



2-Hexenal: Human health tier II assessment

12 December 2019

- Chemicals in this assessment
- Preface
- Grouping Rationale
- Import, Manufacture and Use
- Restrictions
- Existing Worker Health and Safety Controls
- Health Hazard Information
- Risk Characterisation
- NICNAS Recommendation
- References

Chemicals in this assessment

Chemical Name in the Inventory	CAS Number
2-Hexenal	505-57-7
2-Hexenal, (E)-	6728-26-3

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

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 using a range of sources, including information from databases maintained by third parties, which include data supplied by industry. NICNAS has not verified and cannot guarantee the correctness of all information obtained from those databases. Reproduction or further distribution of this information may be subject to copyright protection. Use of this information without obtaining the permission from the owner(s) of the respective information might violate the rights of the owner. NICNAS does not take any responsibility whatsoever for any copyright or other infringements that may be caused by using this information.

ACRONYMS & ABBREVIATIONS

Grouping Rationale

Chemicals in this group are the α,β -unsaturated aldehydes 2-hexenal (mixed cis/trans isomers; CAS No. 505-57-7) and trans-2-hexenal (CAS No. 6728-26-3). The isomers of 2-hexenal are expected to have similar toxicological properties. Trans-2-hexenal is the predominant form in use; however, in some studies 2-hexenal is referred to by the CAS No. for the mixed isomers.

Import, Manufacture and Use

Australian

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

International

Trans-2-hexenal (CAS No. 6728-26-3) and the unspecified isomer of 2-hexenal (CAS No. 505-57-7) have cosmetic uses as fragrances (CpCat; CosIng).

The chemicals are listed on the International Fragrances Association (IFRA) transparency list (IFRA).

Trans-2-hexenal is used as a fragrance in domestic products including air fresheners at concentrations of 0.1–1 % (US HPD).

Trans-2-hexenal (CAS No. 6728-26-3) has reported non-industrial uses as a food additive and as an excipient in medicines (EFSA, 2018; TGA, 2019).

Trans-2-hexenal is an ingredient in e-cigarette liquids (NICNAS, 2019).

Restrictions

Australian

No restrictions for industrial use have been identified for 2-hexenal in Australia.

Trans-2-hexenal (CAS No. 6728-26-3) has restrictions for its non-industrial use as an excipient in medicines. The Therapeutic Goods Administration (TGA) permits for use 'only in combination with other permitted ingredients as a flavour or a fragrance. If used in a flavour, the total flavour concentration in a medicine must be no more than 5 %. If used in a fragrance, the total fragrance concentration in a medicine must be no more than 1 %' (TGA, 2019).

International

Trans-2-hexenal (CAS No. 6728-26-3) is listed in (Galleria Chemica):

- the EU Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products. Annex III: List of Substances which cosmetic products must not contain except subject to the restrictions laid down. The maximum allowable concentration in oral and other products is 0.002 % (CosIng); and
- the New Zealand Cosmetic Products Group Standard - Schedule 5 - Table 1: Components Cosmetic Products Must Not Contain Except Subject to the Restrictions and Conditions Laid Down with a concentration limit of 0.02 % in oral and other products.

Depending on the product, the concentration limits for trans-2-hexenal recommended by IFRA are 0.001–0.02 % (IFRA, 2009).

Existing Worker Health and Safety Controls

Hazard Classification

These chemicals are 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

These chemicals are linear α,β -unsaturated aldehydes that naturally occur in fruits and vegetables and may be used in flavouring and fragrances. Data from structurally similar α,β -unsaturated aldehydes or aldehydes with extended conjugation (such as (E,E)-2,4-hexadienal, CAS No. 142-83-6) are used to support the assessment conclusions where data are otherwise insufficient.

Toxicokinetics

Linear α,β -unsaturated aldehydes including trans-2-hexenal are rapidly absorbed, distributed, metabolised and excreted, predominantly in urine, with a small amount in faeces (Adams et al., 2008).

