REVIEW

Workplace exposure standards and biological exposure indices

PROPOSAL DOCUMENT

March 2024

Te Kāwanatanga o Aotearoa
New Zealand Government

WORKSAFE
Mahi Haumaru Aotearoa

BACKGROUND

This document is the stakeholder engagement document intended to inform the 2024 proposed changes to the WorkSafe New Zealand special guide *Workplace Exposure Standards (WES) and Biological Exposure Indices (BEI)* (2023).

It contains 58 substance reviews that support WorkSafe's recommendations to adopt, maintain or remove individual WES and BEI values. In previous years, the substance reviews were published on the WorkSafe website as individual documents. However, in 2024, all the reviews are available in this single publication.

Users of this document are reminded that WorkSafe's WES and BEI values are largely not prescribed exposure standards (PES). For more information about WES and PES, visit Applying the workplace exposure standards

Most of the WorkSafe WES and BEI are health-based values intended as guidelines for health risk assessment.

WES and BEI values must not be regarded as fine lines between safe and unsafe levels of an exposure. WES and BEI are determined without regard to non-scientific policy, socio-economic impact, cost, economic or technical feasibility, or impact on sampling methods. Therefore, it is recommended that feedback be limited to the health aspect of the proposed changes.

IMPORTANT INFORMATION

Please read this before continuing

Note: Most of the 58 Substance WES Reviews in this proposal document include Licenced Material reproduced with permission from the American Conference of Governmental Industrial Hygienists' (ACGIH®) publication "*Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition, © ACGIH 2024". The Licensed Material shall be solely used by End Users for their own internal use.

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ACGIH® also requires that links to its Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs® are provided to End Users and encourages End Users to read the TLVs® and BEIs® Guidelines section

Instructions

The first use of a term requiring definition, in each substance review, is hyperlinked to the definition in the Glossary

To navigate through this document, it is recommended that users use the bookmarks pane in conjunction with the home button.

Unless otherwise stated, all substance review proposals relate to workplace exposure standards (WES), not biological exposure indices (BEI).

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Terms that are **bold** (first occurrence only) are further defined in the Glossary

1,1,1,2-TETRACHLORO-2,2-DIFLUOROETHANE

CAS NO: 76-11-9

Summary

Workplace Exposure Standards for 1,1,1,2-tetrachloro-2,2-difluoroethane (CAS: 76-11-9)

	CURRENT	PROPOSED
WES-TWA	500**ppm** (4,170**mg/m³**)	100ppm (830mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for 1,1,1,2-tetrachloro-2,2-difluoroethane

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for 1,1,1,2-tetrachloro-2,2-difluoroethane of 100ppm (830mg/m³).

To protect for central nervous system, liver and kidney effects.

Discussion

1,1,1,2-Tetrachloro-2,2-difluoroethane (**CFC-112a** or **R 112a**) is used as a refrigerant, solvent, corrosion inhibitor, and blowing agent (**Safe Work Australia**, 2020; **ACGIH®**, 2008).

1,1,1,2-Tetrachloro-2,2-difluoroethane has a slight ether-like odour (ACGIH®, 2008; PubChem, 2021).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of 1,1,1,2-tetrachloro-2,2-difluoroethane noted that the critical effects were central nervous system, liver and kidney damage (ACGIH®, 2008).

The ACGIH® review concluded that:

> "There is a very limited database for CFC-112a. CFC-112a is a chemical with relatively low toxicity following either acute or subchronic exposures. Lethality occurred in rats and mice exposed to CFC-112a at concentrations of 15,000 (Clayton *et al*., 1966; Bandman *et al*., 1990) and 20,000ppm (Torkelson *et al*., 1971). Low-level narcotic effects, minimal hepatocyte degeneration, and cloudy swelling of the kidneys were reported in rats exposed to 10,000 and 5,000ppm for seven hours (Torkelson *et al*., 1971). Repeated inhalation studies in rats exposed to 1,000ppm showed no effects (Greenberg and Lester, 1950). On the basis of these data, a **TLV-TWA** of 100ppm is recommended. This value should be sufficient to protect against the central nervous system, hepatic, and renal effects of CFC-112a.
>
> "The acute dermal toxicity is very low, which does not suggest a need for a **Skin** notation." (references cited in ACGIH®, 2008).

The ACGIH® found there was insufficient data available to recommend a **TLV-STEL**, or **SEN** or carcinogenicity notations for 1,1,1,2-tetrachloro-2,2-difluoroethane (ACGIH®, 2008).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of 1,1,1,2-tetrachloro-2,2-difluoroethane noted that the **MAK** value of 200ppm, **peak limitation Category II** with an excursion factor of 2, were based on analogy with the more extensively investigated symmetrical isomer 1,1,2,2-tetrachloro-1,2-difluoroethane (MAK value of 200ppm) that showed systemic effects after 31 days exposure to 1,000ppm (DFG MAK, 2007).

The DFG noted that there was no data available on 1,1,1,2-tetrachloro-2,2-difluoroethane to assess the need for **"H"**, **"Sh"** or **"Sa"** notations (DFG MAK, 2007).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 500ppm (4,170mg/m^3) for 1,1,1,2-tetrachloro-2,2-difluoroethane, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for 1,1,1,2-tetrachloro-2,2-difluoroethane that a WES-TWA of 100ppm (830mg/m^3) is adopted, to protect against central nervous system, liver and kidney effects, based on ACGIH® recommendations. Noting the limited and dated toxicology profile.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/6426#section=Chemical-and-Physical-Properties
CAS Number	76-11-9
Conversion factors	1mg/m^3 = 0.120ppm (25°C; 101.3**kPa**) 1ppm = 8.30mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: None Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2008. *"1,1,1,2-Tetrachloro-2,2-difluoroethane."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2007. *"1,1,1,2-Tetrachlor-2,2-difluorethan."* MAK Value Documentation in German language, 2007; The MAK Collection for Occupational Health and Safety; pp 1-6. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7611d0042

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed September 2021 http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed September 2021. *1,1,1,2-Tetrachloro-2,2-difluoroethane*, CID: 6426. https://pubchem.ncbi.nlm.nih.gov/compound/6426

Safe Work Australia (2020). Safe Work Australia Draft Evaluation Report and Recommendations – *1,1,1,2-Tetrachloro-2,2-difluoroethane*. https://engage.swa.gov.au/65429/widgets/323765/documents/192109

1,1,2-TRICHLORO-1,2,2-TRIFLUOROETHANE

CAS NO: 76-13-1

Summary

Workplace Exposure Standards for 1,1,2-trichloro-1,2,2-trifluoroethane (CAS: 76-13-1)

	CURRENT	PROPOSED
WES-TWA	1,000**ppm** (7,670**mg/m³**)	1,000ppm (7,670mg/m³)
WES-STEL	1,250ppm (9,590mg/m³)	1,250ppm (9,590mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for 1,1,2-trichloro-1,2,2-trifluoroethane

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA of 1,000ppm (7,670mg/m³) for 1,1,2-trichloro-1,2,2-trifluoroethane, and
2. maintain the WES-STEL of 1,250ppm (9,590mg/m³) for 1,1,2-trichloro-1,2,2-trifluoroethane.

To protect for psychomotor impairment.

Discussion

1,1,2-Trichloro-1,2,2-trifluoroethane (**CFC-113**) is used as a refrigerant, heat transfer medium, solvent, and an intermediate in chlorofluorocarbon manufacture (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

1,1,2-Trichloro-1,2,2-trifluoroethane has a slight ether-like odour, with an odour threshold reported at 45ppm (ACGIH®, 2001; PubChem, 2021).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of 1,1,2-trichloro-1,2,2-trifluoroethane noted that the critical effects were narcosis and asphyxia at extremely high concentrations, and potential to induce cardiac arrhythmia (ACGIH®, 2001).

The ACGIH® review concluded that:

> "CFC-113 causes narcosis and asphyxia at extremely high concentrations, and it has the potential to induce cardiac arrhythmia. A **TLV-TWA** of 1,000ppm and a **TLV-STEL** of 1,250ppm are recommended to minimize the potential to systemic toxicity such as mild CNS effects, and cardiac sensitization from exposure to CFC-133. The occurrence of tumors in test animals exposed to CFC-113 were concluded to be not dose-related to CFC-133 exposure (Trochimowicz *et al*., 1988). Studies of exposure of mice to CFC-113 failed to demonstrate any significant relationship to benign or malignant tumors or the data were inadequate for statistical evaluation (Epstein *et al*., 1967). Accordingly, a carcinogenicity notation of **A4, Not Classifiable as a Human Carcinogen**, is assigned to CFC-113." (references cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin** or **SEN** notations for 1,1,2-trichloro-1,2,2-trifluoroethane (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of 1,1,2-trichloro-1,2,2-trifluoroethane noted that the **MAK** value of 500ppm, **peak limitation Category II** with an excursion factor of 2, were based on the results of comparative psychomotor performance tests with 1,1,2-trichloro-1,2,2-trifluoroethane and trichloroethene in volunteers. The threshold for significant effects was about 300ppm for trichloroethene and about 2,500ppm for 1,1,2-trichloro-1,2,2-trifluoroethane. The MAK value for trichloroethene was 50ppm. The MAK value for 1,1,2-trichloro-1,2,2-trifluoroethane was supported by reported liver effects in rats exposed to 1,000ppm (DFG MAK, 1992; DFG MAK, 2002).

The DFG did not assess the need for **"H"**, **"Sh"** or **"Sa"** notations (DFG MAK, 1992).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 1,000ppm (7,670mg/m^3) and WES-STEL of 1,250ppm (9,590mg/m^3) for 1,1,2-trichloro-1,2,2-trifluoroethane, to be adequate to manage health risks from possible workplace exposure. Noting the limited and dated toxicology profile and overseas evaluations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/6428#section=Chemical-and-Physical-Properties"1,1,2-Trichlorotrifluoroethane
CAS Number	76-13-1
Conversion factors	1mg/m^3 = 0.131ppm (25°C; 101.3**kPa**) 1ppm = 7.65mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 1,1,2-Trichlorotrifluoroethane www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/009A9514-B73E-42BA-9D43-3BD47084B8DA Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"1,1,2-Trichloro-1,2,2-trifluoroethane."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1992. *"1,1,2-Trichloro-1,2,2-trifluoroethane."* MAK Value Documentation, 1992; The MAK Collection for Occupational Health and Safety; pp 365-370. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7613e0003

Deutsche Forschungsgemeinschaft (DFG), 2002. *"1,1,2-Trichlor-1,2,2-trifluorethan."* MAK Value Documentation in German language, 2002; The MAK Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7613d0034

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed September 2021 http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed September 2021. *1,1,2-Trichlorotrifluoroethane*, CID: 6428. https://pubchem.ncbi.nlm.nih.gov/compound/6428

Safe Work Australia (2020). Safe Work Australia Draft Evaluation Report and Recommendations – *1,1,2-Trichloro-1,2,2-trifluoroethane*. https://engage.swa.gov.au/65429/widgets/323765/documents/192122

2-BUTOXYETHANOL

CAS NO: 111-76-2

Summary

Workplace Exposure Standards for 2-butoxyethanol (CAS: 111-76-2)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (121**mg/m³**)	10ppm (49mg/m³)
WES-STEL	–	20ppm (98mg/m³)
WES-Ceiling	–	–
Notations	**skin**	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for 2-butoxyethanol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for 2-butoxyethanol of 10ppm (49mg/m³)
2. adopt a WES-STEL for 2-butoxyethanol of 20ppm (98mg/m³), and
3. maintain the *skin* notation for 2-butoxyethanol.

To protect for sensory irritative effects.

Discussion

2-Butoxyethanol is used as a solvent in water or organic solvent-based coatings; and, as a component of many hard-surface cleaners, cosmetics, and hair dyes and colours (**Safe Work Australia**, 2019; **ACGIH®**, 2003).

2-Butoxyethanol has an ether-like odour, with reported odour thresholds of 0.1 and 9.3ppm (PubChem, 2021; ACGIH®, 2003).

Cancer risks

The International Agency for Research on Cancer (IARC) evaluation of 2-butoxyethanol concluded that:

> There is ***inadequate evidence in humans*** for the carcinogenicity of 2-butoxyethanol.
>
> There is ***limited evidence in experimental animals*** for the carcinogenicity of 2-butoxyethanol.

With an overall evaluation that:

> 2-Butoxyethanol is *not classifiable as to its carcinogenicity to humans* (**Group 3**). (IARC, 2006).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of 2-butoxyethanol noted that the critical effects were irritative effects (DFG MAK, 2010).

The DFG noted that the **MAK** value of 10ppm for 2-butoxyethanol, **peak limitation Category I** with an excursion factor of 2, were based on **NOAEC** (20ppm) and **LOAEC** (100ppm) for nasal irritation in humans. As the human data was not sufficiently reliable, the MAK value was derived from a LOAEC of 31.2ppm, resulting in a benchmark calculation of 15ppm for a 5% increased incidence of irritative changes in the noses of rats exposed for 2-years. To account for differences in species, the MAK value was lowered to 10ppm. The DFG also noted that volunteers reported no sensory irritation to 20ppm during exposures of 2 hours (DFG MAK, 2010).

The DFG concluded that an **"H"** notation was warranted for 2-butoxyethanol, based on studies indicating that dermal absorption could contribute significantly to systemic toxicity (DFG MAK, 2010).

The DFG reported that there was inadequate data on 2-butoxyethanol to assess **"Sa"** or **"Sh"** notations (DFG MAK, 2010).

The DFG re-evaluation of the carcinogenic potential of 2-butoxyethanol concluded that the non-genotoxic mechanisms of tumour induction in rats and mice were either not relevant to humans, or would only occur at exposure concentrations where irritation and pre-narcotic effects would already be manifest. The previous **Carcinogen Category 4** was withdrawn (DFG, 2018).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of 2-butoxyethanol noted that the critical effect in several animal species is haematotoxicity.

A study indicating a NOAEL of 25ppm (123mg/m^3) for haematological effects in rats, was considered the best available basis for proposing occupational exposure limits. With *in vivo* and *in vitro* studies showing that humans are less sensitive than rats to the haemolytic effects of 2-butoxyethanol, the SEG/SCOEL saw no need for applying an uncertainty factor and recommended an 8 hour TWA of 20ppm (123mg/m^3) and, on the basis of a human volunteer study, recommended a 15 minute STEL of 50ppm (246mg/m^3) to protect from peak exposures that could result in irritation.

Based on skin absorption being likely to considerably increase total body burden, a 'skin' notation was also recommended (SEG, 1996).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of 2-butoxyethanol noted that the critical effects were irritant effects (ACGIH®, 2003).

