Australian Government

**Department of Health** Australian Industrial Chemicals Introduction Scheme

# Benzenepropanol

# **Evaluation statement**

14 January 2022



# **Table of contents**

### Contents

AICIS evaluation statement	4
Subject of the evaluation	4
Chemical in this evaluation	4
Reason for the evaluation	4
Parameters of evaluation	4
Summary of evaluation	4
Summary of introduction, use and end use	4
Human health	4
Conclusions	6
Recommendations	6
Workers	6
Supporting information	8
Chemical identity	8
Relevant physical and chemical properties	8
Introduction and use	9
Australia	9
International	9
Existing Australian regulatory controls	10
AICIS	10
Public	10
Workers	10
International regulatory status	10
Exposure standards	10
Europe	10

Health hazard information10
Toxicokinetics10
Acute toxicity11
Corrosion/Irritation12
Repeat dose toxicity14
Genotoxicity14
Carcinogenicity15
Reproductive and development toxicity15
References16

# **AICIS** evaluation statement

# Subject of the evaluation

Benzenepropanol

# Chemical in this evaluation

Name	CAS number
Benzenepropanol	122-97-4

# Reason for the evaluation

The Evaluation Selection Analysis indicated a potential risk to human health.

# Parameters of evaluation

Benzenepropanol is listed on the Australian Inventory of Industrial Chemicals (the Inventory). This evaluation is a human health risk assessment for all identified uses of the chemical.

# Summary of evaluation

### Summary of introduction, use and end use

There is currently no specific information about the introduction, use and end use of the chemical in Australia. Based on international use information, the chemical is used in cosmetics, primarily as a fragrance. The chemical is typically used at concentrations <0.8% but levels up to 8% have been reported. The chemical also has domestic, commercial, and non-industrial uses, and is reported to be naturally occurring and present in small concentrations in food including fruit. While there are uses in food and synthetic food flavourings as a flavour enhancer reported overseas, these are considered non-industrial uses in Australia.

### Human health

#### Summary of health hazards

The critical health effects for risk characterisation include local effects (skin corrosion and eye damage).

Based on the available data, the chemical is considered to have potential to cause corrosion in vivo. Three guideline in vitro studies determined the chemical to be corrosive. The chemical caused moderate to severe erythema and necrosis when applied to rabbit skin for 24 hours under occlusive conditions. In a limited study in humans, no irritation was observed when exposed to concentrations up to 8%.

No data are available for eye irritation. Chemicals corrosive to the skin are expected to cause serious damage to eyes.

Based on animal data, the chemical has low acute oral and dermal toxicity with median lethal doses (LD50s) of >2000 mg/kg body weight (bw) in rats. There were no inhalation toxicity data available for the chemical. However, due to its lower vapour pressure (35 Pa at 25 °C, equivalent to 0.0234 mm Hg at 25 °C), the chemical is not expected to cause acute inhalation toxicity.

Based on the weight of evidence from in silico, in vitro, and human data, the chemical is not considered to be a skin sensitiser, not genotoxic, and does not cause reproductive or developmental toxicity. The chemical is not expected to be carcinogenic.

Further details on the evaluation of these health hazards is provided in the Supporting Information (refer to **Supporting Information** section).

Health hazard classification

Based on the available data, this chemical satisfies the criteria for classification according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (UNECE, 2017) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical and environmental hazards.

Health hazards	Hazard category	Hazard statement
Irritation/Corrosion	Skin Corr. 1	H314: Causes severe skin burns and eye damage

#### Summary of health risk

#### Public

Based on the available use information, the public may be exposed to the chemical:

- at concentrations up to 8%
- by direct application of the chemical to the skin
- by incidental skin and eye contact with the chemical during use of domestic products
- by inhaling aerosols/vapours.

At the concentrations reported for the chemical corrosive effects are not expected. Therefore, there are no identified risks to the public that require management.

#### Workers

During product formulation and packaging, dermal, ocular 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 the 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 (skin corrosion and eye damage), the chemical could pose a risk to workers. Control measures to minimise dermal, ocular and inhalation exposure are needed to manage the risk to workers (refer to **Recommendations** section).

