Compound		2-Furaldehyde		Data collection sheet
N°CAS 98-01-1 C ₅ H ₄ O ₂ MW=96.08 1 ppb = 3.954 μg/m ³ (23°C	EU- Classification CLP (harmonise Acute tox. 4 (H31 (H331)	on: GHS08, GHS06, GHS02, GHS07 ed): Acute tox. 3 (H301), Eye irrit. 2 (12), STOT SE 3 (H335), Skin irrit. 2 (H		
Organisation name	REACH Registrant	ts German IAQ Guide Values	(Study)	(Workplace, according to GESTIS, 2016)
Risk value name	DNEL repeated dos inhalation, genera population	se RWI (protective) l RWII (health hazard)	RD ₅₀	Workplace Limit value (longtime, 8h average)
Risk value (μg/m³)	8000	RW I=10 RW II=100 (RW I=RW II×0.1)	Mice (B6C3F1) Mice (Swiss-Webster)	5000 (China) 8000 (Australia, Belgium, Canada, Denmark, Finland, Ireland, New Zealand, Singapore, South Korea, Spain, Sweden Switzerland, UK) 10000 (Latvia, Poland) 20000 (Austria, Hungary, USA-OSHA)
Risk value (ppb)			Mice (B6C3F1): 234 ppm (174–327) Mice (Swiss-Webster) 287 ppm (216–402)	
Reference period	subacute	subacute	acute	
Year	2008	2011	1984	
Key study	Not further referenc key study not publisl GLP-Study according OECD Guideline 41	ed, Arts JHE, Muijser H, hed Appel MJ, Kuper CF, Bessems JGM, Woutersen RA: Subacute (28-day) 2 toxicity of furfural in Fisher 344 rats: a comparison of the oral	Steinhagen WH, Barrow S: Sensory irritation structure– activity study of inhaled aldehydes in B6C3F1 and Swiss- Webster mice	Deviation of occupational exposure limits were not known to the author of this worksheet

	Reliability classified as 1 (reliable without	and inhalation route. Food Chem Toxicol 2004;	Toxicology and Applied	
	restriction)	42:1389-1399	Pharmacology 1984; 72:495–503	
Study type	Inhalation	Inhalation	Inhalation	
Species	Rat (Sprague-Dawley)	Rat (Fischer 344)	Mouse (B6C3F1) Mouse (Swiss- Webster)	
Duration of exposure in key study	28 days 0 / 4 / 8 / 20 mg/m ³ (nominal) 0 / 1.93 / 3.7 / 7.38 / 17.05 mg/m ³ (analytical) for 6hrs/day and 5 days/week 10 animals per sex and dose	28 days 0 / 20 / 40 / 80 / 160 / 320 / 640 /1280 mg/m ³ (nominal) 20 / 41 / 80 / 158 / 316 mg/m ³ (analytical) for 6hrs/day and 5 days/week and 160 / 320 / 640 /1280 mg/m ³ (nominal) 157 / 314 / 635 mg/m ³ (analytical) for 3hrs/day and 5 days/week 5 animals per sex and dose / Head-nose only	Head only exposition in body plethysmo- graph, 10 min acclim. / 5 min preexpos. / 10 min expos. / 5 min recov.	
		exposition in Battelle- Tubes		
Critical effect	Histopathology of nasal cavity (hyperplasia and inflammatory cell infiltration) at 20 mg/m ³ (nominal), but no systematic effects	Respiratory epithelial lesions (squamous metaplasia, atypical hyperplasia) in all 6h/day-groups, also transitional epithelium located in the anterior part of the nose was affected in all exposed	RD50	