The ACGIH® review concluded that:

> "Extensive rodent toxicological studies have been reported for 2-butoxyethanol, and toxic effects have been noted at concentrations as low as 77ppm (13 weeks) with a **NOEL** value of 25ppm (Dodd *et al*., 1983). However, ..., the rodent toxicity of 2-butoxyethanol has been ascribed to the ability of its primary metabolite, 2-butoxyacetic acid, to produce **RBC** hemolysis and related toxicity secondary

to RBC lysis. Extensive *in vivo* and *in vitro* studies (Smyth *et al*., 1941; Ghananyem *et al*., 1987; Ghanayem, 1989; Ghanayem & Sullivan, 1993; Udden & Patton, 1994; Udden, 1994) have shown that human RBC were much less susceptible to 2-butoxyacetic acid-induced hemolysis than rodent erythrocytes. Thus, rodent systemic toxicity, which was characterized by RBC hemolysis and its secondary consequences (Gingell *et al*., 1994; Tyler, 1984), likely overestimates the toxicity potential of 2-butoxyethanol in humans when based on applied dose comparisons. In fact, a **PB-PK** model validated against data from both human volunteer and rodent pharmacokinetic studies has provided strong evidence that exposure to either saturated atmospheric concentration of 2-butoxyethanol vapor (approximately 1160ppm) or to a worst-case dermal contact scenario would likely generate human blood 2-butoxyacetic acid concentrations well below those capable of causing human RBC hemolysis (Corley, 1996).

"However, human volunteers exposed at 100 or 200ppm 2-butoxyethanol for 8 hours noted immediate and continued eye and nose irritation, with some reporting nausea and headache during a 7- to 24-hour postexposure period (Carpenter *et al*., 1956). Subjects exposed at 20ppm 2-butoxyethanol for 2 hours, however, did not report any discomfort (Johanson *et al*., 1986). Accordingly, a **TLV-TWA** of 20ppm is recommended to minimize the potential irritant effects from exposure to 2-butoxyethanol."

"The skin notation is no longer recommended for 2-butoxyethanol because 1) primary systemic toxicity in animals is RBC hemolysis (Werner *et al*., 1943a; Werner *et al*., 1943b; Dodd *et al*., 1983; Krasavage, 1986) mediated by butoxyacetic acid, a key metabolite of 2-butoxyethanol (Dodd *et al*., 1983; Ghananyem *et al*., 1987; Ghanayem, 1989; Ghanayem & Sullivan, 1993; Udden & Patton, 1994; Udden, 1994); 2) *in vitro* findings have indicated that human RBC, including those from potentially susceptible populations (elderly, sickle cell anemia, etc.), are significantly more resistant to 2-butoxyacetic acid induced hemolysis (Smyth *et al*., 1941; Ghananyem *et al*., 1987; Ghanayem, 1989; Ghanayem & Sullivan, 1993; Udden & Patton, 1994; Udden, 1994); and 3) a validated PB-PK model, applying a reasonable estimate of dermal absorption of 2-butoxyethanol, predicted that blood butoxyacetic acid concentrations would not approach those sufficient to cause hemolysis in humans (Corley, 1996)." (references cited in ACGIH®, 2003).

The ACGIH® noted that a negative result in volunteers indicated that a **SEN** notation was not warranted for 2-butoxyethanol (ACGIH®, 2003).

The ACGIH® found there was insufficient data available to recommend a **TLV-STEL** for 2-butoxyethanol (ACGIH®, 2003).

NIOSH

National Institute for Occupational Safety and Health (**NIOSH**) Skin Notation Profile for 2-butoxyethanol summarised:

"Sufficient information was available from human and animal dermal toxicokinetic studies *in vivo* and *in vitro* [Bartnik *et al*. 1987; Sabourin *et al*. 1992, 1993; Jakasa *et al*. 2004] and from dermal toxicity studies [Carpenter *et al*. 1956; Duprat and Gradiski 1979] to demonstrate that **BE** is absorbed through the skin, is systemically available, and can elicit systemic effects such as hemoglobinuria (and other blood effects and changes in body weight). Positive results from the single human repeat-insult patch test [Greenspan *et al*. 1995] and from the clinical studies in experimental animals [Union Carbide Corporation 1972; Duprat and Gradiski 1979; Zissu 1995] sufficiently

demonstrate that BE is a mild to moderate skin irritant. Although a limited number of human and animal studies were identified concerning the potential of the substance to be a skin sensitizer, negative results in the human repeat-insult patch study [Greenspan *et al*. 1995], and the guinea pig maximization test [Zissu 1995] are sufficient to demonstrate that BE is not likely to be a skin sensitizer in humans or animals. Therefore, on the basis of these assessments, BE is assigned a composite skin notation of **SK: SYS-DIR (IRR)**." (references cited in NIOSH, 2011).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 25ppm (121mg/m³) for 2-butoxyethanol, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for 2-butoxyethanol that a WES-TWA of 10ppm (49mg/m³) and a WES-STEL of 20ppm (98mg/m³) are adopted, to protect against sensory irritative effects, based on the DFG recommendations. The *skin* notation should be retained.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/2-Butoxyethanol#section=Chemical-and-Physical-Properties
CAS Number	111-76-2
Conversion factors	1mg/m³ = 0.207ppm (25°C; 101.3**kPa**) 1ppm = 4.83mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Ethanol, 2-butoxy Approved hazardous substances with controls Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"2-Butoxyethanol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2010. *"2-Butoxyethanol (Ethylene glycol monobutyl ether)."* MAK Value Documentation, 2010; The MAK Collection for Occupational Health and Safety; pp 107-142. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb11176e0026

Deutsche Forschungsgemeinschaft (DFG), 2018. *"2-Butoxyethanol (Ethylene glycol monobutyl ether)."* MAK Value Documentation, 2018; The MAK Collection for Occupational Health and Safety 2019, Vol 4, No 1; p 20-35. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb11176e6419

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed July 2021 http://limitvalue.ifa.dguv.de

International Agency for Research on Cancer (IARC), 2006. *"IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 88: Formaldehyde, 2-Butoxyethanol and 1-tert-Butoxypropan-2-ol."* Lyon, France. pp 329-421. https://publications.iarc.fr/106

National Center for Biotechnology Information. PubChem Database. Accessed July 2021. *2-Butoxyethanol*, CID: 8133. https://pubchem.ncbi.nlm.nih.gov/compound/2-Butoxyethanol

National Institute for Occupational Safety and Health (NIOSH), 2011. *"Skin Notation Profile – 2-Butoxyethanol (BE)."* NIOSH Publication No.: 2011-152. www.cdc.gov/niosh/docs/2011-152/default.html

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *2-Butoxyethanol*. https://engage.swa.gov.au/49158/widgets/259717/documents/115586

Scientific Expert Group on Occupational Exposure Limits (SEG), 1996. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for 2-butoxyethanol."* SEG/SUM/70

2-CHLOROETHANOL

CAS NO: 107-07-3

Summary

Workplace Exposure Standards for 2-chloroethanol (CAS: 107-07-3)

	CURRENT	PROPOSED
WES-TWA	–	–
WES-STEL	–	–
WES-Ceiling	1**ppm** (3.3**mg/m³**)	1ppm (3.3mg/m³)
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for 2-chloroethanol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-Ceiling for 2-chloroethanol of 1ppm (3.3mg/m³), and
2. maintain the *skin* notation for 2-chloroethanol.

To protect for multiple systemic effects with a steep dose-response relationship and local irritation effects.

Discussion

2-Chloroethanol is used as a solvent for cellulose esters, and in the production of ethylene glycol and ethylene oxide (**Safe Work Australia**, 2019; **ACGIH®**, 2001). 2-Chloroethanol is formed during ethylene oxide sterilisation processes (ACGIH®, 2001).

2-Chloroethanol has a faint sweet, ethereal odour, with an odour threshold reported at 0.4ppm (PubChem, 2022; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of 2-chloroethanol noted that the critical effects were high systemic toxicity with a steep dose-response relationship and local irritation (DFG MAK, 2019).

The DFG noted that the **MAK** value of 2ppm for 2-chloroethanol, **peak limitation Category II** with an excursion factor of 1, were based on oral and dermal studies in animals, as there were no suitable human or inhalation study data in animals to derive a MAK value (DFG MAK, 2019). The DFG noted a **NOAEL** of 45**mg/kg b.w./day** from a 12-week gavage study in rats adjusted into a possible air limit value (toxicokinetic conversion). However, the DFG also noted that gavage bolus administration led to a strong first-pass effect (through the liver), with glutathione depletion and formation of 2-chloroacetaldehyde (a putative toxic metabolite), and considered a worst case scenario that would not occur from dermal or inhalation exposure (slower uptake and no first-pass) (DFG MAK, 2019).

An **"H"** notation was assigned to 2-chloroethanol, based on the comparatively low dermal **LD_{50}** value from acute animal studies and reports of poisoning after dermal contact in the workplace (DFG MAK, 2019). **"Sa"** and **"Sh"** notations were not assigned for 2-chloroethanol, based on lack of positive findings in humans and a negative local lymph node assay in mice (DFG MAK, 2019).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of 2-chloroethanol (ethylene chlorohydrin) noted that the critical effects were multiple systemic effects and local irritation effects (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Sites of the biological effects of ethylene chlorohydrin are central nervous system (respiratory depression, paralysis, mental disturbances, brain damage) (Goldblatt and Chiesman, 1944; Bush *et al*., 1949); cardiovascular system (myocardiopathy, sinus tachycardia, circulatory shock); liver (glutathione depletion, inactivation of drug-metabolizing enzymes, degeneration) (Friedman *et al*., 1977); kidney (polyuria, disorders in excretion of electrolytes and nitrogen, degeneration) (Lewis, 1997); gastrointestinal (nausea, vomiting, epigastric pain) (Bush *et al*., 1949); skin (erythema, nuclear pyknosis, blisters); and eyes (irritation) (Bush *et al*., 1949). Accordingly, a **TLV-Ceiling** of 1ppm is recommended for ethylene chlorohydrin in view of the serious systemic responses noted above. Because of the potential for skin absorption, a **Skin** notation is also recommended (Lawrence *et al*., 1971; Wahlberg and Boman, 1978). Skin painting studies with ethylene chlorohydrin yielded no evidence of carcinogenic activity in male and female Fischer 344 rats and Swiss mice (U.S. NTP, 1985). Accordingly, an **A4**, **Not Classifiable as a Human Carcinogen**, notation is assigned to ethylene chlorohydrin." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to assign **SEN** notations for 2-chloroethanol (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DGF and ACGIH® reviews, WorkSafe considers its current WES-Ceiling of 1ppm (3.3mg/m^3) with a skin notation for 2-chloroethanol to be adequate to manage health risks from possible workplace exposure.

It is recommended for 2-chloroethanol that the WES-Ceiling of 1ppm (3.3mg/m^3) is maintained, to protect against multiple systemic effects with a steep dose-response relationship and local irritation effects, based on ACGIH® recommendation. The skin notation should also be maintained for 2-chloroethanol.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/34#section=Chemical-and-Physical-Properties
CAS Number	107-07-3
Conversion factors	1ppm = 3.31mg/m^3 (25°C; 101.3**kPa**) 1mg/m^3 = 0.302ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Ethylene chlorohydrin www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/404807B9-5C86-461C-8F4D-607F777D0FCD

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"Ethylene chlorohydrin."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2019. *"2-Chlorethanol"* MAK Value Documentation in German language, 2019. The MAK-Collection for Occupational Health and Safety, Vol 4, No 2; pp 559-612. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10707d0067

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2-DIETHYLAMINOETHANOL

CAS NO: 100-37-8

Summary

Workplace Exposure Standards for 2-diethylaminoethanol (CAS: 100-37-8)

	CURRENT	PROPOSED
WES-TWA	10**ppm** (48**mg/m³**)	2ppm (9.7mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for 2-diethylaminoethanol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for 2-diethylaminoethanol of 2ppm (9.7mg/m³), and
2. maintain the *skin* notation for 2-diethylaminoethanol.

To protect for mucous membrane irritation and central nervous system effects.

Discussion

2-Diethylaminoethanol is used as a curing agent for resins; as an emulsifying agent; and, as a fabric softener (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

2-Diethylaminoethanol has a weak, nauseating, ammonia-like odour, with an odour threshold reported at 0.011ppm (PubChem, 2021; ACGIH®, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of 2-diethylaminoethanol noted that the critical effects were mucous membrane irritation and central nervous system effects (ACGIH®, 2001).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 2ppm (9.6mg/m³) is recommended for occupational exposure to 2-diethylaminoethanol (**DEAE**) to minimize the potential for irritation of the nasal mucosa reported in rats and central nervous system (**CNS**) effects that included tremors, convulsions, and ataxia reported for dogs fed 2-diethylaminoethanol for 1 year. A **Skin** notation is recommended, based on the reported dermal **LD_{50}** in rabbits." (ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **DSEN**, **RSEN** or Carcinogenicity notations, or **TLV-STEL** for 2-diethylaminoethanol (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of 2-diethylaminoethanol noted that the critical effects were severe irritation of mucous membranes (DFG MAK, 2000).

The DFG noted that the **MAK** value of 5ppm, **peak limitation Category I** with an excursion factor of 1, were based on studies in rats where short-term exposures at 10ppm revealed no effects, but longer-term exposures caused respiratory irritation, and exposures at 25ppm caused histological changes in the respiratory tract (DFG MAK, 2000; DFG MAK, 2007).

The DFG also noted that visual disturbances observed after exposure to the structurally-related triethylamine and other tertiary amines could not be excluded for 2-diethylaminoethanol, but had not been reported (DFG MAK, 2000). [See WorkSafe WES review for triethylamine 2024].

An **"H"** notation was warranted for 2-diethylaminoethanol, as physico-chemical properties indicated a potentially high rate of dermal penetration (DFG MAK, 2000).

No data was available to evaluate **"Sa"** or **"Sh"** notations (DFG MAK, 2000).

NIOSH

National Institute for Occupational Safety and Health (**NIOSH**) Skin Notation Profile for 2-diethylaminoethanol summarised:

> "Studies that evaluated the potential of **2-DAE** to be absorbed through the skin or to be systemically toxic in humans were limited to models of human skin penetration based on physico-chemical properties [Fiserova-Bergerova 1990; Guy and Potts 1993]. However, these predictions are supported by an acute dermal toxicity study [Smyth and Carpenter 1944]; therefore, this assessment assigns a skin notation of **SK: SYS** for 2-DAE. Taken together, there is limited data in humans and animals to demonstrate that 2-DAE is absorbed through the skin, is systemically available, and is acutely toxic. Based on case reports of skin irritation following accidental dermal exposure to 2-DAE in humans [NIOSH 1981, 1983] and corrosivity observed in experimental animals [Smyth and Carpenter 1944; Potokar *et al*. 1985; Union Carbide, 1990], sufficient information exists to conclude that 2-diethylaminoethanol is corrosive, and that dilute solutions of the substance may irritate the skin. No standard studies conducted in humans were identified that evaluated the potential of the substance to be a skin sensitizer. However, guinea pig maximization tests [Nakamura *et al*. 1994; Leung and Blaszcak 1998] show that 2-DAE was not a skin sensitizer. Therefore, on the basis of these assessments, 2-DAE is assigned a composite skin notation of **SK: SYS-DIR (COR)**." (references cited in NIOSH, 2014).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 10ppm (48mg/m^3) for 2-diethylaminoethanol, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for 2-diethylaminoethanol that a WES-TWA of 2ppm (9.7mg/m^3) with a *skin* notation is adopted to protect against mucous membrane irritation and central nervous system effects, based on the ACGIH® recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/2-diethylaminoethanol#section=Chemical-and-Physical-Properties
CAS Number	100-37-8
Conversion factors	1mg/m³ = 0.21ppm (25°C; 101.3**kPa**) 1ppm = 4.83mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"2-Diethylaminoethanol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2000. *"2-Diethylaminoethanol."* MAK Value Documentation, 2000; The MAK Collection for Occupational Health and Safety; pp 91-99. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10037e0014

Deutsche Forschungsgemeinschaft (DFG), 2007. *"2-Diethylaminoethanol."* MAK Value Documentation in German language, 2007; The MAK Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10037d0043

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National Institute for Occupational Safety and Health (NIOSH), 2014. *"Skin Notation Profile – 2-Diethylaminoethanol."* NIOSH Publication No.: 2014-140. www.cdc.gov/niosh/docs/2014-140/default.html

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ACETONITRILE

CAS NO: 75-05-8

Summary

Workplace Exposure Standards for acetonitrile (CAS: 75-05-8)

	CURRENT	PROPOSED
WES-TWA	40**ppm** (67**mg/m³**)	10ppm (17mg/m³)
WES-STEL	60ppm (101mg/m³)	20ppm (34mg/m³)
WES-Ceiling	-	-
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for acetonitrile

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for acetonitrile of 10ppm (17mg/m³)
2. adopt a WES-STEL for acetonitrile of 20ppm (34mg/m³), and
3. maintain the skin notation.