# Conclusions

The conclusions of this evaluation are based on the information described in this statement. Obligations to report additional information about hazards under section 100 of the IC Act apply.

The Executive Director is satisfied that the identified human health risks can be managed within the existing risk management frameworks. This is provided that all requirements are met under environmental, workplace health and safety and poisons legislation as adopted by the relevant state or territory. The proposed means of managing the risks identified during this evaluation are set out in the **Recommendations** section.

# Recommendations

### Workers

**Recommendation to Safe Work Australia** 

It is recommended that Safe Work Australia (SWA) update the HCIS to include classifications relevant to work health and safety.

#### Information on managing identified risks

The information in this report including recommended hazard classifications, should be used by a person conducting a business or undertaking (PCBU) at a workplace (such as an employer) to determine the appropriate controls under the Model Work Health and Safety Regulations.

Control measures that could be implemented to manage the risk arising from dermal, ocular and inhalation exposure to the chemical include, but are not limited to:

- using closed systems or isolating operations
- minimising manual processes and work tasks through automating processes;
- adopting work procedures that minimise splashes and spills
- cleaning equipment and work areas regularly
- using protective equipment that is designed, constructed, and operated to ensure that the worker does not come into contact with the chemical.

Measures required to eliminate, or manage risk from dermal, ocular and inhalation exposure arising from storing, handling and using a hazardous chemical depend on the physical form and the manner in which the chemical is used.

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. Model codes of practice, available from the Safe Work Australia website, provide information on how to manage the risks of hazardous chemicals in the workplace, prepare an SDS and label containers of hazardous chemicals. Your Work Health and Safety regulator should be contacted for information on Work Health and Safety laws and relevant Codes of Practice in your jurisdiction.

# Supporting information

# Chemical identity

Benzenepropanol (also known as 3-phenylpropyl alcohol) is an aliphatic alcohol with a phenyl substituent. It is prepared by hydrogenation of cinnamaldehyde. The chemical is found to be naturally occurring in food, with the highest concentration in bilberries, and to a lesser extent in fruits such as pomes, cinnamon, highbush blueberries, and evergreen blackberries. It has reported applications in the manufacture of fragrances with blossom compositions for its balsamic and oriental notes; and also in food flavouring as a flavour enhancer due to its sweet, anise, and balsam taste (CosIng; Galleria Chemica; IFRA; TGSC; Bhatia et al. 2011; TMIC 2019).

Chemical name	Benzenepropanol
CAS No.	122-97-4
Synonyms	3-phenylpropyl alcohol; hydrocinnamyl alcohol; 1-propanol, 3-phenyl; 3-benzenepropanol; phenylpropanol; and benzylethyl alcohol.
Structural formula	ОН
Molecular formula	C9H12O
Molecular weight (g/mol)	136.19
SMILES	c1(CCCO)ccccc1
Chemical description	Organic compound

# Relevant physical and chemical properties

Physical form	Colourless to pale yellow liquid with a floral, balsamic odour.
Melting point	<-18 °C at 101.3 kPa
Boiling point	235 °C at 101.3 kPa
Vapour pressure	35 Pa at 25 °C (equivalent to 0.0234 mm Hg at 25 °C)
Water solubility	5.68 g/L at 25 °C

pKa (estimated)

15.96 at 25 °C

log Kow

1.88

# Introduction and use

### Australia

No information is available on the industrial use of the chemical in Australia.

### International

The following international uses have been identified through the:

- European Union (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) dossiers
- Chemwatch (Galleria Chemical)
- Substances and Preparations in Nordic countries (SPIN) database
- European Commission Cosmetic Ingredients and Substances (CosIng) database
- International Fragrance Association (IFRA) Transparency List; The Good Scents Company (TGSC)
- United States (US) Personal Care Products Council International Nomenclature of Cosmetic Ingredients (INCI) Dictionary
- US Environmental Protection Agency's Aggregated Computer Toxicology Resource (ACToR)
- US National Library of Medicine's Hazardous Substances Data Bank (HSDB)
- publically available Safety Data Sheet (SDS).

The chemical has reported cosmetic uses, including:

• as a fragrance ingredient/perfuming compound in cosmetic products (including eye shadow; and body, hand, and hair preparations).

