

Substance Information Document

beta-Ionone

1. Substance identity

Name	beta-Ionone
Synonyms	4-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-3-buten-2-one
IUPAC Name	(E)-4-(2,6,6-trimethylcyclohexen-1-yl)but-3-en-2-one
CAS	14901-07-6

2. Toxicological information

In its scientific opinions on α,β -unsaturated alicyclic ketones and precursors, the EFSA CEF Panel concluded that a concern for genotoxic potential could be ruled out for beta-ionone. While results of Ames tests were negative, beta-ionone was mutagenic in an *umu* assay, and produced equivocal results using the MultiCASE chromosomal aberration test in CHL model. Single intraperitoneal injection up to 750 mg beta-ionone/kg bw induced no micronuclei in a OECD TG 474 and GLP compliant study. A NOAEL for developmental toxicity was reported as 500 mg/kg bw/day based on a decrease in pregnancy rate and resorption rate increased at a maternally dose of 1000 mg/kg bw/day.

No skin irritation was seen in human closed patch tests in which ionone was applied to the skin at 2 or 20% for up to 72 hours, or at 100% for 24 hours. 2 out of 205 contact dermatitis patients had positive sensitization reactions after the 48 hour-application of 5% beta-Ionone (in petrolatum). In rabbits, 100% beta-ionone caused skin erythema and very slight oedema at 24 hours but resolved after 72 hours. Undiluted beta-ionone caused eye irritations in rabbits that were resolved within 24 to 72 hours.

An increase in motility (14%) was reported after groups of four Swiss mice were exposed to a "low concentration" (no details provided) of beta-ionone via inhalation for 1 hour. Areas of bright red tissue were noted in the lungs of mice after a single oral dose of 5000 or 10,000mg/kg bw/day, and labored breathing was reported as a clinical sign of toxicity. 5330 and 7120 mg/kg bw for beta-ionone in mice, and 4950 mg/kg bw for ionone (60% alpha-ionone and 40% beta-ionone) have been reported as acute oral LD₅₀ values in rats, indicating a (very) low order of acute oral toxicity.

A 2-week inhalation study in rats using beta-ionone at concentrations up to 786.5 mg/m³ reported a NOAEC of 79 mg/m³, based on microscopic nasal lesions at the highest dose. 13 weeks oral feeding study determined the NOAEL of trans-beta-ionone for systemic toxicity as 72 and 83 mg/kg bw/day for males and female based on liver, kidney and thyroid findings at 720 and 801 mg/kg bw/day for males and female. In another 90 days study, 100 mg/kg bw/day caused body weight gain reduction in females, and therefore a NOAEL of 10 mg/kg bw/day was reported. No adverse effects were reported in a 90-day study in which rats received diets providing 11.6 (males) and 13.1 (females) mg beta-ionone/kg bw/day. Liver damage occurred at 500 mg/kg bw/day after rats received a diet containing, ionone (60% alpha-and 40% beta-) for 17weeks.

JECFA set a Acceptable Daily Intake of 0-0.1 mg/kg bw for alpha-and beta-ionone. EFSA and JECFA concluded that the use of beta-ionone as a food flavouring is of “no safety concern” at then-current estimated intakes of 130-150 and 100µg/person/day in Europe and the US, respectively.

JECFA	WHO TRS 710 WHO TRS 891
FEMA	3. GRAS Substances(2001-3124)_0.pdf (femaflavor.org)
EFSA	http://www.efsa.europa.eu/en/efsajournal/doc/4244.pdf ; https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2016.4475 ; https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2020.6338
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	beta-Ionone C13H20O - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

No substance-specific addictiveness data were identified. Although SCENIHR did not cite any studies or provide an opinion on the addictiveness of ionone (mixed isomers), it notes that the combination of alpha-and beta-ionone is characteristic of the scent of violets and is used in perfumery and flavouring to recreate their scent. No substance-specific attractiveness data were identified. However, as a flavouring agent it might, depending on the concentration used, increase the attractiveness of an ENDS product containing it.

SCENIHR	Final Opinion on Additives used in tobacco products (Opinion 1) (europa.eu)
EMA	-
PUBMED	-