To protect for liver damage.

Discussion

Acetonitrile is used as a solvent in hydrocarbon extraction; as a speciality solvent and intermediate; and, in the separation of fatty acids from vegetable oils (**ACGIH**®, 2002).

Acetonitrile has a sweet, ethereal odour, with an odour threshold reported at 70mg/m³ (PubChem, 2021).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of acetonitrile noted that the critical effects were induction of basophilic foci in rat livers (DFG MAK, 2018).

The DFG noted that the **MAK** value of 10ppm for acetonitrile, **peak limitation Category II** with an excursion factor of 2, were based on a trend in increasing incidence of basophilic foci in F344 rat livers from 100ppm to statistical significance at 200ppm after chronic exposures, and adjusted to extrapolate from resting rats to working humans (DFG MAK, 2018).

The DFG noted that an **"H"** notation was warranted for acetonitrile, based on dermal LD50 values in rabbits and a human case report (DFG MAK, 2003).

The DFG also noted that an **"S"** notation was designated for acetonitrile (DFG MAK, 2003).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of acetonitrile noted that the critical effects were lung effects (ACGIH®, 2002).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 20ppm is recommended to protect against the potential adverse effects of acetonitrile on the lung. This level is based on the limited human data in which 40ppm, as a single 4-hour exposure, produced no effects in 2 volunteers, and the sensation of cooling in the lungs and slight tightness in the third (Pozzani *et al*., 1959). In animal lifetime inhalation studies (US NTP, 1996), the **NOAEL** in both rats and mice was 200ppm. No increase in cancer incidence was noted in either species, although the combined liver cancers in the high-exposure males were at the upper bound of the background range. Shorter-term inhalation studies also support that 200ppm is not active in rodents, although some evidence of hyperplasia in the forestomach of female mice was observed in a 13-week inhalation study. The degree of response and the lack of a human correlate to this organ diminish the significance of this finding. Acetonitrile is not a developmental toxin and genotoxicity studies are generally negative; although in two mammalian micronucleus studies, weak positives were reported.
>
> "Human experience was limited to case reports, mainly from suicide attempts; however, the data from massive overexposures were relatively consistent. The action of acetonitrile does, to some extent, reflect the metabolism to cyanide. Following exposure to both animals and humans, free cyanide has been detected in both the blood and urine. However, there were not enough data, especially quantitative data, to support a **TLV-STEL**. The current ACGIH recommendation for hydrogen cyanide is a **TLV-CEILING**. This appears overly conservative for acetonitrile, but lowering the TLV-TWA from 40ppm to 20ppm, along with the generally acceptable workplace experience at that level (integrated with the above specific toxicological information), should be protective in the absence of a short-term guidance level.
>
> "A **Skin** notation is recommended based upon the case report of child poisoning from dermal contact (el Ghawabi *et al*., 1975)." (references cited in ACGIH®, 2002).

An **A4**, **Not Classifiable as a Human Carcinogen**, notation was assigned, based on negative results in rodents. The ACGIH® found there was insufficient data available to recommend **SEN** notations or a TLV-STEL for acetonitrile (ACGIH®, 2002).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 40ppm (67mg/m^3) and WES-STEL of 60ppm (101mg/m^3) for acetonitrile with a *skin* notation, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for acetonitrile that a WES-TWA of 10ppm (17mg/m^3) and a WES-STEL of 20ppm (34mg/m^3) are adopted, to protect against liver damage, based on the DFG recommendations. The *skin* notation should be maintained.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/acetonitrile#section=Chemical-and-Physical-Properties
CAS Number	75-05-8
Conversion factors	1mg/m³ = 0.54ppm (25°C; 101.3**kPa**) 1ppm = 1.84mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/9B0F121B-EF59-4B6F-B6DE-183EE22BF37C Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"Acetonitrile."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2003. *"Acetonitrile."* MAK Value Documentation, 2003; The MAK Collection for Occupational Health and Safety; pp 1-41. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7505e0019

Deutsche Forschungsgemeinschaft (DFG), 2018. *"Acetonitril."* MAK Value Documentation in German language, 2018; The MAK Collection for Occupational Health and Safety; pp 606-613. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7505d0065

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AMMONIA, ANHYDROUS

CAS NO: 7664-41-7

Summary

Workplace Exposure Standards for ammonia, anhydrous (CAS: 7664-41-7)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (17**mg/m³**)	20ppm (14mg/m³)
WES-STEL	35ppm (24mg/m³)	40ppm (28mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for ammonia, anhydrous

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for ammonia, anhydrous of 20ppm (14mg/m³), and
2. adopt a WES-STEL for ammonia, anhydrous of 40ppm (28mg/m³).

To protect for acute ocular and respiratory tract irritation, respiratory symptoms and decreased lung function.

Discussion

Ammonia is used as a fertiliser, in chemical manufacture, as a refrigerant, in the nitriding of steel, as a condensation catalyst for polymers, and other applications (**ACGIH®**, 2001).

Ammonia has a sharp, intensely irritating odour, with an odour threshold reported at 0.0266mg/m³ (0.038ppm) (ACGIH®, 2001; PubChem, 2021).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of ammonia noted that the critical effects were acute ocular and respiratory tract irritation (ACGIH®, 2001).

The ACGIH® review concluded that:

> "ACGIH believes that that a time-weighted-average exposure is significant and should be maintained at a lower level than is permissible for brief excursions. The fact that continuous, 24-hour exposures produced effects not observed from considerably higher exposures of the occupational type (Stombaugh *et al*., 1969) can be considered as supporting this conclusion. Accordingly, a **TLV-TWA** of 25ppm is recommended to minimize the potential eye and respiratory tract irritation and minimize discomfort among uninured workers. The **TLV-STEL** of 35ppm is recommended to provide a greater margin of safety against the acute sensory effects from exposure to ammonia." (reference cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations for ammonia (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of ammonia noted that the critical effects were mucous membrane irritation (DFG MAK, 1999).

The DFG noted that the **MAK** value of 20ppm for ammonia, **peak limitation Category I** with an excursion factor of 2, were based on evidence of mucous membrane irritation in experimental animals and humans after exposures to 50ppm, and increased errors in choice reaction tests by humans at >50ppm. Naïve individuals were particularly sensitive. Long-term exposure of workers to 10ppm was reported to be without effect (DFG MAK, 1999; DFG MAK, 2000).

Studies cited in DFG 2020 re-evaluation indicate that 20ppm should be protective for persons with seasonal allergies (DFG MAK, 2020).

The DFG noted that there were inadequate data available to assess **"H"** or **"S"** for ammonia (DFG MAK, 1999).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of ammonia recommended an 8-hour TWA of 20ppm (14mg/m^3) and 15-minute STEL of 50ppm (36mg/m^3), based on a **LOAEL** of 50ppm for mild irritation reported in humans (SEG, 1992).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, ACGIH® and SCOEL reviews, WorkSafe considers its current WES-TWA of 25ppm (17mg/m^3) for ammonia, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for ammonia that a WES-TWA of 20ppm (14mg/m^3) and a WES-STEL of 40ppm (28mg/m^3) are adopted, to protect against acute ocular and respiratory tract irritation, and respiratory symptoms and decreased lung function, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/222#section=Chemical-and-Physical-Properties
CAS Number	7664-41-7
Conversion factors	1mg/m^3 = 0.695ppm (25°C; 101.3**kPa**) 1ppm = 1.44mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/6F4FC34E-2F62-41C5-8284-8310B57C4AA5 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"Ammonia."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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National Center for Biotechnology Information. PubChem Database. Accessed September 2021. *Ammonia*, CID: 222. https://pubchem.ncbi.nlm.nih.gov/compound/222

Scientific Expert Group on Occupational Exposure Limits (SEG), 1992. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for ammonia."* SEG/SUM/20

BARIUM SULPHATE

CAS NO: 7727-43-7

Summary

Workplace Exposure Standards for barium sulphate (CAS: 7727-43-7)

	CURRENT	PROPOSED
WES-TWA	10**mg/m³**	1mg/m³ (r)
WES-STEL	–	5mg/m³ (r)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for barium sulphate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for barium sulphate of 1mg/m³ for **respirable fraction**, and
2. adopt a WES-STEL for barium sulphate of 5mg/m³ for respirable fraction.

To protect for the effects of biopersistent granular particles in the lungs.

Discussion

Barium sulphate is used as a contrast agent in X-ray examinations, and in paints, glass, paper making, and oil well drilling (**Safe Work Australia**, 2019; **ACGIH®**, 2014).

Barium sulphate is reported to be odourless (PubChem, 2021; ACGIH®, 2014).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of barium sulphate noted that the critical effects were due to the substance consisting of biopersistent granular particles (DFG MAK, 2017).

The DFG noted that the **MAK** value of 1.35mg/m³ for the respirable fraction of barium sulphate [0.3mg/m³ x material density of 4.5kg/m³], **peak limitation Category II** with an excursion factor of 8, were based on the lack of data for barium sulphate required to deviate from the general threshold limit value for dusts. The DFG noted that the MAK value of 4mg/m³ for the inhalable fraction should be retained as no data was available for reassessment (DFG MAK, 2017).

In analogy with other biopersistent granular dusts, DFG noted that **"H"**, **"Sa"** or **"Sh"** notations were not warranted for barium sulphate (DFG MAK, 2017).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of barium sulphate noted that the critical effects were pneumoconiosis in chronic rat studies (ACGIH®, 2014).

The ACGIH® review concluded that:

> "Chronic animal studies determined that barium sulfate particles caused an inflammatory response in the lung at 75mg/m³ (i.e., **LOAEL**) but not at 37.5mg/m³ (i.e., **NOAEL**) (Cullen *et al*., 2000), although the particle size was generally greater than what would be considered respirable for a rat. Although a number of case reports have demonstrated that inadvertent aspiration of barium sulfate, when used as a contrast agent in radiography, produces significant lung disease and can result in death, these reports of high-dose poisoning do not provide relevant inhalation dose-response data. In deriving a **TLV** for barium sulfate, it is important to consider the reported LOAEL and NOAEL in rats, but also that a large particle size would have limited the dose of barium sulfate that would reach the lung of a rat. Therefore, because barium sulfate is a relatively low toxicity particle, but high levels of particles can cause inflammation (Cullen *et al*., 2000) or a benign pneumoconiosis (Doig, 1976), a **TLV-TWA** of 5mg/m³ of inhalable particulate matter containing no asbestos and < 1% crystalline silica is recommended." (references cited in ACGIH®, 2014).

The ACGIH® noted that there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations, or a **TLV-STEL** for barium sulfate (ACGIH®, 2014).

Conclusions

Based on the documentation cited and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 10mg/m³ for barium sulphate to be inadequate to manage health risks from possible workplace exposure.

It is recommended for barium sulphate that a WES-TWA of 1mg/m³ is adopted for respirable fraction and a WES-STEL of 5mg/m³ is adopted for respirable fraction, to protect against the effects of biopersistent granular particles in the lungs, based on the DFG recommendations. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Barium-sulfate#section=Chemical-and-Physical-Properties
CAS Number	7727-43-7
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: None

References: PubChem 2021; **IFA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"Barium sulfate."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2017. *"Barium sulfate/barium(2+); sulfate)."* MAK Value Documentations, 2017; The MAK Collection for Occupational Health and Safety 2017, Vol 2, No 4; pp 1465-1472. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb772743stae6217

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed November 2021 http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed November 2021. *Barium sulfate*, CID: 24414. https://pubchem.ncbi.nlm.nih.gov/compound/Barium-sulfate

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Barium sulfate*. https://engage.swa.gov.au/48690/widgets/257444/documents/113558

BUTYL ACETATE ISOMERS (ISOBUYTL ACETATE, n-BUTYL ACETATE, AND SEC-BUYTL ACETATE)

CAS NO: 110-19-0; 123-86-4; 105-46-4

Summary

Workplace Exposure Standards for isobutyl acetate (CAS: 110-19-0)

	CURRENT	PROPOSED
WES-TWA	150**ppm** (713**mg/m³**)	50ppm (238mg/m³)
WES-STEL	–	150ppm (713mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for isobutyl acetate

Workplace Exposure Standards for *n*-butyl acetate (CAS: 123-86-4)

	CURRENT	PROPOSED
WES-TWA	150ppm (713mg/m³)	50ppm (238mg/m³)
WES-STEL	200ppm (950mg/m³)	150ppm (713mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 2: Current and proposed Workplace Exposure Standards (WES) for n-butyl acetate

Workplace Exposure Standards for sec-butyl acetate (CAS: 105-46-4)

	CURRENT	PROPOSED
WES-TWA	200ppm (950mg/m³)	50ppm (238mg/m³)
WES-STEL	–	150ppm (713mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 3: Current and proposed Workplace Exposure Standards (WES) for sec-butyl acetate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for butyl acetate isomers (except tert-butyl acetate) of 50ppm (238mg/m³), and
2. adopt a WES-STEL for butyl acetate isomers (except tert-butyl acetate) of 150ppm (713mg/m³).

To protect for eye and mucous membrane irritation.

Discussion

Butyl acetates are used as a solvent; in the manufacture of lacquers and paint removers; and, as a component of hydraulic fluids (**SCOEL**, 2016).

Isobutyl acetate has a fruity, floral odour, with a reported odour threshold between 0.1 and 20ppm (**ACGIH®**, 2016).

OEL evaluations by ACGIH® (2016) and Safe Work Australia (2019) considered all butyl acetate isomers together, (SCOEL (2016) considered iso-, CAS: 110-19-0, n-, CAS: 123-86-4; and sec-, CAS: 105-46-4; isomers together) due to the commonalities in structure and critical effects, and the potential for workplace exposures to mixtures of isomers, recommending group standards (Safe Work Australia, 2019; SCOEL, 2016; ACGIH®, 2016).