The average maximum use level in cosmetic products (fragrances) has been reported to be 8% with assumption of use of the fragrance oil at levels up to 20% in the final product (TGSC; Bhatia et al. 2011).

The chemical has reported domestic uses, including:

- as an odour agent
- in air fresheners
- a cleaning/washing agent
- in paints, lacquers and varnishes.

The chemical has reported commercial uses, including:

- as a solvent
- as an absorbent and adsorbent.

The chemical has reported non-industrial uses as a flavouring ingredient/flavour enhancer.

# Existing Australian regulatory controls

### AICIS

No specific controls are currently available for the chemical.

### Public

No specific controls are currently available for the chemical.

### Workers

The chemical is not listed on the HCIS and no specific exposure standards are available in Australia (Safe Work Australia).

### International regulatory status

### Exposure standards

No specific exposure standards are available for the chemical.

#### Europe

The chemical is listed on the following (Galleria Chemica):

• EU Cosmetic Directive 76/768/EEC Annex VI— Part 1 of List of preservatives allowed in cosmetic products. The chemical is allowed as a preservative in cosmetic products at a maximum concentration, in ready for use preparations, of 1%.

# Health hazard information

### Toxicokinetics

In an in vitro percutaneous absorption study using the chemical, human abdominal skin samples (approximately 280  $\mu$ m thick) were fixed in 4% formaldehyde and embedded in paraffin. A dose of 5.0 mg/mL of the chemical dissolved in a buffer solution (at a concentration of approximately 75% of its solubility in that medium), was applied for 7 hours. The mean skin permeability coefficient was reported to be 52.35 (±4.98) K<sub>p</sub> (cm/hour) (Bhatia et al. 2011).

The data available for structurally similar cinnamyl alcohol derivatives (i.e. cinnamyl alcohol and a shorter alkyl-chain saturated phenyl alkyl alcohol) support the potential for these relatively small polar organic molecules to undergo rapid absorption either via oral, dermal or inhalation route (although unlikely), making them readily bioavailable. The compounds are metabolised to the respective carboxylic acids, followed by fast and complete excretion primarily in urine. There is no potential for bioaccumulation, neither for the parent compound nor for any of the metabolites (REACH).

### Acute toxicity

#### Oral

Based on the data available, the chemical has low acute oral toxicity.

In acute toxicity studies equivalent to the Organisation for Economic Co-operation and Development (OECD) Test Guideline (TG) 401, Sprague Dawley (SD) rats (10/sex at the top dose; and 5/sex for all other doses) were administered (gavage) a single dose of 1470, 2150, 3160, 4640, or 5000 mg/kg body weight (bw) of the chemical. Mortality was seen in all doses (1 of 5 animals died at the lower doses); however, significant mortality (9 out of 10 animals died) was reported at the top dose of 5000 mg/kg bw. The oral median lethal dose (LD50) was reported to be 2250 mg/kg bw. Treatment-related clinical effects reported included depression, hypopnea, ataxia and piloerection. Gross pathology findings at necroscopy included dark red areas in the lungs of animals at all doses, and distended stomach (REACH; Bhatia et al. 2011).

In another acute toxicity study equivalent to OECD TG 401, rats (10/dose; unspecified sex and strain) were administered (gavage) a single dose of 670, 1310, 2560, or 5000 mg/kg bw of the chemical. Clinical signs including lethargy were reported in rats that were administered the chemical at the second lowest dose of 1310 mg/kg bw. Mortality of all animals was reported at the top dose on day 1 of the study, and at the second lowest dose where 1/10 animals died. Mortality was also reported at the 2560 mg/kg bw dose, where 5/10 animals died by day 2, during the 14 day study. An LD50 of 2300 mg/kg bw was reported (Bhatia et al. 2011; REACH).

In a preliminary screen for an acute oral toxicity study, a 50% solution of the chemical in corn oil was administered orally to 10 rats at a dose level of 5000 mg/kg bw. Clinical signs and mortality were observed at 1 and 4 hours post exposure and then once daily for 14 day. Mortality was reported in 9 out of 10 rats by the end of the study period (Bhatia et al. 2011).