The detoxification of trans-2-hexenal is expected to occur via three pathways: oxidation to 2-hexenoic acid by aldehyde dehydrogenase (ALDH); reduction to 2-hexen-1-ol by aldose reductase (AR); or conjugation with reduced glutathione (GSH) either chemically or by glutathione S-transferase (GST) (EFSA, 2014).

Low levels of trans-2-hexenal (e.g. from food) are expected to be efficiently detoxified (Adams, 2008; EFSA, 2018). High concentrations may deplete intracellular glutathione (GSH), resulting in oxidative stress and the formation of protein and DNA adducts (Adams et al., 2008; EFSA, 2018).

Acute Toxicity

Oral

Based on the reported median lethal dose (LD50) values and in silico predictions, 2-hexenal is expected to have moderate acute toxicity and warrants hazard classification (see **Recommendation** section).

Median lethal dose (LD50) values of 780–1130 mg/kg bw were reported for trans-2-hexenal in rats. Observed sub-lethal effects included salivation, lachrymation and vasodilation. At the higher doses, convulsions preceded mortality (RTECS, Gaunt et al., 1971).

Sub-lethal doses of trans-2-hexenal (200–500 mg/kg bw, oral gavage) induced necrosis and dose-dependent hyperplasia of the forestomach mucosa in male F344 rats (Stout et al., 2008).

The chemical, 2-hexenal, is part of the training set in OASIS TIMES acute toxicity model with a reported LD50 of 780 mg/kg bw. The predicted (in domain) LD50 value was 695 mg/kg bw (OASIS-TIMES).

Dermal

Based on the reported LD50 value of 600 mg/kg bw for trans-2-hexenal in rabbits and LD50 values of structurally similar chemicals, 2-hexenal is expected to have moderate acute toxicity via the dermal route and warrant hazard classification (see **Recommendation** section).

Reported dermal LD50 values for the structurally related chemicals 2,4-hexadienal and trans-2-heptenal (CAS No. 18829-55-5) in rabbits were 240 mg/kg bw and 860 mg/kg bw, respectively (NICNAS; Monograph for trans-2-heptenal, 1988).

Inhalation

No data are available.

Corrosion / Irritation

Skin Irritation

Based on the weight of evidence from available experimental and in silico data, 2-hexenal may be irritating to the skin. However, data is insufficient to warrant hazard classification. Concentrations below 4 % are not expected to be irritating to human skin.

When applied to rabbit skin for 24 hours under occlusion trans-2-hexenal was moderately irritating (Monograph for hexen-2-al, 1979). No further details are available.

A structurally related chemical, 2-heptenal, was irritating to skin in acute toxicity studies in rabbits and guinea pigs after 24 hours under occlusion (Monograph for trans-2-heptenal, 1988).

These chemicals (2-hexenal; unspecified isomer) and 2-heptenal are part of the training set in the OASIS TIMES skin irritation model where they are reported to be irritating to skin based on experimental data. These chemicals were also predicted to be irritating to skin (in domain) with an alert for conjugated unsaturated aldehydes.

Eye Irritation

No data are available.

Observation in humans

In a 48-hour closed-patch test, trans-2-hexenal (4 % in petrolatum) produced no skin irritation (Monograph for hexen-2-al, 1979).

In a 48-hour closed-patch tests the structurally similar chemical, 2-heptenal (4 % in petrolatum), skin reactions were observed in 2/29 and 0/27 human volunteers (Monograph for trans-2-heptenal, 1988).

Sensitisation

Skin Sensitisation

Based available data, 2-hexenal is expected to be a skin sensitiser warranting hazard classification (See **Recommendations** section).

In a local lymph node assay (LLNA) conducted similarly to OECD TG 429, 2-hexenal (0.5, 2.0, 2.5, 5 or 10 % v/v) was applied topically to female CBA/J mice (number of animals not reported) in acetone/olive oil for three days. The reported stimulation indices (SI) were 1.2, 1.2, 2.3, 2.6, 6.4 and 5.5, respectively. The calculated concentration to produce a three-fold increase in lymphocyte proliferation (EC3) was 5.5 % indicating moderate sensitisation potential (REACH; Gerberick et al., 2005).

