

## Substance Information Document

### *gamma-Decalactone*

#### 1. Substance identity

Name	<i>gamma</i> -Decalactone
Synonyms	2-Decalactone 4-Hexyl- <i>gamma</i> -butyrolactone 4-Hydroxydecanoic acid, <i>gamma</i> -lactone 5-Hexyldihydro-2(3H)-furanone Decan-4-olide <i>gamma</i> -Decanolactone Hexyl-4-hydroxybutanoic acid lactone
IUPAC Name	5-hexyloxolan-2-one
CAS	706-14-9

#### 2. Toxicological information

No *gamma*-decalactone-specific data for acute or repeated-dose toxicity were identified in humans and acute or repeated-dose toxicity is very low in laboratory animals. The oral LD50 value in rats and mice has been calculated as >5000 mg/kg bw and 4696 mg/kg bw, respectively. In rabbits, the dermal LD50 value was >5000 mg/kg bw. In an early feeding study in rats, no adverse effects were reported; hence the NOAEL for *gamma*-decalactone was identified as 32 mg/kg bw/day (the only dose tested).

An EFSA CEF Expert Panel noted that although genotoxicity data were limited for a group of lactones (for which *gamma*-decalactone was identified as a supporting substance), there were no indications of concerns for genotoxicity (EFSA, 2012). According to a RIFM Expert Panel, *gamma*-decalactone is not expected to be genotoxic. This conclusion was largely based on read-across data from a bacterial reverse mutation (Ames) assay on *gamma*-octalactone (CAS 104-50-7) and an in vivo micronucleus test on *gamma*-nonalactone (CAS 104-61-0). With regards to carcinogenicity, investigators from the US FDA's CTP using four in silico models for rodent carcinogenicity predicted *gamma*-decalactone to be negative (non-carcinogenic) in all four models.

No indications of reproductive or developmental effects [extent of examination unclear] were identified in an early study with rats; hence the NOAEL was identified as 32 mg/kg bw/day (the only dose tested). With regards to local effects, *gamma*-Decalactone was only found to be "moderately irritating" to the skin of rabbits, when applied neat to the intact or abraded skin for 24 hours under occlusion. A RIFM expert panel concluded that *gamma*-decalactone "does not present a concern for skin sensitisation".

JECFA	<a href="#">908. Aliphatic lactones (WHO Food Additives Series 40) (inchem.org)</a>
FEMA	<a href="#">3. GRAS Substances(2001-3124) 0.pdf (femaflavor.org)</a>

EFSA	<a href="#">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 - - 2012 - EFSA Journal - Wiley Online Library</a>
ECHA – REACH dossier	<a href="#">Registration Dossier - ECHA (europa.eu)</a>
PUBCHEM	<a href="#">gamma-Decalactone   C10H18O2 - PubChem (nih.gov)</a>
CIR	-
OSHA	-

### 3. Addictiveness and attractiveness

The European Commission’s Scientific Committee on Emerging and Newly Identified Health Risks note that various aliphatic lactones, including *gamma*-decalactone, may increase the bioavailability of nicotine, for example by inhibiting nicotine metabolism. However, they provide no summaries of studies investigating the addictiveness of *gamma*-decalactone, nor do they provide an opinion or highlight a concern for such an effect. In addition, *gamma*-decalactone strongly increases membrane fluidity of living cells. It rapidly diffused into model phospholipid bilayers (within 2 min), modifying their general physical state; and strongly increased membrane fluidity in yeast (*Yarrowia lipolytica*). “This property can have a possible influence in the fluidity of the lung epithelium”, [which may increase the bioavailability of nicotine].

In an investigation into the most common flavouring ingredients added to e-liquids on the Dutch market, *gamma*-decalactone (reportedly providing a “coconut-peach” flavour) was identified in 18.2% of e-liquid samples. The investigators noted that such flavourings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	<a href="#">Final Opinion on Additives used in tobacco products (Opinion 1) (europa.eu)</a>
EMA	-
PUBMED	<a href="#">Interaction of an odorant lactone with model phospholipid bilayers and its strong fluidizing action in yeast membrane - PubMed (nih.gov)</a>  <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>