#### Dermal

Based on the weight of evidence from the data available, the chemical is expected to have low acute dermal toxicity.

In a limited acute dermal toxicity study (equivalent to OECD TG 402 with restrictions) in male and female New Zealand White (NZW) rabbits (6/sex/dose), a single dose of 5000 mg/kg bw of the chemical was dermally applied to the clipped, intact or abraded skin for 24 hours, under occlusive conditions. Mortality was reported on days 1, 3 and 4. Observations at necropsy reported lung haemorrhages in 2/6 animals by day 1; with white nodules in the liver and abscessed ovaries in 2/6 animals by day 3. Clinical effects were observed on the skin of the animals that died, including discolouration (1/6 animals), moderate to severe erythema (6/6 rabbits), severe oedema (5/6 rabbits), scaling (2/6 animals), and necrosis (5/6 animals). The LD50 was reported to be <5000 mg/kg bw (REACH; Bhatia et al. 2011).

In a similar acute dermal toxicity study (equivalent to OECD TG 402 with restrictions), the chemical was dermally applied to the intact or abraded skin of rabbits (unspecified strain and sex) in 4 animal at the 2500 mg/kg bw dose; and 6 animals at the 5000 mg/kg bw dose. No mortality and clinical effects were reported at 2500 mg/kg bw. However, mortality was observed in 3/6 animals at 5000 mg/kg. Clinical signs reported at this higher dose included slight lethargy (1/6 animals), anorexia (2/6 animals), diarrhoea (2/6 animals) and a flaccid muscle tone (1/6 animals). The LD50 value was reported to be 5000 mg/kg bw (REACH; Bhatia et al. 2011).

#### Inhalation

No data are available.

#### Corrosion/Irritation

#### Skin irritation

Based on the data available, the chemical is considered to have potential to cause corrosion in vivo. There is sufficient evidence to warrant hazard classification as 'Skin Corrosion – Category 1.'

In an in vitro skin corrosion assay reported to be conducted in accordance with OECD TG 431, the chemical (100% concentration; no vehicle) was applied to reconstructed human epidermis (RHE) EpiDerm<sup>™</sup>. The mean tissue viability was 108.1% and 7.1% after 3 and 60 minutes respectively. Substances that reduced viability to less than 15% after 60 minutes are classified as corrosive. Limited study details are available (REACH).

In another similar skin corrosion study (OECD TG 431), 50  $\mu$ L of the chemical (100% concentration; no vehicle) was reported to be corrosive to skin in the EpiDerm<sup>TM</sup> model, as the cell viability was calculated to be 104.5% and 8.6% after 3 and 60 minutes respectively. Limited study details are available (REACH).

In an in vitro skin irritation study reported to be conducted according to OECD TG 439 (in vitro reconstructed human epidermis (RHE) test method for skin irritation. The chemical (100% concentration; no vehicle), was applied topically to a three dimensional RHE human skin model (EpiDerm<sup>™</sup>) for 1 hour. A mean tissue viability of 5.1% was reported for the chemical in this study, and it was determined to be at least irritating to the skin. Interpretation of results obtained from OECD TG 439 do not allow for distinction between irritation and corrosion (REACH).

The previously reported acute dermal toxicity/irritation study in rabbits showed dermal effects, under occlusive conditions at doses of 2500 and 5000 mg/kg bw. These included moderate erythema (4/4 animals), slight oedema (2/4 animals), and moderate oedema (2/4 animals) at 2500 mg/kg bw. Four out of 6 animals showed moderate erythema at 5000 mg/kg bw while 2/6 animals showed severe erythema and 6/6 animals were observed with moderate oedema (REACH; Bhatia et al., 2011) (refer to **Acute toxicity: dermal** section).

In another reported acute dermal toxicity/irritation study, at a dose of 5000 mg/kg bw for 24 hours, under occlusion conditions in rabbits, irritant effects were reported. It was reported that moderate to severe erythema was observed in 6/6 animals, severe oedema in 5/6 animals, scaling in 2/6 animals, and necrosis in 5/6 animals (Bhatia et al. 2011) (refer to **Acute toxicity: dermal** section).

