Substance Information Document

Phenethyl Isovalerate

1. Substance identity

Name	Phenethyl Isovalerate
Synonyms	2-Phenylethyl 3-methylbutanoate 2-Phenylethyl isovalerate
IUPAC Name	2-phenylethyl 3-methylbutanoate
CAS	140-26-1

2. Toxicological information

Phenethyl isovalerate is a naturally occurring compound in food. It belongs to the Phenethyl ester group, which has been extensively assessed by JECFA. It has been observed with other compounds in the same group as phenethyl isovalerate that upon entry within the human body the chemical is metabolized to relatively non-toxic metabolites and eliminated out of the human body via excretion primarily in the urine. Based on this information it can be concluded that the chemical Phenethyl isovalerate is likely to exhibit a low bio-accumulation potential.

Acute toxicity of phenethyl isovalerate when administered dermally has been demonstrated to be very low in rabbits. The LD50 value has been found to be greater than 5000 mg/kg bw. Phenethyl isovalerate has not been tested in any acute oral toxicity study, however, the LD50 values of members in the same chemical group were shown to be range from 1500 mg/kg bw for phenethyl alcohol (CAS no. 60-12-8) to greater than 15,000 mg/kg bw for phenethyl phenylacetate (CAS no. 102-20-5). This indicates that the acute oral toxicity of phenethyl isovalerate is likely to be low. No inhalation data were available.

The dermal irritation potential of phenethyl isovalerate has been evaluated with OECD TG 439. Results indicated that the chemical is considered to be not irritating to the human skin. No eye irritation study was available but based on QSAR prediction, the chemical is likely not an eye irritant. No skin sensitization study is available on phenethyl isovalerate, but based on QSAR prediction, the chemical is likely not sensitizing to human skin.

No repeated dose toxicity study was identified for phenethyl isovalerate. But several studies were available for other members of the chemical group. The lowest reported NOEL is < 1.5 mg/kg bw/day for phenethyl senecioate (CAS no. 42078-65-9), which is based on observed kidney lesion in a 90-day oral toxicity study in rats.

Based on QSAR prediction, phenethyl isovalerate is not mutagenic in vitro in Salmonella typhimurium strain TA 97 and TA 102 with and without S9 metabolic activation system. The prediction can be further supported by the data from other members in the chemical group showing that when tested at concentrations up to 5000 µg/ml or 50 mg/plate, none of the group members (i.e., Phenethyl alcohol, phenylacetaldehyde, phenylacetic acid, ethyl phenylacetate, isobutyl phenylacetate, isoamyl phenylacetate, and para-tolylacetaldehyde) was mutagenic in various strains of Salmonella typhimurium (e.g., TA98, TA100, TA1535, TA1537 and TA1538).

No reproductive toxicity study was available for phenethyl isovalerate. But studies with phenethyl alcohol given orally (Bottomley et al., 1987) or dermally (Palmer et al., 1986) at high dose indicated that this group of chemicals has little reproductive or developmental toxicity.

No information on carcinogenicity was available.

JECFA	Phenylethyl Alcohol, Aldehyde, Acid and Related Acetals and Esters and Related Substances (JECFA Food Additives Series 50) (inchem.org)
FEMA	PHENETHYL ISOVALERATE | FEMA (femaflavor.org)
EFSA	Scientific Opinion on the safety and efficacy of phenyl ethyl alcohols, phenylacetic acids, related esters, phenoxyacetic acids and related esters (chemical group 15) when used as flavourings for all animal species - - 2012 - EFSA Journal - Wiley Online Library
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	Phenethyl isovalerate | C13H18O2 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

No substance specific data were identified.

SCENIHR	-
EMA	-
PUBMED	RIFM fragrance ingredient safety assessment phenethyl isovalerate, CAS Registry Number 140-26-1 - PubMed (nih.gov)

Reference

- Bottomley, A.M., Ratcliffe, H.E., John, D.M., Anderson, A. & Dawe, I.S. (1987) Effect of dietary administration of micro-encapsulated phenylethyl alcohol on pregnancy of the rat (embryotoxicity study). Unpublished report to RIFM. Submitted to WHO by Flavor and Extract Manufacturers' Association of the United States.
- Palmer, A.K., Bottomley, A.M., Ratcliffe, H.E., Clark, R. & John, D.M. (1986) Effect of phenylethyl alcohol (PEA) on pregnancy of the rat. Unpublished report from Huntingdon Research Center to RIFM. Submitted to WHO by Flavor and Extract Manufacturers' Association of the United States.