SCOEL

The Scientific Committee on Occupational Exposure Limits (SCOEL) evaluation of butyl acetate isomers noted that the critical effects of isobutyl acetate exposure were irritation, although the available data was limited (SCOEL, 2016).

The SCOEL review concluded that:

> "Regarding the critical effect of acute irritation in humans, the **LOAEC** of 150ppm (700mg/m^3) in the study by Iregren *et al* (1993) is the starting point for recommending an OEL. Due to the exposure duration of 4 hours and the minimal effects, an uncertainty factor of 3 is proposed for deriving the recommended OEL. An OEL of 50ppm (240mg/m^3) is proposed for all three butyl acetates to protect workers against both local toxic and systemic effects during an 8-hour exposure.
>
> "Two subchronic inhalation studies in rats (David *et al*. 1998 & 2001) showed **NOAEC**s of each 500ppm which are not in contradiction to the OEL derived above but rather support it.
>
> "A **STEL** is recommended to avoid possible irritating effects by the parent compounds n-butyl, *sec*- and isobutyl acetate and the metabolite acetic acid as well as irritating and central nervous effects caused by isobutanol, a metabolite of isobutyl acetate. Based on the sensory irritation potency (**RD_{50}**), the STEL should be equivalent for the three acetates. A STEL of 150ppm (700mg/m^3) is proposed."
>
> "*n*-Butyl acetate was not sensitising to the skin after dermal exposure of either humans or animals. In the absence of specific data, by analogy to *n*-butyl acetate, no skin sensitising potential is assumed for iso-butyl acetate and sec-butyl acetate."
>
> "In principle, *n*-butyl acetate may be absorbed through human skin (Spasovski and Bencev 1971). However, its permeability through human skin appears to be low owing to its high vapour pressure (ACGIH 2001a). As *sec*-butyl and iso-butyl acetate have even higher vapour pressures, no "skin" notation is proposed for the three compounds." (references cited in SCOEL, 2016).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of butyl acetate isomers noted that the critical effects were eye and mucous membrane irritation reported from human observations (ACGIH®, 2016).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 50ppm (238mg/m^3) is recommended for butyl acetate isomers to minimize the potential risk of irritation reported in volunteers exposed to 147ppm of n-butyl acetate for 4 hours (Iregren *et al*., 1993) and confirmed by experimentally determined eye irritation thresholds of 113 and 177ppm for 10-second exposures to n-butyl acetate and tert-butyl acetate (Cain and Schmidt, 2009). Data from anosmics suggest that n- and sec-butyl acetate have similar thresholds for nasal pungency and irritation and that for tert-butyl acetate is somewhat higher (Abraham *et al*., 1996). Therefore, all butyl acetates are being treated as similarly potent.
>
> "The TWA should protect against transient hyperactivity seen in mice subchronically exposed to 400ppm tert-butyl acetate and increased motor activity in male rats seen at 1600ppm (Faber *et al*., 2014) and against possible reproductive effects of n- and tert-butyl acetate where adverse effects on development of the fetus are probably secondary to maternal toxicity (Saillenfait *et al*., 2007; Yang *et al*., 2007)."
>
> "A **TLV-STEL** of 150ppm (712mg/m^3) is recommended to control mucous membrane irritation in the volunteers at exposures of 200 to 300ppm for 3 to 20 minutes (Nelson *et al*., 1943; Iregren *et al*., 1993)." (references cited in ACGIH®, 2016).

The ACGIH® noted that dermal application of n-butyl acetate to rabbits and guinea pigs did not elicit systemic toxicity, so a **Skin** notation was not warranted; and, there was insufficient data available to recommend **RSEN**, **DSEN** or carcinogenicity notations for butyl acetate isomers (ACGIH®, 2016).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of isobutyl acetate noted that the critical effects were irritative effects, and set a **MAK** value the same as that for the better investigated *n*-butyl acetate, 100ppm (DFG MAK, 2003a). The DFG re-evaluation of *n*-butyl acetate noted that the critical effects were irritative effects of the eyes, nasal mucosa and throat, and recommended a MAK value of 100ppm, peak limitation Category II with an excursion factor of 2 (DFG MAK, 2003b). The DFG has not evaluated sec-butyl acetate.

However, due to prevalent view that all butyl acetate isomers should be considered together, it is pertinent to consider the most up-to-date DFG evaluation of *tert*-butyl acetate. The DFG recommended a MAK value of 20ppm, **peak limitation Category II** with an excursion factor of 2. These values were recently adopted by WorkSafe in 2023. However, the MAK for *tert*-butyl acetate was based on a critical endpoint of acute transient CNS effects while the MAK for other isomers was based on irritation. Given the potential for different endpoints setting different WES for *tert*-butyl acetate from other isomers.

The DFG also noted that dermal absorption might occur, based on data from the isomer n-butyl acetate, but the amounts were unlikely to be relevant for systemic toxicity, so an **"H"** designation was not warranted (DFG MAK, 2014). Sensitisation studies were limited with one study in animals giving a negative result, **"Sa"** or **"Sh"** designations were not considered warranted (DFG MAK, 2014).

Conclusions

Based on the documentation cited, and informed by the conclusions of the SCOEL, ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 150ppm (713mg/m^3) for butyl acetate isomers (except *tert*-butyl acetate), to be inadequate to manage health risks from possible workplace exposure.

It is recommended for all butyl acetate isomers (except *tert*-butyl acetate), that a WES-TWA of 50ppm (238mg/m^3) and a WES-STEL of 150ppm (713mg/m^3) are adopted, to protect against eye and mucous membrane irritation, based on the SCOEL and ACGIH® recommendations; and, noting the potential additive effects of co-exposure with other butyl acetate isomers.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Isobutyl-acetate#section=Chemical-and-Physical-Properties https://pubchem.ncbi.nlm.nih.gov/compound/31272#section=Chemical-and-Physical-Properties https://pubchem.ncbi.nlm.nih.gov/compound/7758#section=Chemical-and-Physical-Properties
CAS Number	isobutyl acetate 110-19-0 n-butyl acetate 123-86-4 sec-butyl acetate 105-46-4
Conversion factors	1mg/m^3 = 0.21ppm (25°C; 101.3**kPa**) 1ppm = 4.75mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Acetic acid, 2-methylpropyl ester www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/120FA943-B214-42F3-AAE8-6029D20955DF HSNO Classification: Acetic acid, butyl ester www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/FF23990A-E631-4F26-A263-4A3EE05EFE5A HSNO Classification: Acetic acid, 1-methylpropyl ester www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/AC8860D4-C357-4AF3-9AD8-4D4C732E16DC Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2001. *"Butyl Acetates, all Isomers."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2003a. *"Isobutyl acetate."* MAK Value Documentation, 2003; The MAK Collection for Occupational Health and Safety 2003; pp 211-215. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb11019e0019

Deutsche Forschungsgemeinschaft (DFG), 2003b. *"n-Butyl acetate."* MAK Value Documentation, 2003; The MAK Collection for Occupational Health and Safety 2003; pp 79-88. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb12386e0019

Deutsche Forschungsgemeinschaft (DFG), 2014. "tert-*Butyl acetate*." The MAK Collection for Occupational Health and Safety 2016, Vol 1, No 2; pp 578-596. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb54088e5716

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National Center for Biotechnology Information. PubChem Database. Accessed July 2021. *Isobutyl acetate*, CID: 8038. https://pubchem.ncbi.nlm.nih.gov/compound/Isobutyl-acetate

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Butyl acetate (all isomers)*. https://engage.swa.gov.au/49158/widgets/259717/documents/115591

Scientific Committee on Occupational Exposure Limits (SCOEL), 2016. "n-*Butyl acetate*, sec-*Butyl acetate and Isobutyl acetate – Recommendation from the Scientific Committee on Occupational Exposure Limits*." SCOEL/REC/184. https://op.europa.eu/en/publication-detail/-/publication/c16eed5e-0a16-11e7-8a35-01aa75ed71a1/language-en/format-PDF/source-213239981

CALCIUM OXIDE

CAS NO: 1305-78-8

Summary

Workplace Exposure Standards for calcium oxide (CAS: 1305-78-8)

	CURRENT	PROPOSED
WES-TWA	2**mg/m³**	1mg/m³
WES-STEL	–	2mg/m³
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for calcium oxide

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for calcium oxide of 1mg/m³, and
2. adopt a WES-STEL for calcium oxide of 2mg/m³.

To protect for irritant effects of the nose, eyes, and throat.

Discussion

Calcium oxide is used in the manufacture of steel, aluminium, glass, and paper; and used in building and construction materials (for example: cement, plaster, mortar, and stucco) (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Calcium oxide is reported to be odourless (PubChem, 2021).

Calcium oxide is hydrolysed to the strongly alkaline calcium hydroxide that is responsible for the local irritative effects of calcium oxide (see the WorkSafe New Zealand WES Review of Calcium hydroxide 2022).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) evaluation of calcium oxide noted that the critical effects were local irritation (DFG MAK, 2014).

The DFG noted that the **MAK** value of 1mg/m³ for calcium oxide, **peak limitation Category I** with an excursion factor of 2, were based on the MAK value for calcium hydroxide (1mg/m³) which is the strongly alkaline hydrolysis product responsible for the local irritative effects of calcium oxide (DFG MAK, 2014). The MAK value for calcium hydroxide was based on volunteer studies that reported mild nasal irritation after 30 minutes exposure to calcium oxide (which hydrolyses to calcium hydroxide in an aqueous environment) at 2.5mg/m³, but not after 20 minutes exposure to 2mg/m³. The study authors reporting that irritative effects did not plateau until after 30 minutes exposure. The peak limit excursion factor of 2 was based on adverse nasal effects at 5mg/m³ from the same set of volunteer studies. These values were supported by a study reporting no relevant respiratory symptoms in workers exposed to calcium oxide at 1.2mg/m³ (0.4-5.8mg/m³) total dust (DFG MAK, 2013).

In analogy with calcium hydroxide, DFG noted that **"H"**, **"Sa"** or **"Sh"** notations were not warranted for calcium oxide (DFG MAK, 2014).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of calcium oxide noted that the critical effects were sensory irritation and decreased lung function at higher concentrations (SCOEL, 2008).

The SCOEL review summarised:

> "The effects of **CaO** and **$Ca(OH)_2$** are considered to be limited to the external surfaces of the body and no systemic effect is foreseen. At low-level exposures, sensory irritation and a decrease of the lung function parameters at long-term exposures are considered to be the critical effects.
>
> "From a well conducted acute study (Cain *et al*., 2004), sensory irritation is expected to be prevented by 1mg/m³ respirable dust. A **STEL** is also set at 4mg/m³ respirable dust to prevent sensory irritation as the exposure in the controlled chamber study (Cain *et al*. 2004) is considered to be to respirable dust and no relation to inhalable dust could be derived.
>
> "No relevant respiratory effect was found as an exposure level at 1mg/m³ (range: 0.4-5.8mg/m³) of total dust among kiln workers producing (Torén *et al*. 1996). That 1mg/m³ is protective against long-term exposure to CaO and Ca(OH)2 is supportive from cement dust exposures that has a similar alkalinity.
>
> "High exposure levels may cause skin and eye burns. Skin absorption is not considered a relevant parameter and, thus, no skin notation is needed." (references cited in SCOEL, 2008).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of calcium oxide noted that the critical effects were eye, mucous membrane, nasal, and moist skin irritation (ACGIH®, 2001).

The ACGIH® review concluded that:

> "By analogy with calcium hydroxide … and because calcium oxide appears to be more irritating than calcium hydroxide, a **TLV-TWA** of 2mg/m³ is believed to be adequate to prevent undue irritation." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations, or a **TLV-STEL** for calcium oxide (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, SCOEL and ACGIH® reviews, WorkSafe considers its current WES-TWA of 2mg/m³ for calcium oxide, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for calcium oxide that a WES-TWA of 1mg/m³ and a WES-STEL of 2mg/m³ are adopted, to protect against irritant effects of the nose, eyes, and throat, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Calcium-oxide#section=Chemical-and-Physical-Properties
CAS Number	1305-78-8
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Calcium oxide www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/5B281CF9-F597-449C-B38C-E147D7F9FDD6

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2008. *"Calcium oxide."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2013. *"Calcium hydroxide."* MAK Value Documentations, 2013; The MAK Collection for Occupational Health and Safety 2016, Vol 1, No 1; pp 12-25. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb130562yole5416

Deutsche Forschungsgemeinschaft (DFG), 2014. *"Calcium oxide."* MAK Value Documentation, 2014; The MAK Collection for Occupational Health and Safety; pp 1119-1121. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb130578e5617

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Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed November 2021 http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed November 2021. *Calcium oxide*, CID: 14778. https://pubchem.ncbi.nlm.nih.gov/compound/Calcium-oxide

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Calcium oxide*. https://engage.swa.gov.au/49436/widgets/260877/documents/116801

Scientific Committee on Occupational Exposure Limits (SCOEL), 2008. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for Calcium oxide (CaO) and calcium hydroxide ($Ca(OH)_2$)."* SCOEL/SUM/137

CHLORINE

CAS NO: 7782-50-5

Summary

Workplace Exposure Standards for chlorine (CAS: 7782-50-5)

	CURRENT	PROPOSED
WES-TWA	0.5**ppm** (1.5**mg/m³**)	–
WES-STEL	1ppm (2.9mg/m³)	0.5ppm (1.5mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for chlorine

Recommendation and basis for WES

It is proposed that WorkSafe:

1. remove the WES-TWA for chlorine, and
2. adopt a WES-STEL for chlorine of 0.5ppm (1.5mg/m³).

To protect for eye irritation and respiratory tract irritation.

Discussion

Chlorine is used as a disinfectant; an oxidising or chlorinating agent; for purifying water and sewage; and, in shrink-proofing wool (**Safe Work Australia**, 2019; **ACGIH®**, 2018).

Chlorine has a pungent, irritating, suffocating odour, with an odour threshold reported at 0.2-0.4ppm (PubChem, 2022; ACGIH®, 2018).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of chlorine noted that the critical effects were respiratory tract irritation, airway hyperreactivity and pulmonary oedema (ACGIH®, 2018).

The ACGIH® review recommended a **TLV-TWA** of 0.1ppm (0.29mg/m³) and a **TLV-STEL** of 0.4ppm (1.16mg/m³) to protect against eye, nasal and lower respiratory tract irritation.

> "A TLV-TWA of 0.1ppm (0.29mg/m³) and a TLV-STEL of 0.4ppm (1.16mg/m³) are recommended for occupational exposure to chlorine (**Cl_2**) in order to minimize eye, nasal, and lower respiratory tract irritation. Chlorine can cause a variety of lung injuries depending mainly on the intensity of the exposure: airway irritation, pulmonary edema, restrictive lung disease, and airway hyperresponsiveness with or without persistent airflow obstruction. Residual effects of chlorine exposure are a function of the intensity of exposure, minute ventilation during exposure, and host factors such as cigarette smoking and atopy (Evans, 2005). Inflammation of the eye or respiratory tract usually resolves after 48 hours, but airway hyperresponsiveness may persist indefinitely.