In a skin irritation study conducted in NZW rabbits, a 0.5 mL aliquot of the chemical was applied to intact and abraded skin for 24 hours, under occlusion. At 24 and 27 hours post-application, moderate irritation and necrosis were observed in 3/6 animals and a primary irritation index of 3.1 was reported (Bhatia et al. 2011).

#### **Observation in humans**

In a limited study in human volunteers, 0.05%–0.5% of the chemical (in a base cream or in 99% ethanol) was dermally applied to the back, the forearm and the inside of the upper arm

of 82 subjects (for 24–48 hours under occlusive conditions) in a closed patch test. No skin reactions/irritation were reported during 30 min post patch removal (REACH; Bhatia et al., 2011).

No signs of skin irritation were observed in human maximisation pre-test with 8% of the chemical in petrolatum (after a 48-hour closed patch test), and during the induction phase of a Human Repeated Insult Patch Test (HRIPT) at 4% of the chemical in petrolatum (Bhatia et al., 2011) (refer to **Skin sensitisation: Observation in humans** section).

#### Skin sensitisation

Based on the data available, the chemical is not considered to be a skin sensitiser. The chemical was negative in the in vitro assays for the first 2 key events (KE) in the adverse outcome pathway (AOP) for skin sensitisation.

In an in vitro study conducted in accordance to OECD TG 442C (in chemico skin sensitisation: direct peptide reactivity assay (DPRA)), the chemical was dissolved in acetonitrile and mixed with cysteine- and lysine-containing peptides using defined ratios of peptide to test item (1:10 cysteine peptide, 1:50 lysine peptide). The chemical was reported as negative for peptide depletion, indicating that the chemical is not likely to have protein binding ability (REACH). This finding is consistent with in silico data reported below.

In an in vitro study conducted in accordance with OECD TG 442D (in vitro skin sensitisation: antioxidant response element (ARE)-Nrf2 luciferase LuSens test method), the activation of the ARE-dependent pathway was assessed by measuring luminescence induction. When tested in 1% DMSO (dimethyl sulfoxide) on the keratinocyte cell line LuSens for 48 hours at concentrations of 0.5–2000  $\mu$ g/mL, the chemical did not induce significant luciferase activity as fold induction remained <1.5 in at least 2 consecutive concentrations of statistical significance (where relative viability remained ≤70%). It was reported that the test substance did not have keratinocyte activating potential and therefore, was negative for the second KE in the AOP for skin sensitisation (REACH).

The EU Scientific Committee on Consumer Safety (SCCS) as part of its '*Opinion on fragrance allergens in cosmetic products*,' determined that there is insufficient evidence for the chemical to be classified as an '*established contact allergen in humans*' (based on limited human evidence, and predicted as a non-sensitiser based on structural alerts) (SCCS, 2012).

The chemical did not give protein binding alerts for skin sensitisation and respiratory sensitisation based on its molecular structure as profiled (in silico) by the Organisation for Economic Co-operation and Development (OECD) Quantitative Structure–Activity Relationship (QSAR) Toolbox v4.4.1(QSAR, 2021).

#### **Observation in humans**

In a human patch test with limited data, 218 subjects (with established contact allergy to fragrance ingredients) were administered the chemical via the epicutaneous route, under occlusive conditions. The induction phase consisted of a patch application of 5% concentration of the undiluted chemical (unspecified purity), with patch removal and evaluation of test site on days 2 and 4 post exposure. The subjects were then challenged at a 5% concentration of the chemical (in petrolatum), using the same dose method described for the induction phase. Between day 2 and 5 following, 48 hours after patch removal, 20/218 of subjects (0.9%) reported a positive dermal response. The challenge concentrations were

evaluated after treatment of 20 control subjects (without evidence of fragrance allergy) (REACH; Bhatia et al., 2011; SCCS, 2012).

No signs of skin sensitisation were observed in human maximisation pre-test with 8% chemical in petrolatum on 25 human subjects (17 female; and 8 males). The chemical was dermally applied to the forearms or backs of subjects under occlusive conditions), for 5 alternated ay 48 hour periods. Patch sites were then pre-treated with 2.5% of aqueous sodium lauryl sulfate (SLS) (under occlusive conditions). After a 10 day rest period, the challenge patches were applied to fresh sites for 48 hours (under occlusive conditions). Challenge sites were also pre-treated with aqueous SLS, and were observed 24 hours post patch removal (Bhatia et al. 2011).

