Substance Information Document

cis-3-Hexen-1-yl acetate

1. Substance identity

Name	cis-3-Hexen-1-yl acetate
Synonyms	(Z)-3-Hexenyl acetate; (Z)-Hex-3-enyl acetate; cis-3-Hexenyl acetate; cis-3-Hexenyl ethanoate
IUPAC Name	[(Z)-hex-3-enyl] acetate
CAS	3681-71-8 (refers to the cis isomer)

2. Toxicological information

Genotoxicity testing (chromosome aberration test and Ames test) on cis-3-hexen-1-yl acetate were negative. No substance-specific carcinogenicity data were identified. In a 48-hour patch test, cis-3-hexen-1-yl acetate in petrolatum at 10% was not irritating when applied under occlusive conditions to the skin of a small number of subjects. No irritation was detected after undiluted cis-3-hexen-1-yl acetate was applied on rabbit skin 24 hours under occlusion.

The oral LD50 value of cis-3-hexen-1-yl acetate was determined to be >5000 mg/kg bw in rats indicating a very low order of acute oral toxicity. A 24-hour dermal LD50 value of >5000 mg/kg bw for cis-3-hexen-1-yl acetate was reported in rabbits (Wohl, 1974), indicating a very low order of acute dermal toxicity.

Repeated-dose oral toxicity study on cis-3-hexen-1-yl acetate with reproduction/developmental toxicity screening test in rats determined the NOAEL for reproductive and developmental toxicity to be 1000 mg/kg bw/day (the highest tested dose), however, the NOEL for systemic toxicity was determined to be 300 mg/kg bw/day based on these effects in male rats (weights of the seminal vesicles and prostate gland were increased in males at the top dose of 1000 mg/kg bw/day).

EFSA noted that the oral rat NOAEL of 127 mg/kg bw/day derived from a repeated-dose toxicity study on hex-3(cis)-en-1-ol (CAS RN 928-96-1) (cis-3-hexen-1-ol via drinking water) can be extrapolated to cis-3-hexen-1-yl acetate, based on “similarity in structure and metabolism”.

The Joint FAO/WHO Expert Committee on Food Additives concluded that the use of cis-3-hexen-1-yl acetate as a food flavouring is of “no safety concern” at then-current estimated intakes of 640 and 57 µg/person/day in Europe and the US, respectively.

JECFA	910. Esters/aliphatic acyclic prim. alcohols/aliphatic linear saturated carb. acids (WHO Food Additives Series 40) (inchem.org) 9789241660679_eng.pdf (who.int)
FEMA	4. GRAS Substances (3125-3249).pdf (femaflavor.org)
EFSA	Scientific Opinion on Flavouring Group Evaluation 06, Revision 4 (FGE.06Rev4): Straight- and branched-chain aliphatic unsaturated

	primary alcohols, aldehydes, carboxylic acids and esters from chemical groups 1, 3 and 4 (wiley.com) Safety and efficacy of non-conjugated and accumulated unsaturated straight-chain and branched-chain, aliphatic primary alcohols, aldehydes, acids, acetals and esters belonging to chemical group 4 when used as flavourings for all animal species - - 2016 - EFSA Journal - Wiley Online Library
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	cis-3-Hexenyl acetate | C8H14O2 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

No substance-specific addictiveness data were identified. In an investigation into the most common flavouring ingredients added to e-liquids on the Dutch market, cis-3-hexen-1-yl acetate was identified in 9.18% of e-liquid samples. The investigators noted that such flavourings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	-
EMA	-
PUBMED	Comprehensive overview of common e-liquid ingredients and how they can be used to predict an e-liquid's flavour category - PubMed (nih.gov)