In another LLNA (with limited details available), topical applications of 0.5, 2.0, 2.5, 5 or 10 % (v/v) of trans-2-hexenal in ethanol/diethyl phthalate resulted in an EC3 value of 2.5 % (REACH).

An EC3 value of 1012 mg/cm² (corresponding to a concentration of ~4 %) was reported based on the weighted mean of 2 different LLNA studies listed in the RIFM database (Api et al., 2008).

Observation in humans

In a human repeated insult patch test (HRIPT), 50 volunteers were treated with 0.02 % (v/v) trans-2-hexenal in ethanol/diethyl phthalate on the upper back under occlusion. The treatment was repeated 9 times during the induction period. After ~14 days, challenge patches were applied on untreated test sites and scored after 24, 48, and 72 hours. One skin reaction was observed upon challenge with 2-hexenal (REACH).

In a human maximisation test in 25 volunteers no dermal reactions were observed at 4 % 2-hexenal in petrolatum (Monograph for hexen-2-al, 1979).

Repeated Dose Toxicity

Oral

Based on the available data, 2-hexenal is not expected to cause harmful systemic effects following repeated oral exposure. The main adverse effect of 2-hexenal is irritation of the forestomach when administered by gavage. This effect is not observed when the chemical is administered via the diet. Therefore, the forestomach local effect can be considered as irritation from direct contact with the chemical rather than a systemic effect.

In a repeat dose toxicity study, male F344 rats were administered 0, 10, 30 or 100 mg/kg bw (5 days/week for 4 weeks) trans-2-hexenal by gavage. Reduced body weights were observed. No haematological or biochemical changes attributed to treatment were observed. Epithelial hyperplasia at doses ≥ 30 mg/kg bw/day, and inflammation and necrosis at 100 mg/kg bw/day were reported in the forestomach (Stout et al., 2008).

In a 13-week feeding study, Carworth Farms Elias (CFE) rats (15/sex/dose) received trans-2-hexenal at 260, 640, 1600 or 4000 ppm in the diet equivalent to approximately 20, 50, 120 or 280 mg/kg bw/day for 13 weeks. There was a small reduction in food intake and bodyweight gain at the highest dose; however, this was attributed to a lower palatability of the diet. Male rats had non-dose related decreases in haemoglobin concentration and erythrocyte counts. Haematology in females was not affected. Serum and urinary analysis was normal. Relative ovary weights were increased at all dose levels. However, the effect was not dose-dependent and not accompanied by any histopathological changes in the ovaries or any other reproductive organ. Ovary weights were not increased in a follow up study, in rats receiving 4000 ppm in diet. No other changes in organ weights were reported from either of the studies (Gaunt et al., 1971).

Daily gavage administration of trans-2-hexenal at 200 mg/kg bw in rabbits for 13 weeks resulted in gastric haemorrhage and ulcers. Ovary weights were not affected (Gaunt et al., 1971).

Dermal

No data are available.

Inhalation

No data are available.

Genotoxicity

Based on the weight of evidence from the available genotoxicity studies, these chemicals may be genotoxic in vitro particularly, without metabolic activation, in sensitive bacterial strains (TA100/104) and mammalian cell lines with low detoxification capability (e.g. low GST and ALDH). In vivo mutagenicity and clastogenicity studies were mainly negative.

This suggests that although the chemicals in this group are highly reactive and bind to DNA, effects may be limited to the point of contact with the body. While the available data is not sufficient for classification, genotoxicity cannot be ruled out.