In a Human Repeated Insult Patch Test (HRIPT), 50 male and female subjects were dermally induced with 4% of the chemical in petrolatum through an occlusive patch applied to the upper arms' of subjects for a period of 3 days a week (for a total of 15 applications). After a 14 day rest period, the subjects were then challenged at the same site for 24 hours. No skin reactions were reported 24 hours and 48 hours post patch removal (Bhatia et al. 2011).

### Repeat dose toxicity

Oral

Based on the data available, the chemical is not expected to cause serious systemic health effects following repeated oral exposure.

In a combined repeated dose/reproductive/developmental oral toxicity study (equivalent to OECD TG 422), male and female SD rats (12/sex/dose) were administered the chemical (by oral gavage in vehicle: corn oil) once daily at doses of 0, 100, 300, or 1000 mg/kg bw/day, 7 days a week (refer to **Reproductive & Developmental Toxicity** section). No significant adverse treatment-related effects were reported. The no observed adverse effect level (NOAEL) for systemic toxicity for the chemical was reported to be 1000 mg/kg bw/day for both sexes (the highest dose tested) (REACH).

Dermal

No data are available.

Inhalation

No data are available.

#### Genotoxicity

Based on the available in vitro data, the chemical is not considered to have genotoxic potential. No in vivo studies were available.

Several in vitro assays using the chemical gave negative results (REACH; Bhatia et al., 2011) in the following studies:

Bacterial mutation assays (various Salmonella typhimurium strains: TA 1535, TA 1537, TA 98, TA 100, and TA 102) with and without metabolic activation at doses up to 5000 μg/mL).

- A micronucleus test in human peripheral blood lymphocytes (doses up to 1362 µg/mL) with and without metabolic activation.
- Gene mutation assays (hypoxanthine-guanine phosphoribosyltransferase (HPRT) locus) in Chinese hamster lung fibroblasts (V79) cells with and without metabolic activation (doses up to 1600 µg/mL).

The chemical structure did not give DNA binding alerts for genotoxicity as profiled (in silico) by the OECD QSAR Toolbox v4.4.1 (QSAR 2021; REACH).

### Carcinogenicity

No data are available. Related compounds which are expected to be more reactive than benzenepropanol: cinnamyl alcohol and cinnamaldehyde, were not found to be carcinogenic (Belsito et al. 2011; NICNASa 2016; NICNASb 2016).

The chemical structure did not contain an alert for genotoxic carcinogenicity as profiled (in silico) by the OECD QSAR Toolbox v4.4.1 (QSAR 2021).

### Reproductive and development toxicity

Based on the data available, the chemical is not expected to cause specific reproductive or developmental toxicity effects. Any reproductive and developmental effects reported were only observed secondary to maternal toxicity and only at the highest dose.

In a combined repeated dose/reproductive and developmental toxicity study (OECD 422) previously described (refer to Repeated dose toxicity: Oral section), both sexes were dosed for 2 weeks prior to mating and continued through the day before sacrifice in males (at least 50 days), and continued through the lactation day (LD) 13 in females. Additional animals in recovery groups at 0 and 1000 mg/kg bw/day (6/sex/dose) were also orally administered the chemical but not mated, and then assigned to 2 weeks of recovery period after the completion of administration. No significant treatment related effects were reported in regard to general toxicity. At the highest dose (1000 mg kg bw/day), an increased number of dead or cannibalised pups and a decrease in viability index was reported (litter loss of 20 pups). However, it was reported other litters of this dose group were not significantly affected. Statistically significant decreased body weight in F1 generation pups of the highest dose group was reported on post-natal day (PND) 4 (94% of control) and PND 13 (92% of control) but were not considered adverse effects, as they were reported to be secondary to maternal toxicity of parental animals of the highest dose group. The NOAEL for reproduction/developmental toxicity was reported to be 300 mg/kg bw/day based on viability, body weight, and weight gain (REACH).

