Substance Information Document

gamma-Valerolactone

1. Substance identity

Name	gamma-Valerolactone
Synonyms	*gamma*-Pentalactone Dihydro-5-methyl-2(3H)-furanone 4-Methyl-4-hydroxybutanoic acid lactone 4-Valerolactone 4-Pentanolide Pentano-1,4-lactone 4-Hydroxypentanoic acid lactone 5-Methyldihydro-2(3H)-furanone
IUPAC Name	5-methyloxolan-2-one
CAS	108-29-2

2. Toxicological information

No respiratory, oral, and eye irritation/sensitization human data are available. No irritation was reported when *gamma*-valerolactone at a concentration of 10% was applied to the skin of an unspecified number of subjects in a 48-hour occluded patch test. RIFM concluded that *gamma*-valerolactone "does not present a concern for skin sensitisation under the current, declared levels of use".

No substance specific data were identified for oral, Inhalation, and dermal acute and repeated-dose toxicity in humans. In rats, the oral and dermal LD_{50} value was reported as >5000 mg/kg bw for acute administration. In inhalation studies, repeated doses of *gamma*-valerolactone were administered by inhalation to rats and rabbits, showing no signs of illness (800-10,000 mg/m^3). Among four studies assessing repeated oral administration, *gamma*-valerolactone showed signs of toxicity only in one, with a NOEL of 500 mg/kg bw/day. Repeated dermal administration (33 days) did not show signs of systemic illness up to 2000 mg/kg bw.

Based on an Ames assay, an in vitro micronucleus test, and a bluescreen assay, RIFM Expert Panel concluded that *gamma*-valerolactone is not expected to be genotoxic.

No human carcinogenicity data were found. In mice exposed to 67 mg/kg bw/injection for 3 weeks (and followed up to 24 months), no tumors developed.

No reproductive and developmental toxicity data are available in human. No reproductive and developmental toxicity was found in rats.

JECFA	908. Aliphatic lactones (WHO Food Additives Series 40) (inchem.org)
FEMA	GAMMA-VALEROLACTONE | FEMA (femaflavor.org)

EFSA	Scientific Opinion on Flavouring Group Evaluation 10, Revision 3 (FGE.10Rev3): Aliphatic primary and secondary saturated and unsaturated alcohols, aldehydes, acetals, carboxylic acids and esters containing an additional oxygenated functional group and lactones from chemical groups 9, 13 and 30 (wiley.com)
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	gamma-Valerolactone | C5H8O2 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

Gamma-Valerolactone has been reported to be a mild to weak inhibitor of CYP2A6, a cytochrome P450 enzyme involved in the metabolism of nicotine. However, the SCENIHR noted that "it seems unlikely that these compounds (including *gamma*-valerolactone) will inhibit nicotine metabolism at the concentrations used in cigarettes". Also, *gamma*-lactones, including *gamma*-valerolactone, are used as flavouring agents in many consumer products, potentially increasing the attractiveness of an ENDS product containing them.

Gamma-Valerolactone was found in 0.74% of the e-liquids in the Dutch market. The investigators noted that such flavorings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	Final Opinion on Additives used in tobacco products (Opinion 1) (europa.eu)
EMA	-
PUBMED	Comprehensive overview of common e-liquid ingredients and how they can be used to predict an e-liquid's flavour category