Substance Information Document

2,5-Dimethylpyrazine

1. Substance identity

Name	2,5-Dimethylpyrazine
Synonyms	2,5-Dimethyl-1,4-diazine
IUPAC Name	2,5-dimethylpyrazine
CAS	123-32-0

2. Toxicological information

Expert-group described 2,5-dimethylpyrazine as respiratory tract irritant, however no sufficient data were identified. No acute toxicity data were recognised by the exert group. One study reported an oral LD50 value of 1000 mg/kg/bw in rats after administration of 2,5-dimethylpyrazine by gavage and observation for 14 days. The result indicated a moderate-low acute oral systemic toxicity.

EFSA experts considered existing data on pyrazine derivatives and concluded that "no genotoxic potential at gene or chromosome level is indicated for this group of flavourings". 2,5-Dimethylpyrazine was predicted as a known negative (non-genotoxic) in both mutagenicity models and negative in all clastogenicity models.

JECFA and EFSA concluded that the use of 2,5-dimethylpyrazine as a food flavouring is of "no safety concern", the current estimated intakes of 19-22 and 8 µg/person/day in Europe and the US was given.

No substance-specific existing expert-group inhalation, oral and dermal HBGVs 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	2,5-Dimethylpyrazine | C6H8N2 - PubChem (nih.gov)
CIR	-
OSHA	-

3. Addictiveness and attractiveness

In a study pyrazines derivative (including 2,5-dimethylpyrazine) were investigated in traditional cigarettes. In the research paper, they note that pyrazines act by chemosensory effects which results in enhanced dopamine release independently of nicotine.

One study result showed a mild tranquilising action of 2,5-dimethylpyrazine after administration (injection) of 100 mg/kg bw in mice.

In an investigation into the most common flavouring ingredients added to e-liquids on the Dutch market, 2,5-dimethylpyrazine was identified in 1.54% of e-liquid samples providing the specific “nuts” flavour category. The investigators noted that such flavourings increase e-cigarette attractiveness and use and thereby exposure to potentially toxic ingredients.

SCENIHR	-
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) A study of pyrazines in cigarettes and how additives might be used to enhance tobacco addiction - PubMed (nih.gov)