				1
		were observed in animals		
		exposed for 3h/day,		
		however, at a lower		
		incidence and degree		
Critical dose value	8 mg/m ³ NOAEC (local)	20 mg/m^3		
Adjusted critical dose	Chronical inhalative	Chronical inhalative		
	exposition for general	exposition for general		
	population	population		
	8 mg/m^3	0.1 mg/m ³ RWII		
Single assessment	No factors applied	Exposure 24/6 × 7/5=5.6		
factors (see table		subacute to acute=6		
R.8.6)		Intraspecies		
		(irritation)=5		
		children=2		
		TAF=336		
Other effects		Olfactory epithelial		
		changes (epithelial		
		disarrangement) in		
		6hrs/day-groups ≥ 80		
		mg/m ³		
		Experiment stopped for \geq		
		640 mg/m ³ (6hrs/d)		
		because of many deaths		
Absolute odour threshold (from HSDB) 0.024 mg/m ³ (odour low); 20.0 mg/m ³ (odour high)				
Ruth JH: Odor Thresholds and Irritation Levels of Several Chemical Substances: A Review. American Industrial Hygiene Association				
Journal 1986;47: A-142–51				
Odour recognition threshold (from HSDB) 1 mg/m ³				
Verschueren K: Handbook of Environmental Data on Organic Chemicals. Volumes 1–2. 4th ed. John Wiley & Sons. New York, NY. 2001,				
p. 1183				
*Kuwabara Y, Alexeeff GV, Broadwin R, Salmon AG: Evaluation and application of the RD50 for determining acceptable exposure				
levels of airborne sensory irritants for the general public. Environmental Health Perspectives 2007; 115:1609–1616				
**Wolkoff P: Indoor air pollutants in office environments: Assessment of comfort, health, and performance. International Journal of				
Hygiene and Environmental Health 2013; 216:371–394				

Compound	2-Furaldehyde		Factsheet	
Parameter	Note	Comments	Value / descriptor	
EU-LCI value and status				
EU-LCI value	1	Mass/volume [µg/m ³]	10	
EU-LCI status	2	Draft/final	Final	
EU-LCI year of issue	3	Year when the EU-LCI value has been issued	2017	
General information				
CLP-INDEX-No.	4	INDEX	605-010-00-4	
EC-No.	5	EINECS – ELINCS - NLP	202-627-7	
CAS-No.	6	Chemical Abstracts Service number	98-01-1	
Harmonised CLP classification	7	Human health risk related classification	Acute tox. 3 (H301); Eye irrit. 2; Carc. 2; Acute tox. 4 (H312) STOT SE 3; Skin irrit. 2; Acute tox. 3 (H331)	
Molar mass and conversion factor	8	[g/mol] and [ppm – mg/m ³]	96.08 1 ppm = 3.95 mg/m ³	
Key data / database				
Key study, author(s), year	9	Critical study with lowest relevant effect level	Arts et al. (2004)	
Read across compound	10	Where applicable		
Species	11	Rat, human etc.	Rat (Fischer 344)	
Route/type of study	12	Inhalation, oral feed, etc.	Inhalation	
Study length	13	Days, subchronic, chronic	28 days (subacute)	
Exposure duration	14	Hrs/day, days/week	6hrs/day, 5 days/week	
Critical endpoint	15	Effect(s), site of	Epithelium lesions (nose, respiratory tract)	
Point of departure (POD)	16	LOAEC*L, NOAEC*L, NOEC*L, Benchmark dose, etc.	LOAEC	
POD value	17	[mg/m ³] or [ppm] or [mg/kg _{BW} ×d]	20 mg/m ³	
Assessment factors (AF)	18			
Adjustment for exposure duration	19	Study exposure hrs/day, days/week	5.6	
Study length	20	$sa \rightarrow sc \rightarrow c$ (R8-5)	6	
Route-to-route extrapolation factor	21		1	
Dose-response	22 a	Reliability of dose-response, LOAEL \rightarrow NOAEL	3	
	22 b	Severity of effect (R 8-6d)	1	
Interspecies differences	23 a	Allometric Metabolic rate (<i>R8-3</i>)	1	
	23 b	Kinetic + dynamic	2.5	
Intraspecies differences	24	Kinetic + dynamic Worker - general population	10	
AF (sensitive population)	25	Children or other sensitive groups	1	
Other adjustment factors	26	Completeness and consistency	1	

Quality of whole database		Reliability of alternative data (R8-6 d,e)	
Result			
Summary of assessment factors	27	Total Assessment Factor (TAF)	2520
POD/TAF	28	Calculated value (µg/m ³ and ppb)	7.94 $\mu g/m^3$ and 2.01 ppb
Molar adjustment factor	29	Used in read-across	-
Rounded value	30	[µg/m³]	10
Additional comments	31		
Rationale section	32		

Effects on exposed mucous membranes of the airways seem to be the most sensitive endpoint for inhalation of 2-furaldehyde. Two sub-acute 28-day studies with rats exposed at 6 hours a day for 5 days a week reported the same LOAEL of 20 mg/m³.

