5-Methyl-2-furanmethanol

Toxicity monograph (with existing HCVs)

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Prepared by:

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INTRODUCTION

(b) (4) was asked to produce a toxicity monograph of 5-methyl-2-furanmethanol (CAS RN[1] 3857-25-8), focussing on the inhalation route of exposure, with inclusion of existing Health Criteria Values (HCVs) where available. Data on the inhalation of tobacco smoke containing the substance (if available) have not been included in this monograph.

EXPERTISE

(b) was founded[2] in 1961 to provide independent, high-quality research, information and advice on chemical toxicology to industry and governmental departments. Its risk assessors have been working together for many years (more than 40 years in some instances) and have a record of objectivity and scientific excellence. All senior and principal scientists in the current team are accredited and listed in the European (Eurotox) and UK Royal Society of Biology/British Toxicology Society Registers of Toxicologists and are thus bound by their specific codes of conduct.

TOXICITY DATA SEARCH CRITERIA[3]

Searches of the (b) (4) (see Appendix for details) identified the JECFA (2012) review, on which this monograph is based. A subsequent search of the primary literature was restricted to (b) (4) and Toxline (the toxicity subset of Medline, via TOXNET) in an attempt to identify more recent data since the 2012 review. The remainder of the TOXNET system (which includes HSDB, GENETOX, DART, CCRIS, IRIS, ITER and CPDB) and eChemPortal was also consulted. Since the key review focussed on the use of 5-methyl-2-furanmethanol (and structurally-related substances) in food and, as such, could not necessarily be relied upon to identify all critical local and systemic inhalation data, no date restriction was placed on searches in PubMed tailored to identify such information (and also cardiopulmonary data).

All searches were conducted in May 2018 using the CAS RN(s) and (in PubMed only) name and/or synonym(s) identified below, as appropriate.

The data summarised in this report refers to the unheated form unless otherwise stated.

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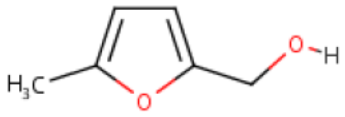
[1] Chemical Abstracts Service Registry Number.

[2] as the (b) (4)

[3] Disclaimer: searches are valid and complete as of the date of searching. (b) accepts no responsibility for the accuracy, completeness or sufficiency of any databases or searching platforms employed.

IDENTIFICATION, REACH STATUS AND EU CLASSIFICATION

Identifier	
Name	5-Methyl-2-furanmethanol
Synonyms(s)	5-Methylfurfuryl alcohol (5-methylfuran-2-yl)methanol
CAS RN	3857-25-8
REACH registration number[4]	Not REACH registered
Molecular formula	$C_6H_8O_2$
Molecular weight	112.13
Structure	
Classification, according to EU CLP (EC 1272/2008)	**Harmonised classification:** None available
	REACH joint registrants: None available

ADME[5]

No substance-specific data were identified on the ADME of inhaled 5-methyl-2-furanmethanol[6].

According to JECFA, systemically absorbed 5-methyl-2-furanmethanol is expected to undergo oxidation to 5-methyl-2-furoic acid (JECFA, 2012). No further ADME data on 5-methyl-2-furanmethanol were included in this 2012 JECFA review[7].

TOXICOLOGY

LOCAL EFFECTS

Respiratory tract irritation

No substance-specific data were identified.

[4] REACH registration numbers are substance and company specific. Therefore, the substance-specific part of the registration number is included here, from data disseminated on the ECHA 'registered substance' website.

[5] Absorption, Distribution, Metabolism and Excretion.

[6] ADME predictions could be estimated on the basis of the structure and physic-chemical properties, if required.

[7] According to JECFA (2012), ADME data on structurally-related furfuryl compounds is evidently available in earlier JECFA reports. 5-Methyl-3-furanmethanol was not, however, included in JECFA's older assessments, therefore these reports have not been consulted at this time.

Skin irritation
No substance-specific data were identified.

Eye irritation
No substance-specific data were identified.

Other local effects
No substance-specific data were identified.

SENSITISATION AND INTOLERANCE
Respiratory tract sensitisation
No substance-specific data were identified.

Skin sensitisation
No substance-specific data were identified.

Oral allergy/intolerance
No substance-specific data were identified.

INHALATION TOXICITY STUDIES – SYSTEMIC EFFECTS
Single dose toxicity
No substance-specific data were identified.

Repeated dose toxicity
No substance-specific data were identified.

TOXICITY STUDIES – OTHER EXPOSURE ROUTES
Single dose toxicity
No substance-specific data were identified.

Repeated dose toxicity
No substance-specific data were identified.

GENOTOXICITY
Expert-group opinions

In its evaluation of furfuryl alcohol "and related substances"[8], *in vitro* and *in vivo* studies [including the *in vitro* positive study on 5-methyl-2-furanmethanol described below] raised concerns regarding the potential genotoxicity of this group of related compounds (JECFA, 2012).