### References

NICNASa (National Industrial Chemicals Notification and Assessment Scheme) (2016) <u>IMAP</u> <u>Single Assessment Report - Chemical: Human health tier II assessment: 2-Propenal, 3-</u> <u>phenyl (Cinnamaldehyde; CAS No. 104-55-2)</u>, NICNAS, accessed August 2021.

NICNASb (National Industrial Chemicals Notification and Assessment Scheme) (2016) <u>IMAP</u> <u>Single Assessment Report - Chemical: Human health tier II assessment: 2-Propen-1-ol, 3-</u> <u>phenyl (Cinnamyl alcohol; CAS No. 104-54-1)</u>, NICNAS, accessed August 2021.

Belsito et al., 2011 (Belsito D; Bickers D; Bruze M; Calow P; Dagli M; Fryer A; Greim H; Miyachi Y; Saurat J and Sipes I (2011)). A toxicologic and dermatologic assessment of cinnamyl phenylpropyl compounds when used as fragrance ingredients. *Food and Chemical Toxicology* 49(2):S256–S257, doi: <u>https://doi.org/10.1016/j.fct.2011.07.053</u>

Bhatia et al., 2011 (Bhatia S, Wellington G; Cocchiara J; Lalka J; Letizia C and Api A (2011)). Fragrance material review on 3-phenyl-1-propanol. *Food and Chemical Toxicology* 49(2):S246–S251, doi: <u>https://doi.org/10.1016/j.fct.2011.07.050</u>

Chemwatch (n.d.) Galleria Chemica, Chemwatch website, accessed August 2021.

EC (European Commission) (n.d.) <u>Cosmetic Ingredient (CosIng)</u>, EC website, accessed July 2021.

IFRA (International Fragrance Association) (n.d.) <u>*Transparency List*</u>, IFRA website, accessed July 2021.

NLM (National Library of Medicine) (n.d.) <u>ChemIDplus Advanced Database</u>, NLM website, accessed August 2021.

OECD (Organisation for Economic Co-operation and Development) (2021) <u>Quantitative</u> <u>Structure-Activity Relationship Toolbox (Version 4.4.1)</u> [Computer software], OECD, accessed July 2021.

Personal Care Products Council (n.d.) <u>*Cosmetic Ingredient Identification Database*</u>, Personal Care Products Council website, accessed August 2021.

REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) (n.d.). <u>Registered Dossier for 3-phenylpropan-1-ol (CAS No. 122-97-4)</u>, European Chemicals Agency website, accessed July 2021.

SCCS (European Commission Scientific Committee on Consumer Safety) (2012) <u>Opinion on</u> fragrance allergens in cosmetic products (SCCS/1459/11), SCCS, accessed July 2021.

SPIN (Substances in Preparation in Nordic Countries) (n.d.) <u>SPIN Database</u>, SPIN website, accessed July 2021.

SWA (Safe Work Australia) (n.d.) <u>Hazardous Chemical Information System (HCIS)</u>, SWA website, accessed July 2021.

TGA (Therapeutic Goods Administration) (2021) <u>Standard for the Uniform Scheduling of</u> <u>Medicines and Poisons No.34 (Poisons Standard October 2021)</u>, TGA, accessed October 2021.

TGSC (The Good Scents Company). *Information System on 3-phenyl propyl alcohol (CAS No. 122-97-4)*, accessed July 2021.

TMIC (The Metabolomics Innovation Centre), 2019. <u>*Compound 3-Phenyl-1-propanol</u>* (FDB012188), accessed August 2021.</u>

UNECE (United Nations Economic Commission for Europe) (2017) <u>Globally Harmonized</u> <u>System of Classification and Labelling of Chemicals (GHS), Seventh Revised Edition,</u> UNECE, accessed July 2021.

US Environmental Protection Agency's Aggregated Computational Toxicology Resource (ACToR), <u>3-Phenylpropanol (CAS No. 122-97-4)</u>, accessed July 2021.

US HSDB (US National Library of Medicine's Hazardous Substances Database). <u>3-</u> <u>Phenylpropanol (CAS No. 122-97-4)</u>, accessed July 2021.

