Substance Information Document

Citral

1. Substance identity

Name	Citral
Synonyms	Citral GERANIAL (2E)-3,7-dimethylocta-2,6-dienal trans-Citral *(non-exhaustive list)*
IUPAC Name	(2E)-3,7-dimethylocta-2,6-dienal
CAS	5392-40-5

2. Toxicological information

The local NOAEC for respiratory irritation was at 20 mg/m^3 (from a rat 13-week inhalation study involving 6-hour exposures (5 days/week)). In shorter-term inhalation studies, a NOAEC for eye irritation was at 230 mg/m^3. The NOAEC for oral or gastrointestinal irritation was also at 230 mg/m^3 (from a rat 21-day inhalation study or from exposure by gavage in repeated-dose studies).

Citral is classified as a skin irritant (Under EU Classification, Labelling and Packaging (CLP)), although 48-hour exposures to 1-8% were not irritating to humans. It is also recognized as a skin sensitizer. An no expected sensitization induction level (NESIL) was reported for human skin at 1400 µg/cm2. However, a modified local lymph node assay (LLNA) did not identify statistically significant evidence of respiratory sensitization in mice.

Citral exhibits low acute toxicity by the inhalation, oral and dermal routes. An inhalation LC50 in rodents was at 83,800 mg/m^3. The oral LD50 values were 4950-6800 mg/kg BW in rats and 2007-3297 mg/kg BW in mice (note, one lower rat LD50 of 500 mg/kg BW was reported). Dermal LD50 values in rats and rabbits were reported starting at 2000 mg/kg BW.

A systemic NOAEC from repeated-dose toxicity tests (including a 13-week inhalation study) in rats was at 65 mg/m^3. A chronic oral NOAEL (based on reduced growth) in rats was at 100 mg/kg BW/day. In the equivalent mouse study, a NOAEL or a LOAEL at 60 mg/kg BW/day was considered.

Citral is considered non-genotoxic. A NOAEL for reproductive toxicity in rat was at 1000 mg/kg BW and a NOAEL for developmental toxicity (in rabbit) was at 60 mg/kg BW/day. No adverse effects on the reproduction or development of rats were reported after gavage up to 250 mg/kg BW/day. There were no adverse effects on reproduction or development at 230 mg/m^3 in a rat inhalation study.

Inhalation Health-Based Guidance Value (HBGVs) were not identified, but oral HBGVs were available (0.6 mg/kg BW/day' RIFM).

JECFA	WHO | JECFA
FEMA	24. GRAS Substances (4430-4666).pdf (femaflavor.org)
EFSA	http://dx.doi.org/10.2903/j.efsa.2016.4512 http://dx.doi.org/10.2903/j.efsa.2013.3392 http://dx.doi.org/10.2903/j.efsa.2011.2139 http://dx.doi.org/10.2903/j.efsa.2010.1402 http://dx.doi.org/10.2903/j.efsa.2009.1081
ECHA – REACH dossier	Substance Information - ECHA (europa.eu)
PUBCHEM	Citral | C10H16O - 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, citral, geranial, and neral were identified in 5.62, 0.8 and 0.75% of e-liquid samples, respectively. The investigators noted that such flavorings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	Opinion of the Scientific Committee on Consumer Products on dermal sensitisation quantitative risk assessment (citral, farneso (europa.eu)
EMA	-
PUBMED	-