Substance Information Document

Guaiacol

1. Substance identity

Name	Guaiacol
Synonyms	1-Hydroxy-2-methoxybenzene 2-Methoxyphenol o-Methylcatechol
IUPAC Name	2-methoxyphenol
CAS	90-05-1

*Non answered, IUPAC Name was not found.

2. Toxicological information

Guaiacol is included in SCHEER's priority list of tobacco additives. Among reasons for its inclusion in the list was that guaiacol is reported to be a respiratory tract, skin and eye irritant. No guaiacol-specific data were identified a low repeated-dose toxicity following inhalation or dermal treatment in laboratory animals or humans. In rats, oral treatment of a structurally-related compound (4-methoxyphenol) yielded a NOAEL of 0.25% corresponding to 125 mg/kg bw/day. The permissible concentration of guaiacol vapours is 0.02 mg/L. The oral LD50 of guaiacol in rats is 520-725 (mg/kg bw). When given subcutaneously, the fatal dose [of guaiacol] for guinea pigs and rats is 0.9 g/kg. Subcutaneous administration (6.25-400 µL/40 g [0.17-11 mg/kg bw]) of guaiacol to male Swiss Webster mice produced tachycardia and hyperactivity, followed by sedation, hypnosis, high hypothermic effect and in higher doses (25-400 µL/40 g [0.70-11 mg/kg bw]), had a lethal effect.

With regards to genotoxicity, guaiacol is included in SCHEER's priority list of tobacco additives due the fact that apart from the absence of mutagenicity tested with the Ames test, the only genotoxicity test on mammalian cells gave positive results (SCE16 in human lymphocytes) and concluded that these data have to be confirmed or denied by means of results coming from appropriate in silico/in vitro methods.

Guaiacol was predicted as positive (carcinogenic) in male rats and negative (non-carcinogenic) in female rats and in male and female mice by investigators from the US FDA's CTP using four *in silico* models for rodent carcinogenicity. Administration for 104 weeks of 4-methoxyphenol caused an increase in atypical hyperplasia followed by the presence of papillomas and squamous cell carcinomas.

No guaiacol-specific data were identified for reproductive and developmental toxicity.

JECFA	PHENOL AND PHENOL DERIVATIVES (inchem.org)
FEMA	0320 FEMA GRAS 29 (femaflavor.org)

EFSA	Flavouring Group Evaluation 58 (FGE.58) Consideration of phenol derivatives evaluated by JECFA (55th meeting) structurally related to ring substituted phenolic substances evaluated by EFSA in FGE.22 (2006) (Commission Regulation (EC) No 1565/2000 of 18 July 2000) - Opinion of the Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in contact with Food (AFC) (wiley.com) Scientific Opinion on Flavouring Group Evaluation 22, Revision 1 (FGE.22Rev1): Ring-substituted phenolic substances from chemical groups 21 and 25 - - 2011 - EFSA Journal - Wiley Online Library
ECHA – REACH dossier	Registration Dossier - ECHA (europa.eu)
PUBCHEM	Guaiacol | C7H8O2 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

Neither the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks nor the Scientific Committee on Health, Environmental and Emerging Risks provide summaries of studies specifically investigating its addictiveness, nor do they provide an opinion or highlight a concern for such an effect. Guaiacol is included in SCHEER's priority list of tobacco additives. Among reasons for its inclusion was that "guaiacol is a known flavouring agent for food and is added to tobacco products for flavouring (one of the factors potentially contributing to attractiveness). More data are needed on the amount of guaiacol that imparts a noticeable flavour other than tobacco. Its use as a local anaesthetic can enhance smoke inhalation, thus potentially contributing to addictiveness". "In line with its function as a dental pulp sedative, guaiacol, depending on the absorbed dose, can cause neurological, hemodynamic (shock), respiratory, metabolic (metabolic acidosis), renal (acute tubular necrosis), digestive and hematologic adverse effects". "Its use as local anaesthetic can favour the smoke inhalation, thus potentially contributing to addictiveness ... There is a possibility that its use results in a characterising flavour: Odour detection threshold: 3-21ppb".

Scientists from the Dutch National Institute for Public Health and the Environment (RIVM) identified guaiacol as an ingredient added to at least 100 e-liquids of the EU-CEG dataset and it was reported to be present in 6.05% of all e-liquids and within several flavour categories. The investigators noted that such flavourings 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 - PubMed (nih.gov)