

## Substance Information Document

gamma-dodecalactone

### 1. Substance identity

Name	gamma-dodecalactone
Synonyms	gamma-Dodecalactone 4-Dodecanolide 5-octyloxolan-2-one 2(3H)-Furanone, dihydro-5-octyl-
IUPAC Name	5-octyloxolan-2-one
CAS	2305-05-7

### 2. Toxicological information

Acute oral toxicity was assessed in Wistar rats administered a single dose of gamma-dodecalactone at 2000 mg/kg by gavage. No mortality and no signs of toxicity were observed during the first 4 hours in females or the 14-day observation period thereafter. During necropsy, no macroscopic findings were observed. Acute oral toxicity was assessed in Wistar rats following dermal application of gamma-dodecalactone and 0.5, 1, 2, 4 and 6 hours later. Each animal was inspected daily for the next 14 days. gamma-dodecalactone applied to 3 females at a limit dose of 2000 mg/kg body weight did not cause death. No signs of toxicity were observed at the dosage of 2000 mg/kg body weight during the first 4 hours or 14-day observation period. During necropsy no macroscopic findings were noticed. In a repeated-dose toxicity study in Wistar rats orally administered with 50, 300 and 750 mg/kg of body weight/day, gamma-dodecalactone did not cause mortality and had no visible toxic effects. NOAEL for systemic toxicity and reproduction toxicity in males and females was concluded to be 750 mg/kg. The mutagenic potential of gamma-dodecalactone was assessed using *S. typhimurium* and *E. coli*. gamma-dodecalactone showed no genotoxicity. gamma-dodecalactone showed no toxicity to reproduction in Wistar rats orally administered with 50, 300 and 750 mg/kg of body weight/day. NOAEL for males and females was concluded to be 750 mg/kg. Aliphatic lactones, such as gamma-dodecalactone, are generally metabolised to innocuous products (many of which are endogenous in humans); at the estimated level of intake as flavouring substances (below the thresholds of concern of 1800 µg/person/day for structural class I).

JECFA	<a href="https://www.fao.org/food-safety-quality">Food safety and quality: details (fao.org)</a>
FEMA	<a href="https://www.femaflavor.org/GAMMA-DODECALACTONE">GAMMA-DODECALACTONE   FEMA (femaflavor.org)</a>
EFSA	<a href="https://www.efsa.europa.eu/en/efsajournal/doc/25122/attachment/68122">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-Dodecalactone   C12H22O2 - PubChem (nih.gov)</a>
CIR	-
OSHA	-

### 3. Addictiveness and attractiveness

The addictive effect of nicotine may be increased due to a higher bioavailability of nicotine if the metabolism rate of nicotine is reduced. gamma-dodecalactone is a mild to weak inhibitor of CYP2A6, an enzyme within the P450 enzyme system, involved in the metabolism of nicotine. However, with IC50-values in the range 560-12,000 µM, it seems unlikely that these compounds will inhibit nicotine metabolism at the concentrations used in cigarettes. Regarding attractiveness, lactones are known flavouring agents for food and are added to tobacco products for flavouring (in addition to also being tobacco constituents) and providing coumarinic and coconut tastes.

SCENIHR	<a href="http://ec.europa.eu/health/scientific_committees/emerging/docs/scenih_r_o_051.pdf">http://ec.europa.eu/health/scientific_committees/emerging/docs/scenih_r_o_051.pdf</a>
EMA	-
PUBMED	<a href="#">RIFM fragrance ingredient safety assessment, γ-dodecalactone, CAS Registry Number 2305-05-7 - ScienceDirect</a>