In vitro

The chemical, 2-hexenal, was:

- Positive without metabolic activation in two bacterial reverse mutation assays in *Salmonella typhimurium* TA 104 at concentrations of up to 196 $\mu\text{g}/\text{plate}$ and >490 $\mu\text{g}/\text{plate}$ (EFSA, 2018);
- Positive without metabolic activation in several bacterial reverse mutation assays in *S. Typhimurium* TA 100 at concentrations up to 2500 $\mu\text{g}/\text{plate}$ (EFSA, 2018)
- Negative in multiple in point mutation studies in *S. typhimurium* strains TA98, TA102, TA1535 and TA1537 and at concentrations up to 5000 $\mu\text{g}/\text{plate}$ (concentrations above 200 $\mu\text{g}/\text{plate}$ were bacteriostatic) (REACH; EFSA, 2018; Adams, 2008);
- Negative in a bacterial reverse mutation assay in *S. typhimurium* TA 100 at concentrations of 0.01–0.50 $\mu\text{L}/\text{plate}$ with a standard cell density, but positive in a 3-fold bacterial cell density assay (Eder et al., 1992; EFSA, 2014);

- Negative in an SOS chromosome assay in *Escherichia coli* strains PQ37 and PQ243 at concentrations up to 43 µg/plate (EFSA, 2014);
- Positive in an unscheduled DNA synthesis (UDS) in rat hepatocytes at concentrations of up to 700 nmol/mL (EFSA, 2018).
- Positive in a DNA single strand break assay in L1210 mouse leukemia cells at concentrations up to 50 µg/plate (Eder et al., 1993; EFSA, 2014).
- Positive in a sister chromatid exchange (SCE) and micronucleus assay in primary human blood lymphocytes and human B-lymphocytes (Namalva cells) at concentrations of up to 250 µM (EFSA, 2018).
- Positive in a chromosomal aberration assay in human lymphocytes (Namalva cells; from 100 µM), but negative in human lymphocytes at concentrations up to 250 µM (EFSA, 2018).

Trans-2-hexenal has been shown to form DNA adducts in a ³²P-postlabelling assay in rat and human primary colon mucosa (concentrations as low as 0.4 mM) (Adams et al., 2008).

In vivo

In a combined comet and micronucleus assay conducted in accordance with OECD TG 474 and OECD TG 489, trans-2-hexenal (in corn oil) was administered to male Han Wistar rats (6/dose) at doses of 87.5, 175 or 350 mg/kg bw/day (oral gavage) for 3 days. No significant difference in the mean micronucleus frequency was reported compared to the negative control (EFSA, 2018). Due to the variability in response in some of the treatment groups, the comet assay was repeated (n=3). Overall, results were inconsistent or fell within the range of the laboratory historical control data. It was concluded that the increase in mean tail intensity reported in some animals was not reproducible or biologically relevant (EFSA, 2018).

In a Muta(TM)Mouse (lacZ/GalE) assay combined with an in vivo micronucleus assay male, CD2-lacZ80/HazfBR mice received trans-2-hexenal (120, 235 or 350 mg/kg bw, n=6/dose) by oral gavage for 28 days. No significant increase in mutation frequency was reported in the liver or duodenum. The micronucleus assay was conducted in peripheral normochromatic erythrocytes (NCE) 4 and 31 days post-treatment (OECD TG 474 recommends once at 36–48 hours following final treatment). No significant increase in the frequency of micronuclei was reported (EFSA, 2018).

In an in vivo micronucleus assay in bone marrow performed in accordance with OECD TG 474, mice (n=5/dose/sex) received trans-2-hexenal (250, 500 or 1000 mg/kg bw). No significant increase in the frequency of micronuclei was reported. Notably, at the highest dose a 35 % reduction in the polychromatic erythrocytes was reported, indicating the chemical was cytotoxic to bone marrow at this dose (EFSA, 2018)

In an in vivo UDS assay performed in accordance with OECD TG 486, male rats received 2-hexenal (unspecified isomer, 200 or 500 mg/kg bw). No significant increase in the net nuclear grain counts were reported (EFSA, 2018)

Trans-2-hexenal has been shown to form DNA adducts in a ³²P-postlabelling assay in male Fischer 344 rats (n=4/group, 50-500 mg/kg bw) (EFSA 2018). DNA adducts were reported in the forestomach, but not in liver after exposure to 100 mg/kg bw/day (5 days/week) trans-2-hexenal for 1 or 4 weeks. Similar effects were not seen at lower doses (10 or 30 mg/kg bw/day) and suggest genotoxicity was limited to the site of contact (forestomach) (Stout et al., 2008, EFSA, 2018).