"The recommended TLV-TWA is based on a 2-year inhalation exposure study in rats and mice that showed concentration-dependent injury to nasal and olfactory tissues in animals exposed to 0, 0.4, 1.0 and 2.0ppm Cl_2 for 6 hours/day, 5 days/week for 2 years (Wolf *et al*., 1995). Adjusting the observed lowest-observed-adverse-effect level (**LOAEL**) of 0.4ppm from a 6-hour to an 8-hour exposure, and going from a LOAEL to a no-observed-adverse-effect level (**NOAEL**) for relatively mild effects observed at 0.4ppm, leads to a TLV-TWA of 0.1ppm for chlorine gas.

"Short-term "peak" exposures to chlorine appear to be important in the initiation of Reactive Airways Dysfunction Syndrome (**RADS**), and the resulting airway hyperresponsiveness may persist for several years (Malo *et al*., 1994). Chlorine may be the only environmental irritant to which persons with airway allergies or asthma can be "predictably hyperresponsive" (Rotman, *et al*., 1983; D'Alessandro *et al*., 1996). The TLV-STEL is based on D'Alessandro *et al*. (1996) findings of significant pulmonary function changes in 10 human volunteers, 5 with airway hyper-reactivity (**AHR**) and 5 without AHR after 60-minute exposures to 1ppm Cl_2. Lung function changes did not persist when measured after 24 hours. Exposure to 0.4ppm for 60 minutes elicited small pulmonary function changes that were not statistically significant in 5 subjects with AHR. Based on these findings, a TLV-STEL of 0.4ppm should be protective for sensitive individuals. (Note: this **TLV** is likely below the odor threshold for chlorine in many workers; therefore, odor is a very unreliable indicator of exposure.)

"Based on equivocal carcinogenicity findings in animals fed chlorinated water, and inadequate cancer data in humans (IARC, 1991), an **A4**, **Not Classifiable as a Human Carcinogen**, carcinogenicity notation is assigned.

"Exposure to chlorine can exacerbate asthma (Rotman *et al*., 1983) but there is no evidence that individuals become sensitized to chlorine *per se*. Therefore, an **RSEN** or **DSEN** notation is not assigned." (references cited in ACGIH®, 2018).

The ACGIH® noted that there was insufficient data available to support a **Skin** notation for chlorine (ACGIH®, 2018).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of chlorine noted that the critical effects were irritation of the eyes and respiratory tract (DFG MAK, 2004).

The DFG noted that the **MAK** value of 0.5ppm for chlorine, **peak limitation Category I** with an excursion factor of 1, were based on the results of short-term, repeated exposure and epidemiological studies at the workplace that indicated exposures to 0.5ppm chlorine did not induce statistically significant adverse changes. The DFG reported repeat inhalation studies in rats, mice and rhesus monkeys that potentially gave lower NOAEL/LOAEL values, but concluded that, due to difficulties in the study or differences in anatomy and physiology of respiratory tracts with humans, the MAK value of 0.5ppm was robust (DFG MAK, 2004).

The DFG also noted that **"H"**, **"Sa"** or **"Sh"** notations could not be assessed due to lack of data for chlorine (DFG MAK, 2004).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of chlorine noted that the critical effects were irritation of the eyes and respiratory tract (SCOEL, 1998).

The SCOEL review summarised:

> "A constant exposure to 0.5ppm (1.5mg/m^3) has been shown to be without effect in two human studies, and also in rhesus monkeys, whereas there is clear evidence of irritation at 1.0ppm (2.95mg/m^3). On this basis, the SCOEL considered that occupational exposure levels should not exceed 0.5ppm (1.5mg/m^3), which is therefore proposed as a STEL (15 mins). Because the effects appear to be related to concentration in the air and not to duration of exposure, there is no requirement for an 8-hour TWA.
>
> "No "skin" notation was considered to be necessary." (SCOEL, 1998).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SCOEL reviews, WorkSafe considers its current WES-TWA of 0.5ppm (1.5mg/m^3) and WES-STEL of 1ppm (2.9mg/m^3) for chlorine to be inadequate to manage health risks from possible workplace exposure.

It is recommended for chlorine that the WES-TWA is removed and a WES-STEL of 0.5ppm (1.5mg/m^3) is adopted, to protect against eye irritation and respiratory tract irritation, based on the DFG and SCOEL recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/chlorine#section=Chemical-and-Physical-Properties
CAS Number	7782-50-5
Conversion factors	1ppm = 2.90mg/m^3 (25°C; 101.3**kPa**) 1mg/m^3 = 0.344ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/BCEB1151-22A4-4FE3-853F-692E11E35696

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Chlorine."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2004. *"Chlorine."* MAK Value Documentation, 2004; The MAK Collection for Occupational Health and Safety, 2014; pp 1-27. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb778250e3814

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2022. GESTIS International Limit Values. Accessed January 2022. http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed January 2022. *Chlorine*, CID: 24526. https://pubchem.ncbi.nlm.nih.gov/compound/chlorine

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Chlorine*. https://engage.swa.gov.au/50013/widgets/263308/documents/117899

Scientific Committee on Occupational Exposure Limits (SCOEL), 1998. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for chlorine."* SCOEL/SUM/76

CHLOROBENZENE

CAS NO: 108-90-7

Summary

Workplace Exposure Standards for chlorobenzene (CAS: 108-90-7)

	CURRENT	PROPOSED
WES-TWA	10**ppm** (46**mg/m³**)	5ppm (23mg/m³)
WES-STEL	–	10ppm (46mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for chlorobenzene

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for chlorobenzene of 5ppm (23mg/m³), and
2. adopt a WES-STEL of 10ppm (46mg/m³).

To protect for central nervous system effects.

Discussion

Chlorobenzene is used as a solvent; a chemical intermediate; and, as a heat transfer medium (**Safe Work Australia**, 2019; **ACGIH**®, 2001).

Chlorobenzene has a mild aromatic, or almond-like odour, with an odour threshold reported at 0.21ppm (PubChem, 2021; **SCOEL**, 2003; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of chlorobenzene noted that the critical effects were central nervous system effects reported in humans, and liver and kidney changes in animals (DFG MAK, 2018).

The DFG noted that the **MAK** value of 5ppm, **peak limitation Category II** with an excursion factor of 2, were based on a **NOAEC** of 50ppm from a 2-generation inhalation study in rats with liver and kidney toxicity reported at 150ppm, and scaled for the workplace (DFG MAK, 2018). The MAK value was supported by data from volunteers reporting sleepiness, headache, and pain in the eyes after exposure to 60.2ppm for several hours, but not after exposure to 11.8ppm (DFG MAK, 2018).

The DFG noted that there was no robust data available to evaluate **"Sa"** or **"Sh"** notations (DFG MAK, 2018). No data was reported for potential dermal absorption, and the dermal $\mathbf{LD_{50}}$ was reported as greater than 2212**mg/kg b.w.** in rabbits (DFG MAK, 2018).

SCOEL

The Scientific Committee on Occupational Exposure Limits (SCOEL) evaluation of chlorobenzene (monochlorobenzene) recommended:

> "Weighing the total body of data obtained in genotoxicity and carcinogenicity studies of monochlorobenzene (one positive *in vitro* gene mutation test and several negative *in vitro* genotoxicity assays, and one negative long-term mouse and one negative long-term rat carcinogenicity study), the committee concludes that occupational exposure to monochlorobenzene under normal conditions is of no health concern with respect to potential genotoxic or carcinogenic effects.
>
> "The committee has selected the **LOAEL** of 50ppm obtained in the two-generation rat inhalation reproduction study (Nair *et al*. 1987) as the starting point for deriving an occupational exposure limit. Applying an uncertainty factor of 10 to allow for intra- and interspecies variation and for the absence of a **NOAEL** in the selected two-generation rat study, the committee recommends an occupatinal (*sic.*) exposure limit for monochlorobenzene of 5ppm (23mg/m^3) as a **TWA** over 8-hours. The committee emphasizes that the proposed value is considered ~~to~~ (sic) protective for workers against potential haematotoxic effects as found in mice after prolonged inhalational exposure to 21ppm (100mg/m^3) monochlorobenzene (Zub, 1978), and also against sensory irritation as seen in human volunteers exposed to 60ppm (282mg/m^3) with no effects at 12ppm (55mg/m^3) (Ogata *et al*, 1991).
>
> "A **STEL** (15 mins) of 15ppm (70mg/m^3) is proposed to limit peaks in exposure which could result in irritation.
>
> "No "**skin**" notation is considered to be necessary, since acute dermal application of monochlorobenzene in a dose of more than 2,000**mg/kg** body weight was not lethal to rabbits." (references cited in SCOEL, 2003).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of chlorobenzene noted that the potential critical effects were liver changes (increased weight and congestion) as reported in animals (ACGIH®, 2001).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 10ppm is recommended for chlorobenzene. This primarily follows from the inhalation data in which subtle effects, particularly those in the liver, occurred in rats exposed repeatedly at 75ppm (Dilley & Lewis, 1978) and the slight liver weight increase seen in one of two generations of males exposed at 50ppm (Nair *et al*., 1987). A rather complete battery of animal studies following both acute and repeated exposures are available to support this position. The chemical does not appear to be a mutagen or a developmental toxin. Based on the slight increases in the frequency of neoplastic nodules in male rats in a 2-year feeding study with chlorobenzene (US NTP, 1985), a carcinogenicity notation of **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, is assigned to chlorobenzene." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **Skin**, **DSEN** or **RSEN** notations, or a **TLV-STEL** for chlorobenzene (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, SCOEL and ACGIH® reviews, WorkSafe considers its current WES-TWA of 10ppm (46mg/m^3) for chlorobenzene, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for chlorobenzene that a WES-TWA of 5ppm (23mg/m^3) and a WES-STEL of 10ppm (46mg/m^3) are adopted to protect against CNS effects, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/chlorobenzene#section=Chemical-and-Physical-Properties
CAS Number	108-90-7
Conversion factors	1mg/m^3 = 0.216ppm (25°C; 101.3**kPa**) 1ppm = 4.62mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Benzene, chloro www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/D4C4ECD8-B5B6-4446-B3A8-229564BBD3FA Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Monochlorobenzene."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2018. *"Chlorobenzene."* MAK Value Documentation, 2018; The MAK Collection for Occupational Health and Safety 2019, Vol 4, No 4; pp 1893-1909. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10890e6519

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed July 2021 http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed July 2021. *Methylcyclohexane*, CID: 7964. https://pubchem.ncbi.nlm.nih.gov/compound/chlorobenzene

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Chlorobenzene*. https://engage.swa.gov.au/50013/widgets/263308/documents/117901

Scientific Committee on Occupational Exposure Limits (SCOEL), 2003. *"Recommendation of the Scientific Committee on Occupational Exposure Limits for Monochlorobenzene."* SCOEL/SUM/42

CHLORODIFLUOROMETHANE

CAS NO: 75-45-6

Summary

Workplace Exposure Standards for chlorodifluoromethane (CAS: 75-45-6)

	CURRENT	PROPOSED
WES-TWA	1,000**ppm** (3,540**mg/m³**)	1,000ppm (3,540mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for chlorodifluoromethane

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA of 1,000ppm (3,540mg/m³) for chlorodifluoromethane.

To prevent chronic toxicity.

Discussion

Chlorodifluoromethane (**FC-22**) is used as an aerosol propellant, refrigerant, low-temperature solvent, and as a component of fluorocarbon resins (**ACGIH®**, 2001; **Safe Work Australia**, 2019).

Chlorodifluoromethane has a faint, sweetish odour (PubChem, 2021; **SEG**, 1993).

Cancer risks

The International Agency for Research on Cancer (IARC) evaluation of chlorofluoromethane concluded that:

> There is ***inadequate evidence in humans*** for the carcinogenicity of chlorofluoromethane.
>
> There is ***limited evidence in experimental animals*** for the carcinogenicity of chlorofluoromethane.

With an overall evaluation that:

> Chlorofluoromethane is *not classifiable as to its carcinogenicity to humans* (**Group 3**). (IARC, 1999).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of chlorodifluoromethane noted that the substance indicated very low toxicity in rats and mice (DFG MAK, 1992).

The DFG noted that the **MAK** value of 500ppm for chlorodifluoromethane, **peak limitation Category II** with an excursion factor of 8, were based on a **NOAEL** of about 10,000ppm from long-term studies in rats and mice, with an *appropriate* safety factor (DFG MAK, 1992; DFG MAK, 2002).

The DFG came to no conclusions on **"H"** or **"S"** notations for chlorodifluoromethane (DFG MAK, 1992; DFG MAK, 2002).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of chlorodifluoromethane noted that the critical effects were central nervous system effects and cardiac palpitations at high concentrations (ACGIH®, 2001).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 1,000ppm FC-22 is recommended as a guide for good occupational hygiene practice for vapors of low toxicity. Neoplastic findings in rats exposed by inhalation 6 hours/day, 5 days/week for 104 weeks at 4.1, 41 or 82mg/m^3 FC-22 were similar to those in control rats (Seckar *et al*., 1986). Accordingly, a carcinogenicity notation of **A4**, **Not Classifiable as a Human Carcinogen**, is assigned to FC-22." (reference cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin** or **SEN** notations for chlorodifluoromethane (ACGIH®, 2001).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of chlorodifluoromethane recommended an 8-hour TWA of 1,000ppm (3,600mg/m^3), based on:

> "The studies of Tinston *et al* (1981a and b) and Palmer *et al* (1978a and b), indicating a NOAEL of 10,000 ppm (36 g/m^3) for chronic toxicity and teratogenicity in rats, was considered to be the best available basis for proposing an 8-hour TWA. An uncertainty factor of 10 was applied to allow for the absence of human data. The recommended 8-hour TWA is 1,000 ppm (3,600 mg/m^3). This value refers to pure CFC22 only. No **STEL** or "**skin**" notation was considered to be necessary." (reference cited in SEG, 1993).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, SCOEL, and ACGIH® reviews, WorkSafe considers its current WES-TWA of 1,000ppm (3,540mg/m^3) for chlorodifluoromethane, to be adequate to manage health risks from possible workplace exposure. Noting the limited and dated toxicology profile and overseas risk assessments.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/chlorodifluoromethane#section=Chemical-and-Physical-Properties
CAS Number	75-45-6
Conversion factors	1mg/m³ = 0.54ppm (25°C; 101.3**kPa**) 1ppm = 1.84mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: None

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Chlorodifluoromethane."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1992. *"Chlorodifluoromethane."* MAK Value Documentation, 1992; The MAK Collection for Occupational Health and Safety; pp 63-71. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7545e0003

Deutsche Forschungsgemeinschaft (DFG), 2002. *"Monochlorodifluormethan."* MAK Value Documentation in German language, 2002; The MAK Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7545d0034

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2021. GESTIS International Limit Values. Accessed September 2021 http://limitvalue.ifa.dguv.de

International Agency for Research on Cancer (IARC), 1999. *"IARC Monographs on the Identification of Carcinogenic Hazards to Humans Volume 71: Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide (Part 1, Part 2, Part 3)."* Lyon, France. pp 1339-1343. https://publications.iarc.fr/89

National Center for Biotechnology Information. PubChem Database. Accessed September 2021. *Chlorodifluoromethane*, CID: 6372. https://pubchem.ncbi.nlm.nih.gov/compound/chlorodifluoromethane

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Chlorodifluoromethane*. https://engage.swa.gov.au/49436/widgets/260877/documents/116919

Scientific Expert Group on Occupational Exposure Limits (SEG), 1993. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for Chlorodifluoromethane."* SEG/SUM/36

CUMENE

CAS NO: 98-82-8

Summary

Workplace Exposure Standards for cumene (CAS: 98-82-8)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (125**mg/m³**)	10ppm (50mg/m³)
WES-STEL	75ppm (375mg/m³)	50ppm (250mg/m³)
WES-Ceiling	–	–
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for cumene

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for cumene of 10ppm (50mg/m³)
2. adopt a WES-STEL for cumene of 50ppm (250mg/m³), and
3. maintain the *skin* notation for cumene.

