

## Substance Information Document

### Hexanoic acid

#### 1. Substance identity

Name	Hexanoic acid
Synonyms	Caproic acid Capronic acid Hexoic acid Pentanecarboxylic acid
IUPAC Name	hexanoic acid
CAS	142-62-1

#### 2. Toxicological information

Hexanoic acid was reported to be a skin irritant in several laboratory animal studies, and in vitro assays and an Expert Panel for the US CIR concluded that it is corrosive at concentrations of 70%. Erythema was seen in 1/10 and 7/10 volunteers receiving daily patches of 5.8 or 11.6% hexanoic acid, respectively. Hexanoic acid was also severely irritating to the eyes of rabbits when tested at 15% and was indicated as corrosive to the bovine eye in a guideline in vitro assay. No respiratory tract irritation data are available.

A RIFM Expert Panel recently concluded that hexanoic acid is not considered a skin sensitizer, based on the existing substance-specific data, and data on the read-across compound heptanoic acid. In maximization tests, no skin sensitization was seen in humans exposed to 1% hexanoic acid or guinea pigs tested with up to 100% heptanoic acid.

Hexanoic acid appears to be of low acute inhalation systemic toxicity (no deaths in rats exposed to vapour approaching saturation (1368 mg/m<sup>3</sup>) for 8 hours, and in mice a 2-hour inhalation LC50 of 4100 mg/m<sup>3</sup> was determined). It displays a moderate order of acute oral systemic toxicity in rats (LD50 value of 1886 mg/kg bw) and low toxicity in mice (LD50 value of 5000 mg/kg bw). Results from acute dermal studies have been mixed, with rabbit LD50 values ranging from 580->5000 mg/kg bw.

Repeated-dose studies on hexanoic acid are generally of limited quality. In a reproductive study of unknown reliability, the only significant finding was "unspecified" clinical observations in maternal rats at 1000 mg/kg bw/day. The REACH registrants considered repeated-dose toxicity data on the read-across compound docosanoic acid key in their evaluation of hexanoic acid. In a high-quality combined repeated-dose toxicity and reproduction/developmental toxicity screening test, the NOAEL was 1000 mg/kg bw/day (the highest tested dose). RIFM recently concluded that hexanoic acid does not present a concern for genotoxicity. This conclusion was based on guideline bacterial reverse mutation (Ames) assays on hexanoic acid and the read-across compound nonanoic acid, and a guideline in vitro micronucleus test on nonanoic acid. No carcinogenicity data are available.

The TCEQ has established a chronic general population RfC of 0.001 mg/m<sup>3</sup> for inhaled hexanoic acid.

JECFA	<a href="#">906. Saturated aliphatic acyclic linear primary alcohols, aldehydes and acids (WHO Food Additives Series 40) (inchem.org)</a>
FEMA	<a href="#">0320 FEMA GRAS 29 (femaflavor.org)</a>
EFSA	<a href="#">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)</a>
ECHA – REACH dossier	<a href="#">Registration Dossier - ECHA (europa.eu)</a>
PUBCHEM	<a href="#">Hexanoic acid   C6H12O2 - PubChem (nih.gov)</a>
CIR	<a href="#">facids042019finalrep.pdf (cir-safety.org)</a>
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, hexanoic acid (reportedly providing a “heavy, fatty, cheesey-sweaty” flavour) was identified in 11% 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	<a href="#">Comprehensive overview of common e-liquid ingredients and how they can be used to predict an e-liquid's flavour category - PubMed (nih.gov)</a>