Observations in humans

The chemical was administered to healthy volunteers (n=7/study) as an aqueous mouthwash (10 ppm). This resulted in a 2-fold increase in the number of micronuclei present in exfoliated buccal mucosa cells over the subsequent 4 day observation period (Dittberner et al., 1997).

Carcinogenicity

Based on the limited data available, there is insufficient evidence of carcinogenicity to warrant hazard classification.

High doses resulting in necrosis at the site of contact (see **Repeat Dose Toxicity: Oral** section) and regenerative cell proliferation or formation of DNA adducts following GSH depletion may contribute to carcinogenicity.

In a 3-day epigenetics study, mice (CBA/CA(H-2K), AKR/J(H-2K and C3He-mg(H-2K) and rats (Long Evans, Fischer 344 and Wistar) (n=6/sex/dose) were administered 50 mg/kg bw/day of trans-2-hexenal via intraperitoneal injection (i.p.) and necropsied at 24, 48 or 72 hours. No significant differences between treated and control groups were reported. Over-expression of the Ha-ras and p53 gene were not observed (Nadasi et al., 2005).

In an 18-month study, mice and rats received 3 doses of 50 mg/kg bw trans-2-hexenal on day 1, 8 and 15. No tumours were reported in the CBA/Ca mice, one AKR/J mouse developed leukaemia and three C3He-mg mice had malignant diseases (liver carcinoma and kidney tumours). One of the Long Evans rats had carcinoma of the parotid gland and one had an adenocarcinoma, additional details were not available. Two lung tumours were found in the F344 rats and Wistar rats (Nadasi et al., 2005).

Reproductive and Developmental Toxicity

No data are available.

Risk Characterisation

Critical Health Effects

The critical health effects for risk characterisation include systemic acute effects (acute toxicity from oral and dermal exposure) and local effects (skin sensitisation).

Although some α,β -unsaturated aldehydes are positive for genotoxicity in vitro, evidence of in vivo genotoxicity and carcinogenicity occur only following use of highly irritating concentrations of aldehydes, and are not considered relevant to the expected uses (low concentrations as fragrance ingredient) and routes of exposure in humans (Adams, 2008).

Public Risk Characterisation

Although use in cosmetic and domestic products in Australia is not known, the chemicals are reported to be used at low concentrations in cosmetic and domestic products overseas. The use of trans-2-hexenal in cosmetic products is currently restricted in the EU and IFRA has recommended concentration limits of 0.001–0.02 % (IFRA, 2015). Given the uses identified, it is unlikely that the public will be exposed to the chemicals at doses sufficient to cause harm.

Due to lack of data suitable for assessing the inhalation risk (NICNAS, 2019), e-cigarette use has not been assessed in this report. NICNAS will continue to monitor for relevant toxicological data.

Occupational Risk Characterisation

During product formulation, 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 chemicals at lower concentrations could also occur while using formulated products containing the chemicals. The level and route of exposure will vary depending on the method of application and work practices employed.

Given the critical systemic acute and local health effects, the chemicals could pose an unreasonable risk to workers unless adequate control measures to minimise dermal exposure are implemented. Good hygiene practices to minimise oral exposure are expected to be in place. The chemicals 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.

Available data support an amendment to the hazard classification in the Hazardous Chemical Information System (HCIS) (Safe Work Australia) (refer to **Recommendation** section).

NICNAS Recommendation

Further risk management is required. Sufficient information is available to recommend that risks for workplace health and safety be managed through changes to classification and labelling.

