. Identification of the most appropriate/reliable NOAEL (if available) for the critical effect(s).

3. Where appropriate, comparison of the estimated or measured human dose or exposure (EHD) with the appropriate/reliable NOAEL to provide an MOE:

$$MOE = NOAEL/EHD$$

4. Evaluation of whether the MOE obtained by this method indicates a health concern for the human population under consideration.

The MOE provides a measure of the likelihood that a particular adverse health effect will occur under the conditions of exposure. As the MOE increases, the risk of potential adverse effects decreases. To decide whether the MOE is of sufficient magnitude, expert judgement is required. Such judgements are usually made on a case-by-case basis, and should take into account uncertainties arising in the risk assessment process such as the completeness and quality of the database, the nature and severity of effect(s) and intra/inter species variability.

Taking into account the interspecies and intraspecies assessment factors of 10, the acceptable MOE for a NOAEL-based assessment is 100.

In this assessment, the MOE methodology was used for characterising the public health risks from exposure to chemicals in this group through use of cosmetic and personal care products.

## Critical Health Effects and Selection of the NOAEL for Risk Assessment

As indicated in the Tier II assessment for this group of chemicals, the critical health effects for risk characterisation relate to the uncertainty as to the possibility of developmental effects related to metabolism to 2-EH.

The chemical 2-EH is classified as hazardous substance toxic to reproduction (Category 2), with the risk phrase ‘Suspected of damaging the unborn child’ (H361d) in the Hazardous Chemicals Information System (HSIS) (Safe Work Australia), and is the common hydrolysis product for all the chemicals in this group.

The hydrolysis product, 2-EH, was reported to cause developmental toxicity, but not teratogenicity, in rats following treatment via the oral route (NICNAS, 2016). These effects were noted in the absence of signs of marked maternal toxicity, and included markedly reduced mean foetal body weights and a higher number of foetuses with skeletal malformations, variations and retardations (similar to the effects noted in the available developmental toxicity study using 2-ethylhexyl stearate; refer to the Tier II assessment – Reproductive and developmental toxicity section).

The NOAEL for developmental toxicity was reported to be 130 mg/kg bw/day for 2-EH. An estimation of risk based on this NOAEL value is considered appropriate, as 2-EH is the common hydrolysis product across all the chemicals in this group.

## Risk estimates related to use of cosmetics and personal care products

The main route of exposure to these chemicals from cosmetic use in the general population is through dermal contact arising from use of products directly applied to the skin. Oral exposure is also likely to arise though inadvertent ingestion of applied lipstick or lip gloss products. Cosmetic products applied as sprays also present a possibility of incidental inhalation exposure.

Based on the critical health effects of developmental toxicity, the potential risks from cosmetic use are related to long-term exposure through repeated use, especially in regards to leave-on products. The chosen NOAEL value of 130 mg/kg bw/day used for calculating risk estimates for these chemicals has been derived from 2-EH, the common hydrolysis product across all the chemicals in this group, and is associated with the critical health effects of concern.

## Estimation of margin of exposure

The MOE values for 2-EH provided in Tables 6.1 and 6.2 have been calculated based on the internal dose ($D_{int}$) values as derived for each of the product types and exposure routes (refer to Tables 3, 4 and 5).

**Table 6.1** Calculated MOE for the critical health effect of 2-EH from exposure in adults to 2-ethylhexyl esters for each of the identified cosmetic product types.

| Product and exposure type | Representative 2-EH ester[a] | Ester use concentration[a] (%) | Relative 2-EH concentration[b] (%) | $D_{int}$ of 2-EH[c] (mg/kg bw/day) | NOAEL (mg/kg bw/day) | MOE |
|---|---|---|---|---|---|---|
| **Body Lotion** (dermal) | Palmitate | 5 | 1.8 | 197.4 | 130 | 659 |
| **Face Cream** (dermal) | Hydroxystearate | 10 | 3.2 | 69.4 | 130 | 1873 |
| **Body lotion spray** (inhalation) | Palmitate | 5 | 1.8 | 68.5 | 130 | 1897 |
| **Makeup setting spray** (inhalation) | Isononoate | 10 | 4.8 | 73.6 | 130 | 1766 |
| **Lipstick or lip gloss** (oral) | Hydroxystearate | 20 | 6.3 | 50.3 | 130 | 2585 |

***a*** *Refer to Table 1*

***b*** *Refer to Table 2*

***c*** *Refer to Tables 3, 4 and 5*

The estimated MOE for the general population is greater than 100 at the highest likely (or assumed) use concentrations for all cosmetic uses and exposure routes identified (Table 7.1). Further, given that the available 2-EH concentrations among this group of esters differs by less than a factor of two, use of a lower molecular weight ester would not give rise to a MOE below 100. This indicates that for cosmetic products the risk for the general population of potential developmental toxicity from use of these products is low under this scenario.

Based on exposure estimates for children from use of body lotions containing 2-ethylhexyl palmitate (refer to Table 5), the MOE for the critical health effects of 2-EH exposure was found not to demonstrate an unacceptable risk (MOE of greater than 100) at the highest likely use concentration of 5 % (as the ester), as presented in Table 6.2.

**Table 6.2** Calculated MOEs for the critical health effect of 2-EH from dermal exposure in children to 2-ethylhexyl esters in body lotions.

| Infant age | $D_{int,derm}$ (mg/kg bw/day) | NOAEL (mg/kg bw/day) | MOE |
|---|---|---|---|

| Infant age | $D_{int,derm}$ (mg/kg bw/day) | NOAEL (mg/kg bw/day) | MOE |
|---|---|---|---|
| **Newborn** | 454 | 130 | 286 |
| **6 months** | 355 | 130 | 366 |
| **12 months** | 316 | 130 | 411 |

This indicates that the risk of potential developmental toxicity from the use of cosmetic products containing 2-ethylhexyl esters, likely to be available to consumers, is low. Compared with esters of 2-ethylhexanoic acid (NICNAS, 2013b), the risk is reduced both due to the lower developmental toxicity and lower dermal absorption of 2-ethylhexanol.

### Uncertainties in the risk estimate

Uncertainties involved in the risk characterisation for the general population from cosmetic use result from database limitations in addition to the lack of specific data on bioavailability of the esters and limited available data on product use concentrations.

Australian data on the use patterns of consumer products are not available; therefore, there is no precise exposure assessment for cosmetics. Given the limited available data, conservative plausible assumptions have been used to determine the risk to consumers.

## NICNAS Recommendation

No further assessment or risk management is required. Based on the quantitative risk assessment, public exposure to cosmetic products containing waxy 2-ethylhexyl esters, at expected use concentrations, is unlikely to present a health risk in relation to the potential developmental toxicity of 2-EH formed on hydrolysis of the ester.

### Advice for consumers

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

### Advice for industry

The advice provided in the human health Tier II IMAP report remains unchanged.

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

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### What is IMAP?

A framework we work in to accelerate the assessment of unassessed chemicals on AICS.

### Selected 2-ethylhexyl esters: Human health tier II assessment

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.