To protect for cancer, and neurological and haematological effects at higher concentrations.

Discussion

Cumene is used primarily as an intermediate in the production of phenol and acetone. Other uses include: in chemical manufacture; as a catalyst for acrylic and polyester-type resins; as a thinner for paints; as a solvent for fats and resins; and, in printing and rubber manufacture (**Safe Work Australia**, 2019; **IARC**, 2012). Cumene occurs naturally in crude oil and can be released into workplaces through petrol engine emissions and while handling fossil fuels (IARC, 2012).

Cumene has a sharp, penetrating, aromatic odour, with odour thresholds of 0.008ppm and 0.012ppm reported (PubChem, 2021).

Cancer risks

The International Agency for Research on Cancer (IARC) evaluation of cumene and its putative metabolite α-methylstyrene concluded that:

> No data were available to the Working Group [for cancer in humans].
>
> There is ***sufficient evidence in experimental animals*** for the carcinogenicity cumene.
>
> There is ***sufficient evidence in experimental animals*** for the carcinogenicity α-methylstyrene.

With an overall evaluation that:

> Cumene is possibly carcinogenic to humans (**Group 2B**).
>
> α-Methylstyrene is possibly carcinogenic to humans (Group 2B). (IARC, 2012).

The IARC noted that while cumene has not demonstrated mutagenic activity, one of its metabolites α-methylstyrene oxide has shown mutagenic activity in bacteria and *in vivo* in male rats. The enzymes responsible for generating α-methylstyrene oxide from cumene are present in both rodents and humans. Mouse lung tumours induced by cumene reveal gene mutations and changes in gene expression that are involved in carcinogenesis in both mice and humans (IARC, 2012).

A mutational mechanism for cumene-induced lung or nasal tumours would indicate that a threshold may not exist, however no data on cumene-induced cancer in humans was available to confirm or refute this hypothesis.

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of cumene (2-phenylpropane) noted that the critical effects were carcinogenicity reported in rodents (SCOEL, 2018).

The SCOEL review summarised:

> "... the observed difference between rats and mice in lung carcinogenicity may be explained by differences in the local metabolism, as there are more Clara cells in mice than in rats, which contain the ring-oxidising cytochromes **P-450 CYP2F** and **CYP2E1** (Sections 7.1.2./7.9.). As in humans there are even less Clara cells than in rats. A very low susceptibility of humans may be reasonably anticipated. By analogy to other solvents, e.g. phenylethane (ethyl benzene), the renal effects of 2-phenylpropane in male rats (tubular adenomas/carcinomas) may reasonably be related to the specific $\alpha 2_{\mu}$-globulin-nephropathy, which is not relevant to humans. In the case of 2-phenylpropane, this is supported by measurements of $\alpha 2_{\mu}$-globulin in kidneys of rats exposed subchronically (NTP 2009, NTP 2012b; see Section 7.3.2). Damage to rat nasal tissue was not observed in subchronic studies at all concentrations tested, up to 500ppm 2-phenylpropane (Section 7.3.2). In the 2-year study by **NTP** (2009), there were signs of chronic inflammation in the nasal epithelium of rats in conjunction with the occurrence of adenomas of the respiratory epithelium (Section 7.7.2). Based on these arguments, the existence of a threshold for the experimentally observed carcinogenic effects of 2-phenylpropane is very likely. In total, the data suggest that 2-phenylpropene is an overwhelmingly non-genotoxic carcinogen. In consequence, the compound is grouped into SCOEL carcinogenicity group D, for which a health-based **OEL** may be derived.
>
> "The **NOAEC** in rats, based on the studies of Cushman *et al* (1995) and NTP (1999) is 50ppm (Section 7.3.2). This NOAEC is primarily based on hepatic effects. As discussed in Section 7.7.2, there is evidence that the formation of liver tumours in (female) mice cannot be translated to humans based on kinetic and dynamic arguments. But it appears safe to base the OEL derivation on this NOAEC, as this will provide an in-built margin of safety. The derived OEL will therefore in any case be protective against carcinogenic effects seen in animal experiments. The OEL evaluation is based on experimental studies with inhalation exposure. Starting from the NOAEC of 50ppm an uncertainty factor of 5 is applied accounting for the nature of the effect and the remaining uncertainties due to inter- and intra-species differences. Therefore, a health-based OEL of 10 ppm is recommended, based on the preferred value approach. Together with the above mentioned in-built margin of safety, this OEL will provide a sufficient distance to reported adverse effects. A **STEL** of 50ppm can be recommended to protect against possible short-term behavioural effects and is also protective against local irritation." (SCOEL, 2018).

The SCOEL recommended a *"skin notation"* for cumene, based the chemical's high lipophilicity, analogy to benzene and xylene, and modelling estimates of dermal absorption (SCOEL, 2018).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of cumene (isopropyl benzene) noted that the critical effects were tumour-induction and liver effects in rodents (DFG MAK, 2018).

The DFG noted that the **MAK** value of 10ppm for cumene, **peak limitation Category II** with an excursion factor of 4, were based on a NOAEC of 125ppm from a 14-week inhalation study in rats where systemic effects such as increased kidney weights and changes in clinic-chemical parameters were reported at 250ppm. This NOAEC was supported by a **$BMDL_{05}$** of 42ppm from a 2-year inhalation study in rats where nasal adenomas were reported, adjusted accordingly to give a workplace air **NAEC** of 31ppm (DFG MAK, 2018).

The DFG concluded that an **"H"** notation was warranted for cumene, based on mathematical modelling and comparison with structurally related substances, in the absence of experimental data, indicating that dermal absorption could contribute significantly to systemic toxicity (DFG MAK, 2018).

The DFG also noted that **"Sh"** or **"Sa"** notations were not designated for cumene, based on a negative skin sensitisation test in guinea pigs and the absence of sensitisation reports in humans (DFG MAK, 2013).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (**ACGIH®**) review of cumene noted that the critical effects were upper respiratory tract adenoma and neurological effects (ACGIH®, 2020).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 5ppm (25mg/m^3) for cumene is recommended to protect against nasal respiratory epithelial adenoma observed in rats in a 105-week study (U.S. NTP, 2009). These adenomas were significantly increased in all exposed groups of males (250, 500, and 1,000ppm), with a positive statistical trend, and were also seen in 250ppm females. There was no evidence of malignant progression of these adenomas. This value should protect against neurological effects (U.S. NTP, 2009; Cushman *et al*., 1995).
> "The incidences of renal tubule adenoma in all exposed groups of males, renal tubule carcinoma in 500 and 1,000ppm males, and renal tubule adenoma or carcinoma (combined) in all exposed groups of males were increased. The difference from chamber controls for the combined incidence was significant at 500ppm. The incidences of hyperplasia of the renal tubule and transitional epithelium of the renal pelvis in males exposed to 500 and 1,000ppm, and mineralization of the renal papilla in all exposed groups of males, were significantly greater than those of the chamber controls.
>
> "Female mice exposed at 125ppm and male mice exposed to 250ppm (the lowest concentration studied for both) developed alveolar/bronchiolar carcinoma. Hepatocellular adenoma or carcinoma was found in female mice exposed to 500ppm (U.S. NTP, 2009)

"An **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, cancer notation is recommended based on the mouse lung and liver carcinomas and rat nasal, testicular, and renal carcinomas observed in the absence of human data. The lack of clear evidence of genotoxicity, the species-specific nature of the tumors observed, the high rate of spontaneous tumors, the lack of progression of some tumor types, and the uncertainty in the relevance of induction of K-ras and p53 oncogenes are consistent with this cancer classification." (references cited in ACGIH®, 2020).

The ACGIH® noted that data did not support a **DSEN**, and found there was insufficient data available to recommend **Skin** or **RSEN** notations, or a **TLV-STEL** for cumene (ACGIH®, 2020).

Conclusions

Based on the documentation cited, and informed by the conclusions of the SCOEL, DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 25ppm (125mg/m³) and WES-STEL of 75ppm (375mg/m³) with a *skin* notation for cumene, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for cumene that a WES-TWA of 10ppm (50mg/m³) and a WES-STEL of 50ppm (250mg/m³) are adopted, to protect against cancer and neurological and haematological effects at higher concentrations, based on the SCOEL and DFG recommendations. The *skin* notation should be maintained.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/cumene#section=Chemical-and-Physical-Properties
CAS Number	98-82-8
Conversion factors	1mg/m³ = 0.2ppm (25°C; 101.3**kPa**) 1ppm = 4.92mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Benzene, (1-methylethyl) www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/5821A596-F802-47A4-987D-FB59F84F54CE Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Cumene."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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CYCLOHEXANONE

CAS NO: 108-94-1

Summary

Workplace Exposure Standards for cyclohexanone (CAS: 108-94-1)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (100**mg/m³**)	10ppm (41mg/m³)
WES-STEL	–	20ppm (82mg/m³)
WES-Ceiling	–	–
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for cyclohexanone

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for cyclohexanone of 10ppm (41mg/m³)
2. adopt a WES-STEL for cyclohexanone of 20ppm (82mg/m³), and
3. maintain the *skin* notation for cyclohexanone.

To protect for irritation of the eyes, nose, and throat.

Discussion

Cyclohexanone is used predominantly in the production of nylon; as a solvent in insecticides, paints, paint and varnish removers, natural and vinyl rubbers, and in the textile and tanning industries (**Safe Work Australia**, 2019; **ACGIH®**, 2003).

Cyclohexanone has an acetone and peppermint-like odour, with an odour threshold reported at 0.88ppm (PubChem, 2021; ACGIH®, 2003).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of cyclohexanone noted that the potential critical effects were central nervous system effects; eye, nose and throat irritation; and, possible liver and kidney effects (ACGIH®, 2003).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 25ppm" [*note this is an error, and is intended to be 20ppm*] "and a **TLV-STEL** of 50ppm are recommended for cyclohexanone to minimize eye, nose, and throat irritation (Schaper, 1993; Nelson *et al*., 1943; Esso, 1965). This value is significantly lower than the intravenous NOEL of 100**mg/kg/day** that was reported in a 28-day subchronic rat study, which would translate to 700mg/m³ (175ppm) in a 150-pound individual assuming a respiratory volume of 10m3 (Greener *et al*., 1982). It is also lower than the lowest-observed-effect level of 190ppm reported to induce just demonstrable changes in the liver and kidneys of rabbits repeatedly exposed for 6 hours/day for 50 days (Treon *et al*., 1943).

"Based on the most likely non-relevant carcinogenic evidence in rat and mouse drinking water studies, cyclohexanone is assigned a carcinogenicity designation of **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans** (Lijinsky & Kovatch, 1986; US EPA, 1998; IARC, 1998). A **Skin** notation is assigned, based on the reported dermal **LD_{50}** data (Smyth *et al*., 1969)." (references cited in ACGIH®, 2003).

The ACGIH® noted that there was insufficient data to recommend **DSEN** or **RSEN** notations for cyclohexanone (ACGIH®, 2003).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of cyclohexanone noted that the critical effects were irritative effects reported in humans, and liver and kidney changes in animals (DFG MAK, 1998).

The DFG noted that a **MAK** value could not be set because the mechanism responsible for the induction of thyroid gland tumours in the rat was unclear (DFG MAK, 1998).

The DFG noted that cyclohexanone was readily absorbed through the skin, and warranted an **"H"** notation (DFG MAK, 1998).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of cyclohexanone recommended:

"The studies of Treon *et al* (1943), indicating a **LOAEL** of 190ppm (775mg/m^3) for systemic effects in rabbits, and of Nelson *et al* (1943), indicating a **NOAEL** of 25ppm (102mg/m^3) for irritation to the throat and eyes of human volunteers, were considered to be the best available bases for proposing a limit. An uncertainty factor of 2 was applied to allow for the limitations of the Nelson study. The recommended 8-hour **TWA** is 10ppm (40.8mg/m^{-3}). This is not contradicted by the study of Greene* *et al* (1982), establishing a NOAEL for systemic effects of 100mg/kg/day by intravenous injection. A S ILL (*sic*) (15 minš) (*sic*) of 20ppm (81.6mg/m^3) is proposed to limit peaks in exposure which could result in irritation. A "skin" notation is also recommended as dermal absorption could contribute substantially to the total body burden." (references cited in SEG, 1992).

NIOSH

National Institute for Occupational Safety and Health (NIOSH) Skin Notation Profile for cyclohexanone summarised:

"The mathematical model predicted that cyclohexanone is considered to be absorbed through the skin following dermal exposure. However, acute toxicity studies in rabbits and guinea pigs [Union Carbide Corporation 1967; Smyth *et al*. 1969; Eastman Kodak Company 1978; EI du Pont de Nemours and Company (DuPont) 1983a] indicate that cyclohexanone is not acutely toxic. While no epidemiological studies, human case reports, or animal chronic dermal toxicity studies were identified, repeat-dose studies [Rengstorff *et al*. 1972; Industrial Health Foundation, Inc. 1983] evaluated

limited systemic endpoints and ophthalmologic and histopathologic changes in the eye, and these studies indicated no treatment-related systemic effects or other effects on the eye. Irritation tests in rabbits and guinea pigs [Gupta *et al*. 1979; Union Carbide 1982; Industrial Health Foundation Inc. 1983; Eastman Kodak Company 1978] indicate that high concentrations of cyclohexanone or repeated dermal exposures are mildly to severely irritating to the skin with the potential to cause necrosis. The available data indicate that cyclohexanone resin may cause allergic contact dermatitis in humans [Bruze *et al*. 1988; Pazzaglia *et al*. 2003]; however, results from predictive tests in animals (GPMTs and MESTs) indicated that cyclohexanone itself is not a skin sensitizer [Gad *et al*. 1986; Bruze *et al*. 1988]. Based on the available information, this assessment assigns a composite skin notation of **SK: DIR (COR)** for cyclohexanone." (references cited in NIOSH, 2020).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SCOEL reviews, WorkSafe considers its current WES-TWA of 25ppm (100mg/m³) for cyclohexanone, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for cyclohexanone that a WES-TWA of 10ppm (41mg/m³) with a WES-STEL of 20ppm (82mg/m³) are adopted, while the skin notation is maintained, to protect against irritation of the eyes, nose, and throat, based on the SCOEL recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/cyclohexanone#section=Chemical-and-Physical-Properties
CAS Number	108-94-1
Conversion factors	1mg/m³ = 0.25ppm (25°C; 101.3**kPa**) 1ppm = 4.01mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/0A683331-518A-4DE8-8745-A9C7737C346C Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

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DIACETONE ALCOHOL

CAS NO: 123-42-2

Summary

Workplace Exposure Standards for diacetone alcohol (CAS: 123-42-2)

	CURRENT	PROPOSED
WES-TWA	50**ppm** (238**mg/m³**)	50ppm (238mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for diacetone alcohol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. retain a WES-TWA for diacetone alcohol of 50ppm (238mg/m³).