Due to lack of data suitable for assessing the inhalation risk (NICNAS, 2019), e-cigarette use has not been assessed in this report. Further assessment may be required should relevant data become available.

Regulatory Control

Work Health and Safety

These chemicals are 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	Harmful if swallowed - Cat. 4 (H302) Toxic in contact with skin - Cat. 3 (H311)
Sensitisation	Not Applicable	May cause an allergic skin reaction - Cat. 1B (H317)

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

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

* Existing Hazard Classification. No change recommended to this classification

Advice for industry

Control measures

Control measures to minimise the risk from oral and dermal exposure to the chemicals 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 chemicals are used. Examples of control measures that could minimise the risk include, but are not limited to:

- health monitoring for any worker who is at risk of exposure to the chemicals, 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 chemicals.

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 chemicals 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 these chemicals has not been undertaken as part of this assessment.

References

Adams TB, Gavin CL, Taylor DV, Waddell WJ, Cohen SM, Feron VJ, Goodman J, Rietjens IMCM, Marnett LJ, Portoghese PS, Smith RL 2008. The FEMA GRAs assessment of alpha, beta-unsaturated aldehydes and related substances used as flavour ingredients. *Food and Chem. Toxicol.*, 26 pp. 2935-2967

Api AM, Basketter DA, Cadby PA, Cano MF, Ellis G, Gerberick GF, Griem P, McNamee PM, Ryan CA & R Safford (2008) Dermal sensitization quantitative risk assessment (QRA) for fragrance ingredients. *Regulatory Toxicology and Pharmacology* 52:3-23.

Cosmetic Ingredients & Substances (CosIng) Database. European Commission. Accessed November 2019 at <http://ec.europa.eu/consumers/cosmetics/cosing/>

Dittberner U, Schmetzera B, Golzerb P, Eisenbrand G, Zankla G 1997. Genotoxic effects of trans-2-hexenal in human buccal mucosa cells in vivo. *Mutat Res Genet Toxicol Environ Mutagen*, 390 pp. 161-165.

European Food Safety Authority (EFSA) 2014. Scientific Opinion on flavouring Group Evaluation 200 (FGE.200): 74 a, b-unsaturated aldehydes and precursors from subgroup 1.1.1 of FGE.19. *EFSA Journal*, 12(6) 3709.

European Food Safety Authority (EFSA) 2018. Scientific Opinion on Flavouring Group Evaluation 200, Revision 1 (FGE.200): 74 a,b-unsaturated aldehydes and precursors from subgroup 1.1.1 of FGE.19. *EFSA Journal*, 16(10):5422

Fragrance raw materials monographs for hexen-2-al. (1979). *Food and Chemical Toxicology*, pp. 424.
<https://doi.org/10.1016/B978-0-08-023775-6.50307-6>

Fragrance raw materials monographs for trans-2-heptenal. (1988). *Food and Chemical Toxicology*, 26(4), 331.
[doi:https://doi.org/10.1016/0278-6915\(88\)90166-4](https://doi.org/10.1016/0278-6915(88)90166-4)

Galleria Chemica. Accessed November 2019 at <http://jr.chemwatch.net/galleria/>

Gaunt IF, Colley J, Wright M, Creasy M, Grasso P, Gangolli SD 1971. Acute and short-term toxicity studies on trans-2-hexenal. Food Cosmet. Toxicol. 9(6) pp. 775-786.

Gerberick FG, Ryan CA, Kern PS, Schlatter H, Dearman RJ, Kimber I, Pattlewicz GY, Basketter DA 2005. Compilation of Historical Local Lymph Node Data for Evaluation of Skin Sensitization Alternative Methods. Dermatitis, 16(4) pp 157-202.

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

International Fragrance Association (IFRA) Transparency List. Accessed November 2019 at <https://ifrafragrance.org/initiatives/transparency/ifra-transparency-list>

Nadasi E, Varjas T, Pajor L, Ember I 2005. Carcinogenic potential of trans-2-hexenal is based on epigenetic effect. In vivo, 19 pp. 559-562.