[8] Including 5-methyl-2-furanmethanol

Mammals (*in vivo*)
No substance-specific data were identified.

Mammalian cells (*in vitro*)
No substance-specific data were identified.

Micro-organisms
In a non-standard bacterial reverse mutation assay, *Salmonella typhimurium* strain TA100 and TA100-derived strains expressing human or rodent sulfotransferase (SULT) enzymes were treated with 5-methyl-2-furanmethanol at concentrations of up to 220 µg/plate[9] without added S9 mix[10]. No evidence of mutagenicity was observed in TA100. However, in TA100 strains expressing SULT 1A1, A2 and 1C2 and murine SULT 1a1, mutagenic effects were detected (Glatt *et al.*, 2012).

The results of this study, as well as other genotoxicity investigations conducted with structurally-related compounds, suggested that furfuryl alcohol [and 5-methyl-2-furanmethanol] is converted by intracellular sulfate conjugation to 2-sulfo-oxymethylfuran, an electrophile capable of reacting with DNA (JECFA, 2012).

Other
No substance-specific data were identified.

CARCINOGENICITY
No substance-specific data were identified.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY
No substance-specific data were identified.

CARDIOPULMONARY EFFECTS[11]
No substance-specific data were identified.

OTHER TOXICITY CONSIDERATIONS
No substance-specific data were identified.

EXISTING HEALTH CRITERIA VALUES (HCVs)
No substance-specific inhalation HCVs were identified.

[9] Low test concentration. Cytotoxicity not specified in JECFA (2012)
[10] Induced mammalian liver post-mitochondrial fraction used for metabolic activation.
[11] Potential effects on the heart, blood vessels and/or respiratory tract.

Although JECFA assigned a group ADI[12] of 0-0.5 mg/kg bw/day for furfuryl alcohol and its derivatives, newly available *in vitro* and *in vivo* studies raised genotoxicity concerns for these substances, and therefore the group ADI previously established "will need to be reconsidered" (JECFA, 2012).

REFERENCES

Glatt H, Schneider H, Murkovic M, Monien BH and Meinl W (2012). Hydroxymethyl-substituted furans: mutagenicity in *Salmonella typhimurium* strains engineered for expression of various human and rodent sulphotransferases. Mutagenesis 27, 41-48 [cited in JECFA, 2012].

JECFA (2012). Safety evaluation of certain food additives. Prepared by the seventy-sixth meeting of the Joint FAO/WHO Expert Committee on Food Additives. WHO Food Additives Series 67.
http://apps.who.int/iris/bitstream/handle/10665/77763/9789241660679_eng.pdf;jsessionid=AD279BC92AB22174827C29451EFBD675?sequence=1

[12] Acceptable Daily Intake.

APPENDIX: The (b) (4) database and databank

(b) (4)

(b) (4) includes information from peer-reviewed toxicology and nutrition journals as well as secondary sources and websites. In addition to primary literature on the health effects of chemicals, (b) covers official publications and evaluations issued by authoritative groups including:

- WHO/IPCS reports and evaluations (including CICADs and EHCs, and IARC, JECFA and JMPR monographs), and the WHO Air Quality and Drinking-Water Quality Guidelines
- OECD SIDS dossiers/SIARS
- IUCLID data sets
- EU Risk Assessment Reports
- EU expert committee opinions (including EU scientific committees, and EFSA scientific panels) and other reports from EU agencies and institutes etc (including ECHA, ECVAM, EMA and CPS&Q)
- ECETOC, HERA, Council of Europe and other pan-European programmes
- UK government agency (including Defra, EA, FSA, DoH, HSE, HPA, PSD and VMD) and advisory committee (e.g. COT, COM, COC, ACNFP, SACN, ACP, ACAF, VPC, VRC and ACRE) reports and evaluations
- Opinions from other UK organisations such as the Royal Society
- US agency reports and evaluations (EPA, ATSDR, FDA, NTP, OSHA, NCEA, CFSAN, CERHR, NIEHS, CDC, OEHHA and ACGIH)
- Health Canada evaluations
- BUA, DFG, BG Chemie and BfR reports and monographs
- Gezondheidsraad opinions, including those from its various committees such as DECOS
- RIVM reports
- Danish EPA reviews
- Reports and other information provided by Swedish governmental organisations, including the National Food Administration and the Swedish Chemicals Agency
- Nordic Expert Group for Criteria Documentation of Health Risks from Chemicals
- Australian agency reviews including NICNAS Priority Existing Chemical Assessments, APMVA reports and (jointly with New Zealand) FSANZ assessments
- Japanese Chemical Industry Ecology-Toxicology & Information Center reports
- CIR, RIFM and other specialist industry groups
- (b) **Toxicity Profiles**