To protect for eye, skin and respiratory tract irritation.

Discussion

Diacetone alcohol is used as a solvent for nitrocellulose, cellulose acetate, celluloid, pigments, waxes, fats, and oils (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Diacetone alcohol has a mint-like odour, with a reported odour threshold of 0.28ppm (PubChem, 2021; ACGIH®, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of diacetone alcohol noted that the critical effects were eye, skin and respiratory tract irritation (ACGIH®, 2001).

The ACGIH® review recommended a **TLV-TWA** of 50ppm based on a human study where irritation occurred at 100ppm (reference cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin**, **DSEN**, **RSEN** or carcinogenicity notations, or a **TLV-STEL** for diacetone alcohol (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of diacetone alcohol (4-hydroxy-4-methylpentan-2-on) noted that the critical effects were mucous membrane irritation (DFG MAK, 2001).

The DFG noted that the **MAK** value of 20ppm for diacetone alcohol, **peak limitation Category I** with an excursion factor of 2, were based on studies with volunteers that reported irritative effects in the majority at 100ppm, but that 50ppm was tolerable for the majority after 8 hours exposure. The MAK value was supported by a **NOEL** of 50ppm from a 6-week inhalation study in rats where marginal effects were reported at 216ppm (DFG MAK, 2001).

The DFG concluded that an **"H"** notation was warranted for diacetone alcohol, based on studies that indicated that dermal absorption could contribute significantly to systemic toxicity (DFG MAK, 2001

The DFG reported that inadequate data on diacetone alcohol was available to assess **"S"** notations (DFG MAK, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 50ppm (238mg/m³) for diacetone alcohol to be adequate to manage health risks from possible workplace exposure.

It is recommended for diacetone alcohol that a WES-TWA of 50ppm (238mg/m³) be retained to protect against eye, skin and respiratory tract irritation, based on the ACGIH recommendations. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Diacetone-alcohol#section=Chemical-and-Physical-Properties
CAS Number	123-42-2
Conversion factors	1mg/m³ = 0.211ppm (25°C; 101.3**kPa**) 1ppm = 4.74mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/4439B71B-CCC5-4106-A104-FAF7C2FA853A Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

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DIETHYL ETHER

CAS NO: 60-29-7

Summary

Workplace Exposure Standards for diethyl ether (CAS: 60-29-7)

	CURRENT	PROPOSED
WES-TWA	400**ppm** (1,210**mg/m³**)	400ppm (1,210mg/m³)
WES-STEL	500ppm (1,520mg/m³)	500ppm (1,520mg/m³)
WES-Ceiling	-	-
Notations	-	-

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for diethyl ether

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA for diethyl ether of 400ppm (1,210mg/m³), and
2. maintain the WES-STEL for diethyl ether of 500ppm (1,520mg/m³).

To protect for eye, nasal, and respiratory tract irritation, and narcosis.

Discussion

Diethyl ether is used as a solvent; reagent in organic syntheses; and, historically as an anaesthetic (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Diethyl ether has an aromatic, ethereal, sweet odour, with odour thresholds reported at 0.83 and 8.9ppm (PubChem, 2021; ACGIH®, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of diethyl ether (ethyl ether) noted that the critical effects were eye, nasal and respiratory tract irritation, and narcosis (ACGIH®, 2001).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 400ppm (1,210mg/m³) and a **TLV-STEL** of 500ppm (1,520mg/m³) are recommended to protect for occupational exposure to ethyl ether to minimize the potential for eye, nasal, and respiratory tract irritation, and narcosis that can lead to general anesthesia. Symptoms in workers from chronic overexposure to ethyl ether are reported to include loss of appetite, headache, exhaustion, sleepiness, dizziness, excitation, and psychic disturbances." (ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **DSEN**, **RSEN**, **Skin** or carcinogenicity notations for diethyl ether (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of diethyl ether noted that the critical effects were mucous membrane irritation and neurotoxicity (DFG MAK, 1999).

The DFG noted that the **MAK** value of 400ppm, **peak limitation Category II** with an excursion factor of 1, were based on animal studies that indicated that exposures to diethyl ether at 1,000 and 2,000ppm for respectively 22 hours daily for 35 days and 7 hours/day, 5 days/week for 35 days did not result in significant systemic toxicity (DFG MAK, 1999).

An **"H"** notation was not warranted for diethyl ether, based on the limited data available (DFG MAK, 1999).

The DFG noted that no robust data was available to assess **"Sa"** and **"Sh"** notations (DFG MAK, 1999).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of diethyl ether recommended an 8-hour TWA of 100ppm (308mg/m^3) and a 15-minute STEL of 200ppm (616mg/m^3), based on a study by Nelson *et al*. (1943) while noting the study had major limitations. Human volunteers reported the first signs of nasal irritation after 3-5 minutes exposure to a calculated level of 200ppm diethyl ether, while a calculated level of 300ppm became objectionable. Most volunteers reported that 100ppm would be acceptable over an 8-hour exposure period (SEG, 1991).

This SEG evaluation remains the basis for the current European Communities Indicative Occupational Exposure Levels (IOEL) (**ECHA REACH**, n.d.). However, the ACGIH® and DFG reviews cited the Nelson *et al*. (1943) study but did not use the data as a basis for their recommendations (ACGIH®, 2001; DFG, 1999).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 400ppm (1,210mg/m^3) and WES-STEL of 500ppm (1,520mg/m^3) for diethyl ether, to be adequate to manage health risks from possible workplace exposure.

It is recommended for diethyl ether that the WES-TWA of 400ppm (1,210mg/m^3) and WES-STEL of 500ppm (1,520mg/m^3) are maintained to protect against eye, nasal, and respiratory tract irritation, and narcosis, based on the ACGIH® recommendations.

It is noted that no new oversea evaluations were available since the previous review.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/3283#section=Chemical-and-Physical-Properties
CAS Number	60-29-7
Conversion factors	1mg/m³ = 0.330ppm (25°C; 101.3**kPa**) 1ppm = 3.03mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Ethane, 1,1'-oxybis www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/7B2ACED9-7454-401B-A628-3AD0113C52DD Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Ethyl Ether"* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1999. *"Diethyl ether."* MAK Value Documentation, 1999; The MAK Collection for Occupational Health and Safety; pp 149-160. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb6029e0013

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DIMETHOXYMETHANE

CAS NO: 109-87-5

Summary

Workplace Exposure Standards for dimethoxymethane (CAS: 109-87-5)

	CURRENT	PROPOSED
WES-TWA	1,000**ppm** (3,110**mg/m³**)	500ppm (1,555mg/m³)
WES-STEL	–	1,000ppm (3,110mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for dimethoxymethane

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for dimethoxymethane of 500ppm (1,555mg/m³), and
2. adopt a WES-STEL for dimethoxymethane of 1,000ppm (3,110mg/m³).

To protect for CNS depression, and eye and mucous membrane irritation.

Discussion

Dimethoxymethane is used as a special purpose fuel; in perfumes; as a solvent in adhesives and coatings; and, as an anaesthetic in surgery (**Safe Work Australia**, 2019; **ACGIH®**, 2004).

Dimethoxymethane has a chloroform-like odour (PubChem, 2021; ACGIH®, 2004).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of dimethoxymethane (dimethoxymethan) noted that the critical effects were central nervous system depression reported in animals (DFG MAK, 2019).

The DFG noted that the **MAK** value of 500ppm, **peak limitation Category II** with an excursion factor of 2, were based on a NOAEC of 1,908ppm from a 13-week inhalation study in rats with CNS depression observed at 10,000ppm, and scaled for the workplace. The MAK value was expected to be protective against eye and mucous membrane irritation, induced by locally produced formaldehyde, reported in animals exposed to 9650ppm dimethoxymethane (DFG MAK, 2019).

The DFG noted that mathematical modelling indicated that dermal absorption of dimethoxymethane was unlikely to significantly contribute to total body burden, so an **"H"** notation was not warranted (DFG MAK, 2019).

The DFG also noted that there was no robust data available to evaluate **"Sa"** or **"Sh"** notations for dimethoxymethane (DFG MAK, 2019).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of dimethoxymethane (methylal) noted that the critical effects were irritation of the eyes and mucous membranes, and central nervous system depression at high concentrations (ACGIH®, 2004).

The ACGIH® review concluded that:

> "Methylal is a minor irritant of the eyes and mucous membranes (Weaver *et al*., 1951), and at high concentrations, it can cause central nervous system depression. Based on the available but very limited animal data and the clinical experience (Weaver *et al*., 1951) with methylal, a **TLV-TWA** of 1,000ppm is recommended. The 1,000ppm TLV-TWA corresponds with the acute and subchronic animal data which indicate that methylal is one of the least toxic organic solvents. There appear to be no occupational exposure experience or data from chronic animal studies to either support or dispute this judgment." (reference cited in ACGIH®, 2004).

The ACGIH® noted that there was insufficient data to recommend **Skin**, **DSEN**, **RSEN** or carcinogenicity notations, or a **TLV-STEL** for dimethoxymethane (ACGIH®, 2004).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 1,000ppm (3,110mg/m³) for dimethoxymethane, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for dimethoxymethane that a WES-TWA of 500ppm (1,555mg/m³) and a WES-STEL of 1,000ppm (3,110mg/m³) are adopted, to protect against CNS depression, and eye and mucous membrane irritation, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Dimethoxymethane#section=Chemical-and-Physical-Properties
CAS Number	109-87-5
Conversion factors	1mg/m³ = 0.322ppm (25°C; 101.3**kPa**) 1ppm = 3.11mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Methane, dimethoxy www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/CC4B92A1-E18D-4704-94E2-1320C666E670 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methylal."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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DIPHENYLAMINE

CAS NO: 122-39-4

Summary

Workplace Exposure Standards for diphenylamine (CAS: 122-39-4)

	CURRENT	PROPOSED
WES-TWA	10**mg/m³**	5mg/m³
WES-STEL	–	10mg/m³
WES-Ceiling	–	–
Notations	–	***skin***

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for diphenylamine

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for diphenylamine of 5mg/m³
2. adopt a WES-STEL for diphenylamine of 10mg/m³, and
3. adopt a *skin* notation for diphenylamine.

To protect for damage to the haematopoietic system, spleen, kidney and liver.

Discussion

Diphenylamine is used as an industrial antioxidant, fungicide and anthelmintic (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Diphenylamine has a "floral" odour, with an odour threshold reported at 0.05ppm (0.35mg/m3) (PubChem, 2021; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of diphenylamine noted that the critical effects were damage to the haematopoietic system, spleen, kidney and liver in test species (DFG MAK, 2013).

The DFG noted that the **MAK** value of 5mg/m³ for diphenylamine, **peak limitation Category II** with an excursion factor of 2, were based on **NOAEL** of 2.5**mg/kg bw/day** for anaemia in dogs, and of 8mg/kg bw/day for damage to spleen and kidney in rats. The **LOAEL** was 25mg/kg bw/day in both species. These NOAEL were scaled to extrapolate to the workplace (DFG MAK, 2013).

The DFG concluded that an **"H"** notation was warranted for diphenylamine, based on modelling that indicated dermal absorption could contribute significantly to systemic toxicity (DFG MAK, 2013).

The DFG noted that there was inadequate data to justify **"Sa"** or **"Sh"** notations for diphenylamine (DFG MAK, 2013).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of diphenylamine noted that the critical effects were kidney, liver or blood dyscrasias reported in dogs and rats (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Due to the unavailability of inhalation data for diphenylamine, the **TLV** must be derived from ingestion studies. The lowest daily dose that yielded no-observed-adverse-toxicological effects in female rats was 0.025% dietary diphenylamine fed over 226 days (Thomas *et al*., 1967a). These rats weighed 200 grams and consumed an average of 9.5g/day, giving a daily dose of 11.875**mg/kg**. Assuming a 70-kg worker has a respiratory exchange of 10m^3 during an 8-hour workday and 100% absorption, a no-effect inhalation dose is estimated as 83mg/m^3. Accordingly, an occupational exposure **TLV-TWA** of 10mg/m^3 is recommended for diphenylamine dust to reduce the potential for adverse kidney, liver, or hematological effects (Thomas *et al*., 1967a, 1967b), and possible skin, eye and mucous membrane irritation (Fairhall, 1957; Calnan, 1978). Evidence reported from 1 to 2-year feeding studies with dogs and rats indicates that diphenylamine is not carcinogenic (Thomas *et al*., 1967a, 1967b)." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **Skin** or **SEN** notations, or a **TLV-STEL** for diphenylamine (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 10mg/m^3 for diphenylamine, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for diphenylamine that a WES-TWA of 5mg/m^3 and a WES-STEL of 10mg/m^3 are adopted with a *skin* notation, to protect against damage to the haematopoietic system, spleen, kidney and liver, based on the DFG recommendations. Noting the limited and dated toxicological database and international assessments for diphenylamine.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Diphenylamine#section=Chemical-and-Physical-Properties
CAS Number	122-39-4
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Diphenylamine www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/1A910098-F06B-4441-8911-72BA15109AED

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Diphenylamine."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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DIPROPYLENE GLYCOL METHYL ETHER

CAS NO: 34590-94-8

Summary

Workplace Exposure Standards for dipropylene glycol methyl ether (CAS: 34590-94-8)

	CURRENT	PROPOSED
WES-TWA	100**ppm** (606**mg/m³**)	50ppm (308mg/m³)
WES-STEL	150ppm (909mg/m³)	–
WES-Ceiling	–	–
Notations	***skin***	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for dipropylene glycol methyl ether

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for dipropylene glycol methyl ether of 50ppm (308mg/m³)
2. remove the WES-STEL for dipropylene glycol methyl ether, and
3. remove the *skin* notation for dipropylene glycol methyl ether.

To protect for eye, nose and throat irritation.

