Substance Information Document

2,3,5-Trimethylpyrazine

1. Substance identity

Name	2,3,5-trimethylpyrazine
Synonyms	Trimethylpyrazine
IUPAC Name	2,3,5-trimethylpyrazine
CAS	14667-55-1

2. Toxicological information

JECFA, EFSA and FEMA have concluded that no human health concerns were identified on 2,3,5-trimethylpyrazine.

No acute or repeated-dose inhalation toxicity data were noted. A single study reported an oral LD50 value of 806 mg/kg bw for rats, suggesting a potentially moderate order of acute oral toxicity. No significant adverse effects were seen in rats fed diets containing 2,3,5-trimethylpyrazine for 90 days, providing about 17-18 mg/kg bw/day. Evaluation included histopathological examination of the major organs and tissues.

EFSA experts concluded that a range of pyrazines and related substances, including 2,3,5-trimethylpyrazine, lack genotoxic potential, based on the absence of mutagenicity in bacteria (Ames test).

No substance-specific local effects, sensitisation or carcinogenicity data were identified. In addition, no good-quality laboratory animal reproductive or developmental toxicity data were identified.

JECFA	PYRAZINE DERIVATIVES (JECFA Food Additives Series 48) (inchem.org)
FEMA	4. GRAS Substances (3125-3249).pdf (femaflavor.org)
EFSA	Scientific Opinion on Flavouring Group Evaluation 17, Revision 3 (FGE.17Rev3): Pyrazine derivatives from chemical group 24 (wiley.com) Safety and efficacy of pyrazine derivatives including saturated ones belonging to chemical group 24 when used as flavourings for all animal species (wiley.com)
ECHA – REACH dossier	-
PUBCHEM	2,3,5-Trimethylpyrazine | C7H10N2 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

In one study, the presence of pyrazines, including 2,3,5-trimethyl pyrazine, in traditional cigarettes has been investigated. In the research paper, it has been noted that pyrazines act by chemosensory effects that reinforce the learned behaviour of smoking and that several pyrazine derivatives might enhanced dopamine release independently of nicotine.

In an investigation into the most common flavouring ingredients added to e-liquids on the Dutch market, 2,3-dimethylpyrazine was identified in 6% of e-liquid samples. The investigators noted that 2,3,5-trimethyl pyrazine providing a “baked potato, roasted nut, cocoa, coffee, burnt” flavour increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	-
EMA	-
PUBMED	A study of pyrazines in cigarettes and how additives might be used to enhance tobacco addiction - PubMed (nih.gov) Comprehensive overview of common e-liquid ingredients and how they can be used to predict an e-liquid's flavour category - PubMed (nih.gov)