

Substance Information Document

Terpinolene

1. Substance identity

Name	Terpinolene
Synonyms	Isoterpinene Terpinolen Tereben Alpha-terpinolene
IUPAC Name	1-methyl-4-propan-2-ylidenecyclohexene
CAS	586-62-9

2. Toxicological information

Respiratory tract irritation – A European Food Safety Authority (EFSA) panel concluded that it should be irritating to the respiratory tract.

Skin irritation – An EFSA panel concluded that it should be irritating to the skin. A study showed that it was not irritating to human skin when applied at a concentration of 20% in a 48-hour close patch test.

Eye irritation – An EFSA panel concluded that it should be considered irritating to the eye. However, because of a rabbit study showing that all signs of irritation (after instillation into one eye of the rabbit) resolved after 7 days, terpinolene does not meet the European Union Classification, Labelling, and Packing (CLP) criteria as a category 2 eye irritant.

Respiratory sensitization – substance-specific data were not identified.

Skin sensitization – An EFSA panel concluded that it should be considered as skin sensitizer. In human, no skin sensitization reactions were produced in a human maximation test in which 24 subjects were treated with terpinolene at 20%. In silico prediction showed that it was predicted to be non-sensitizer; however, several of its metabolites could be weak or strong sensitizers.

Acute inhalation toxicity – Substance-specific data in human was not identified. Exposure to 0.04 or 0.4 mg/cage (but not 0.004 or 4 mg/cage) reduced the spontaneous motor activity of mice significantly, with animals becoming calm 10 minutes after exposure.

Acute oral toxicity – The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) concluded that chemical is expected to have low oral toxicity. Substance-specific data in human were not identified. The oral LD50 was determined at 3753 mg/kg bw (rats) and 3762 mg/kg bw (mice).

Acute dermal toxicity - NICNAS concluded that chemical is expected to have low dermal toxicity. Substance-specific data in human were not identified. The dermal LD50 was reported at >5000 mg/kg/bw (rabbits) and >4330 mg/kg bw (rats).

Repeat-dose inhalation toxicity – Substance-specific data were not identified

Repeat-dose oral toxicity - NICNAS concluded that chemical is not expected to cause serious damage to health. Substance-specific data in humans were not identified. NOAELs at 161.5 mg/kg bw/day (female rats) and 294.6 mg/kg bw/day (male rats) were reported based on the observed changes in body weight gain at the highest dose tested. REACH registrants use the NOAEL of 161.5 mg/kg bw/day to calculate an inhalation DNEL of terpinolene.

Repeat-dose dermal toxicity – Substance-specific data were not identified.

Genotoxicity – NICNAS concluded that chemical is not expected to be genotoxic. Investigators at the US FDA’s CTP concluded that terpinolene was predicted as negative (non-genotoxic) in mutagenicity and clastogenicity (in silico) models.

Carcinogenicity - NICNAS concluded that chemical is not expected to be carcinogenic.

Reproductive and developmental toxicity - NICNAS concluded that chemical is not expected to be specific reproductive or developmental toxicants. REACH registrants use the NOAEL of 161.5 mg/kg bw/day for reproductive and developmental toxicity.

JECFA	JECFA Evaluations-TERPINOLENE- (inchem.org)
FEMA	The FEMA GRAS assessment of aliphatic and aromatic terpene hydrocarbons used as flavor ingredients (femaflavor.org)
EFSA	http://dx.doi.org/10.2903/j.efsa.2019.5721 http://dx.doi.org/10.2903/j.efsa.2015.4067 http://dx.doi.org/10.2903/j.efsa.2015.4053 http://dx.doi.org/10.2903/j.efsa.2011.2178 http://dx.doi.org/10.2903/j.efsa.2009.931
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	Terpinolene C10H16 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

In an investigation into the most common flavoring ingredients added to e-liquids on the Dutch market, terpinolene was identified in 0.84% of e-liquid samples. The investigators noted that such flavorings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	Scientific Committee on Consumer Products (europa.eu)
EMA	-
PUBMED	Biological properties of terpinolene evidenced by in silico, in vitro and in vivo studies: A systematic review - PubMed (nih.gov) The sedative effect of inhaled terpinolene in mice and its structure-activity relationships - PubMed (nih.gov)



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