National Industrial Chemicals Notification and Assessment Scheme (NICNAS) 2019. Non-nicotine liquids for e-cigarette devices in Australia: chemistry and health concerns. Accessed November 2019 at <https://www.nicnas.gov.au>

National Industrial Chemicals Notification and Assessment Scheme (NICNASa). Human Health Tier II assessment for 2,4-hexadienal. Australian Government Department of Health. Available at [nicnas.gov.au](http://www.nicnas.gov.au)

International Fragrance Association (IFRA) 2009. The 43th Amendment of the IFRA Standard – Trans-2-hexenal Accessed December 2019 at <http://www.ifraorg.org/en-us/standards>

Optimised Approach based on Structural Indices Set–Tissue MEtabolism Simulator (OASIS–TIMES) Version 2.28.1. Developed by the Laboratory of Mathematical Chemistry (OASIS LMC). Available at <http://oasis-lmc.org/products/software.aspx>

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Dossier. Trans-2-hexenal (CAS No. 6728-26-3). Accessed November 2019 at <https://echa.europa.eu>

Registry of Toxic Effects of Chemical Substances (RTECS). Accessed November 2019 at <http://ccinfoweb2.ccohs.ca/rtecs/records/CB2450000.html>

Safe Work Australia. Hazardous Chemical Information System (HCIS). Accessed November 2019 at <http://hcis.safeworkaustralia.gov.au/>

Stout MD, Bodes E, Schoonhoven R, Upton PB, Travlos GS and Swenberg JA 2008. Toxicity, DNA binding, and cell proliferation in male F344 rats following short-term gavage exposures to trans-2-hexenal. Toxicol Pathol. 2008 Feb;36(2):232-46.

The Poisons Standard October 2019. The Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No. 25. Accessed November 2019 at <https://www.tga.gov.au/publication/poisons-standard-susmp>

Therapeutic Goods (Permissible Ingredients) Determination No. 3 of 2019. Australian Government Department of Health. Accessed Dec 2019 at <https://www.legislation.gov.au/Details/F2019L01472>

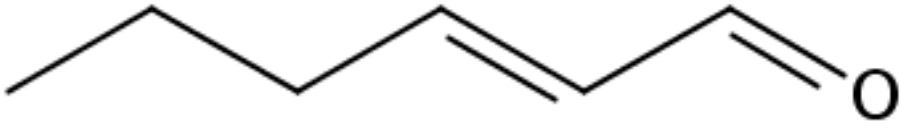
United States Environmental Protection Agency (US EPA) Chemical and Product Categories database (CPCat). Accessed November 2019 at <https://www.epa.gov/chemical-research/chemical-and-products-database-cpdat>

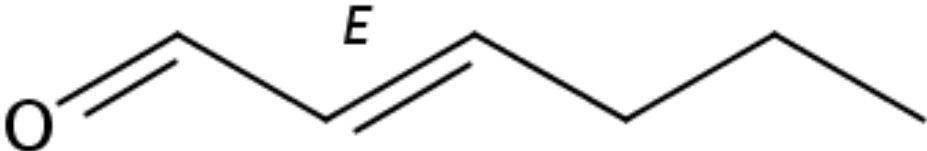
US Household Products Database. US Department of Health and Human Services. Accessed November 2019 at <http://householdproducts.nlm.nih.gov/advancedsearch.htm>

Last Update 12 December 2019

Chemical Identities

Chemical Name in the Inventory and Synonyms	2-Hexenal 2-hexen-1-al
---	----------------------------------

CAS Number	505-57-7
Structural Formula	
Molecular Formula	C6H10O
Molecular Weight	98.14

Chemical Name in the Inventory and Synonyms	2-Hexenal, (E)- 2-Hexenal, trans-leaf aldehyde
CAS Number	6728-26-3
Structural Formula	
Molecular Formula	C6H10O
Molecular Weight	98.14

Share this page