The LOAEL of 20 mg/m³ was taken as the point of departure (POD). The key study was published by Arts et al. (2004).0 The authors described respiratory epithelial lesions (squamous metaplasia, atypical hyperplasia). In addition, transitional epithelium located in the anterior part of the nose was affected in all exposed animals.

The following assessment factors were applied:

5.6=factor line 19 (adjustment for 6 hours/24 hours × 5 days/7 days) 6=factor line 20 (adjustment subacute 28-day exposition to chronic exposition) 2.5=factor line 23b for intraspecies (local) kinetic and dynamic variation 10=factor line 24 for interspecies variation

The total assessment factor (TAF) is 5.6×6×2.5×10=2520 leading to a POD/TAF=7.94 μg/m³ (2.01 ppb at 23°C).

Although the study referenced by the Reach registrants (ECHA registration dossier, 2017) showed that epithelial damage occurring at 20 mg/m³ was reversible within a 28-day post-exposure period, no reduced assessment factors were applied, as the dose-response curve of the substance is very steep. Arts et al. (2004) reported that 4 of 10 animals had died within 8 days of exposure at 640 mg/m³.

According to the rounding rules an EU-LCI of 10 μ g/m³ for 2-furaldehyde was derived.

The ECHA dissemination site displays supporting results of an unpublished study used for the DNEL derivation. In this study, exposed rats (Sprague-Dawley) developed effects on epithelia at nominal 20 mg/m³ (analytical 17 mg/m³). This study additionally tested lower concentrations, and a NOAEC of 8 mg/m³ (analytical, nominal 7.38 mg/m³) was reported (registrants derived a DNEL of 8 mg/m³ for the general population without any assessment factors applied). The DNEL key study, which was performed according to OECD Guideline 412 and complies with GLP standards, was rated by the Reach registrants to be reliable without restrictions. No further reference is available, so this study was not used for the EU-LCI derivation. However, the results support the current EU-LCI derivation. If the measured NOAEC of 7.38 mg/m³ is taken as the POD, and a TAF of 840 (5.6 for exposure, 6 for study length, 2.5 for interspecies and 10 for intraspecies differences) is applied, an alternative LCI of 8.79 µg/m³ can be calculated.

The study by Arts et al. (2004) was also used as the key study for the derivation of the German indoor air quality guide values (Ad-hoc-AG Innenraumrichtwerte, 2011); a RW II (health hazard guide value) of 100 μ g/m³ and a RW I (health precaution guide value) of 10 μ g/m³ were set.

Non inhalative administered 2-furaldehyde caused tumours in rats (cholangiocarcinoma) and mice (liver adenoma and liver carcinoma). These effects seem to be due to chronic inflammation or cytotoxicity at higher doses and not to genotoxicity (Ad-hoc-AG Innenraumrichtwerte, 2011, NTP, 1990). IARC (1995) decided not to classify the substance for its carcinogenicity to humans (Group 3), the CLP harmonised classification is Carc. 2 (suspected of causing cancer).

References

Ad-hoc-AG Innenraumrichtwerte: Richtwerte für 2-Furaldehyd in der Innenraumluft. Bundesgesundheitsblatt 2011; 54:510–5; https://www.umweltbundesamt.de/sites/default/files/medien/pdfs/furaldehyd.pdf (last retrieved on 4.12.2019).

Arts JHE, Muijser H, Appel MJ, Kuper CF, Bessems JGM, Woutersen RA: Subacute (28-day) toxicity of furfural in Fisher 344 rats: a comparison of the oral and inhalation route. Food Chem Toxicol 2004; 42:1389–1399.

ECHA-Registration Dossier for 2-furaldehyde (accessed 2017): Study-result for repeated dose toxicity: inhalation (Anonymous, 2008). https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14883/7/6/3/?document (last retrieved on 4.12.2019).

IARC: IARC monographs on the evaluation of carcinogenic risks to humans. 1995; Vol 63: Chapter 'Furfural' 414–435 http://monographs.iarc.fr/ENG/Monographs/vol63/mono63.pdf (last retrieved on 4.12.2019).

NTP: Toxicology and carcinogenesis studies of furfural (CAS No. 98-01-1) in F344/N rats and B6C3F1 mice (gavage studies). NTP 1990. TR 382; NIH Publication No. 90-2837. https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr382.pdf (last retrieved on 4.12.2019).