Discussion

Dipropylene glycol methyl ether is used as hydraulic fluid, and as a high boiling point solvent (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Dipropylene glycol methyl ether has an ether-like odour (ACGIH®, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of dipropylene glycol methyl ether noted that the critical effects were eye, nose and throat irritation (ACGIH®, 2001).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 100ppm (606mg/m³) and a **TLV-STEL** of 150mg/m³ (*sic.*) (909mg/m³) are recommended for occupational exposure to (2-methoxymethylethoxy)propanol (**DPGME**). This value is intended to minimize the potential for eye, nasal, and throat irritation. It should also provide a wide margin of protection from possible central nervous system effects, primarily narcosis. The recommended TLV-STEL is intended to provide further protection against irritant effects. The **Skin** notation is assigned, based on reported transient weight loss and narcosis in rabbits following dermal application of DPGME." (ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **DSEN**, **RSEN** or carcinogenicity notations for dipropylene glycol methyl ether (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of dipropylene glycol methyl ether (dipropylene glycol monomethyl ether) noted that the critical effects were irritation and unpleasant odour (DFG MAK, 1993).

The DFG noted that the **MAK** value of 50ppm for dipropylene glycol methyl ether, **peak limitation Category I** with an excursion factor of 1, were based on studies with volunteers that reported slight nasal irritation when exposed to concentrations above 35ppm, and eye and respiratory tract irritation above 75ppm (DFG MAK, 1993; DFG MAK, 2000). Subchronic inhalation studies with animals at concentrations up to 300ppm dipropylene glycol methyl ether, when the atmosphere is practically saturated, did not report any significant toxicity (DFG MAK, 1993).

The DFG concluded that an **"H"** notation was not warranted for dipropylene glycol methyl ether, based on studies in animals that indicated that while dermal absorption could cause narcotic effects and death, aerosols that wet the fur of rats for several hours only induced slight narcotic effects (DFG MAK, 1993).

The DFG have not assigned **"S"** notations for dipropylene glycol methyl ether (DFG MAK, 1993; DFG MAK, 2001).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of dipropylene glycol methyl ether (dipropylene glycol monomethyl ether) recommended an 8-hour TWA of 50ppm (308mg/m^3), based on a NOAEL of 200ppm for systemic effects for 90-day inhalation studies in rats and rabbits, and scaled to account for interspecies variation. No 15-minute STEL was considered necessary. A "skin" notation was recommended as dermal absorption was assessed to potentially contribute significantly to total body burden (SEG, 1993).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SEG reviews, WorkSafe considers its current WES-TWA of 100ppm (606mg/m^3) and WES-STEL of 150ppm (909mg/m^3) for dipropylene glycol methyl ether, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for dipropylene glycol methyl ether that a WES-TWA of 50ppm (308mg/m^3) is adopted, to protect against eye, nose and throat irritation, based on DFG recommendations. The WES-STEL of 150ppm (909mg/m^3) should be removed as adverse effects are only seen at very high concentrations, such that an excursion limit would be protective against acute irritant effects or central nervous system impairment. The *skin* notation should be removed as no deaths nor toxic effects were seen in animals at low doses.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/1-_3-Methoxypropoxy_propan-1-ol#section=Chemical-and-Physical-Properties
CAS Number	34590-94-8
Conversion factors	1mg/m³ = 0.165ppm (25°C; 101.3**kPa**) 1ppm = 6.05mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Propanol, 1(or 2)-(2-methoxymethylethoxy) www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/12D091D5-8989-485E-83D6-72C86D9877BE Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"(2-Methoxymethylethoxy)propanol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1993. *"Dipropylene glycol monomethyl ether."* MAK Value Documentation, 1993; The MAK Collection for Occupational Health and Safety; pp 199-204. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb3459094xise0006

Deutsche Forschungsgemeinschaft (DFG), 2000. *"Dipropylenglykolmonomethylether."* MAK Value Documentation in German language, 2000; The MAK Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb3459094xisd0030

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Scientific Expert Group on Occupational Exposure Limits (SEG), 1993. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for Dipropyleneglycol monomethylether."* SEG/SUM/45

ETHYL AMYL KETONE

CAS NO: 541-85-5

Summary

Workplace Exposure Standards for ethyl amyl ketone (CAS: 541-85-5)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (131**mg/m³**)	10ppm (53mg/m³)
WES-STEL	–	20ppm (107mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for ethyl amyl ketone

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for ethyl amyl ketone of 10ppm (53mg/m³), and
2. adopt a WES-STEL for ethyl amyl ketone of 20ppm (107mg/m³).

To protect for neurotoxicity and local irritation.

Discussion

Ethyl amyl ketone is used as a solvent for nitrocellulose-alkyd, nitrocellulose-maleic, and vinyl resins (**Safe Work Australia**, 2019; **ACGIH®**, 2007).

Ethyl amyl ketone has an odour of apricot and peach essence, with an odour threshold reported at approximately 5ppm (ACGIH®, 2007; SEG, 1991).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of ethyl amyl ketone noted that the critical effects were neurotoxicity (ACGIH®, 2007).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 10ppm (52.4mg/m³) is recommended to minimize potential neurotoxic effects. A subchronic oral study in rats (Hosenfeld and Topping, 1990) found that 82**mg/kg/day** was the **NOAEL** for neuropathy. An airborne concentration equivalent to this NOAEL for a 70-kg human who inhales 10m³ in an 8-hour workday is 574mg/m³ or 110ppm." (ACGIH®, 2007).

The ACGIH® found there was insufficient data available to recommend **Skin**, **DSEN**, **RSEN** or carcinogenicity notations for ethyl amyl ketone (ACGIH®, 2007).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of ethyl amyl ketone (5-methylheptan-3-on) noted that the critical effects were eye and mucous membrane irritation (DFG MAK, 2001).

The DFG noted that the **MAK** value of 10ppm for ethyl amyl ketone, **peak limitation Category I** with an excursion factor of 2, were based on studies with volunteers that reported irritation of the nasal mucosa at 25ppm, but not at 5ppm, and reversible eye irritation at concentrations above 25ppm. The MAK value was supported by NOAEL (100mg/kg b.w./day) and LOAEL (500mg/kg b.w./day) for functional neuropathy and clinical symptoms from a 13-week oral study in rats, and by analogy to the structurally related ketones (ethyl butyl ketone (CAS: 106-35-4); methyl isoamyl ketone (CAS: 110-12-3); and, methyl amyl alcohol (CAS: 108-11-2)) (DFG MAK, 2001).

The DFG noted that there was no data available to assess an **"H"** notation (DFG MAK, 2001).

The DFG also noted that **"S"** notations were not warranted, based on negative results in humans and animals (DFG MAK, 2001).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of ethyl amyl ketone (5-methylheptan-3-one) recommended an 8-hour TWA of 10ppm (53mg/m^3) and a 15-minute STEL of 20ppm (107mg/m^3), based on limited data from volunteers (SEG, 1991).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SEG reviews, WorkSafe considers its current WES-TWA of 25ppm (131mg/m^3) for ethyl amyl ketone, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for ethyl amyl ketone that a WES-TWA of 10ppm (53mg/m^3) and a WES-STEL of 20ppm (107mg/m^3) are adopted, to protect against neurotoxicity and local irritation, based on the ACGIH®, DFG and SCOEL recommendations. Noting the limited database and analogy to structurally related ketones.

[See WorkSafe Draft WES Reviews for:

- ethyl butyl ketone (CAS: 106-35-4), 2021: WES-TWA of 10ppm (47mg/m^3) and a WES-STEL of 20ppm (93mg/m^3)
- methyl isoamyl ketone (CAS: 110-12-3), 2021: WES-TWA of 20ppm (93mg/m^3) and a WES-STEL of 50ppm (233mg/m^3), and
- methyl amyl alcohol (CAS: 108-11-2), 2022: WES-TWA of 20ppm (85mg/m^3) and a WES-STEL of 40ppm (167mg/m^3).]

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/5-Methylheptan-3-one
CAS Number	541-85-5
Conversion factors	1mg/m³ = 0.191ppm (25°C; 101.3**kPa**) 1ppm = 5.24mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/B7BE6801-09FA-41AF-B012-EF34FA3B290D Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Ethyl amyl ketone."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2001. *"4-Hydroxy-4-methylpentan-2-on."* MAK Value Documentation in German language, 2001; The MAK Collection for Occupational Health and Safety; pp 1-6. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb12342d0032

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

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National Center for Biotechnology Information. PubChem Database. Accessed July 2021. *5-Methylheptan-3-one*, CID: 7822. https://pubchem.ncbi.nlm.nih.gov/compound/5-Methylheptan-3-one

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *5-Methylheptan-3-one*. https://engage.swa.gov.au/53876/widgets/280057/documents/136944

Scientific Expert Group on Occupational Exposure Limits (SEG), 1991. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for 5-Methylheptan-3-one."* SEG/SUM/9

ETHYL SILICATE

CAS NO: 78-10-4

Summary

Workplace Exposure Standards for ethyl silicate (CAS: 78-10-4)

	CURRENT	PROPOSED
WES-TWA	10**ppm** (85**mg/m³**)	5ppm (44mg/m³)
WES-STEL	–	10ppm (85mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for ethyl silicate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for ethyl silicate of 5ppm (44mg/m³), and
2. adopt a WES-STEL for ethyl silicate of 10ppm (85mg/m³).

To protect for irritation of the mucous membranes and respiratory tract.

Discussion

Ethyl silicate is used to weatherproof and acidproof mortar and cements, in heat- and chemical-resistant paints, and in other coatings (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Ethyl silicate has a sharp ester- or alcohol-like odour, with an odour threshold of 17ppm reported (PubChem, 2021; ACGIH®, 2001).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of ethyl silicate (tetraethylsilicate) noted that the critical effects were irritation of the respiratory tract (SCOEL, 2008).

The SCOEL review concluded that:

> "The database on tetraethylsilicate is poor, but an **OEL** based on nephrotoxicity may be derived.
>
> "The study of Pozzani and Carpenter (1951) and Omae *et al*. (1995) indicate a **NOAEL** of 50ppm (433mg/m³) for kidney effects in mice. However, histopathological changes were still detected in the nasal mucosa of mice exposed to 50 and 100ppm for 14 and 28 days (Omae *et al*., 1995). A NOAEL for local irritation could not be derived from this study.
>
> "Although mice are more sensitive to irritating effects than humans, due to the anatomy of their nasal cavity, the high incidence of the inflammatory effect seen at 50ppm requires a sufficiently large difference between the **NOEL** and the OEL, resulting in an 8-hour **TWA** of 5ppm (44mg/m³). A STEL is needed to prevent from irritation, but the database does not allow deriving one. In any case, a two-fold default value for a **STEL** should not be exceeded.
>
> "No data for a "skin" notation are available." (references cited in SCOEL, 2008).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of ethyl silicate noted that the critical effects were eye and mucous membrane irritation, and kidney damage at higher concentrations (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Ethyl silicate is an irritant of the eyes and mucous membranes. In view of the findings by Rowe *et al*. (1948) of kidney injury in animals exposed at about 100ppm, and the effects noted by Kasper *et al*. (1937) after exposure at 164ppm in less than 4 weeks, a **TLV-TWA** of 10ppm is recommended." (references cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations, or set a **TLV-STEL** for ethyl silicate (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of ethyl silicate noted that the critical effects were irritation of the respiratory tract, and kidney damage at higher concentrations in mice (DFG MAK, 1998).

The DFG noted that the **MAK** value of 10ppm for ethyl silicate, **peak limitation Category I** with an excursion factor of 1, were based on a report of nasal inflammation in mice after exposure to 50ppm (the lowest concentration tested) for 2 or 4 weeks (DFG MAK, 1998; DFG MAK, 2000).

The DFG noted that there were no data available to assess **"H"**, **"Sh"** or **"Sa"** notations for ethyl silicate (DFG MAK, 1998).

Conclusions

Based on the documentation cited, and informed by the conclusions of the SCOEL, ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 10ppm (85mg/m^3) for ethyl silicate, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for ethyl silicate that a WES-TWA of 5ppm (44mg/m^3) and a WES-STEL of 10ppm (85mg/m^3) are adopted, to protect against irritation of the mucous membranes and respiratory tract, based on the SCOEL recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Tetraethyl-orthosilicate#section=Chemical-and-Physical-Properties
CAS Number	78-10-4
Conversion factors	1mg/m³ = 0.118ppm (25°C; 101.3**kPa**) 1ppm = 8.5mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Silicic acid, tetraethyl ester www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/E53C73DA-3A5C-4ED3-8E03-429C9D540C09 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Ethyl silicate."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1998. *"Tetraethylsilicat."* MAK Value Documentation in German language, 1998; The MAK Collection for Occupational Health and Safety; pp 1-3. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7810d0026

Deutsche Forschungsgemeinschaft (DFG), 2000. *"Tetraethylsilicat."* MAK Value Documentation in German language, 2000; The MAK Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7810d0030

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Scientific Committee on Occupational Exposure Limits (SCOEL), 2008. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for tetraethylsilicate."* SCOEL/SUM/64

ETHYLAMINE

CAS NO: 75-04-7

Summary

Workplace Exposure Standards for ethylamine (CAS: 75-04-7)

	CURRENT	PROPOSED
WES-TWA	10**ppm** (18**mg/m³**)	5ppm (9mg/m³)
WES-STEL	–	15ppm (28mg/m³)
WES-Ceiling	–	–
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for ethylamine

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for ethylamine of 5ppm (9mg/m³)
2. adopt a WES-STEL for ethylamine of 15ppm (28mg/m³), and
3. maintain the *skin* notation.

To protect for upper respiratory tract irritation, and eye and lung damage from acute exposures.

Discussion

Ethylamine is used in solvent extraction; in organic synthesis; as a dye intermediate; as a stabiliser for rubber latex; in petroleum refining; and, in chemical production (**Safe Work Australia**, 2019; **ACGIH®**, 2013).

Ethylamine has an ammonia-like odour, with an odour threshold reported at 0.95ppm (ACGIH®, 2013; PubChem, 2021).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of ethylamine noted that the critical effects were nasal irritation (DFG MAK, 2019).

The DFG noted that the **MAK** value of 5ppm for ethylamine, **peak limitation Category I** with an excursion factor of 2, were based on a study in volunteers with diethylamine giving a **LOAEC** of 10ppm, while noting the relative irritant potency and toxicity of ethylamine compared with diethylamine (MAK value of 2ppm) (DFG MAK, 2019).

The DFG noted that model calculations indicated that dermal absorption under workplace conditions was unlikely to significantly contribute to total body burden, so that an **"H"** notation was not warranted for ethylamine (DFG MAK, 2019).

The DFG also noted that there was no data available on ethylamine to assess the need for **"Sh"** or **"Sa"** notations (DFG MAK, 2019).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of ethylamine noted that the critical effects were upper respiratory tract irritation (ACGIH®, 2013).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 5ppm is recommended to minimize the potential risk of irritation produced by repeated, low-level exposures to ethylamine. A **TLV-STEL** of 15ppm is recommended to prevent transient irritation that could be produced at higher concentrations. Repeated inhalation exposures of 50ppm ethylamine vapor by rabbits produced lung damage and corneal injury (Brieger and Hodes, 1951). Exposure at 100ppm also produced kidney change (Brieger and Hodes, 1951). The upper respiratory tract of the rabbits in this study was not evaluated, but it is likely that changes reflecting irritation were produced. No effects were seen in rats following inhalation of ethylamine for 24 weeks at 100ppm (Lynch *et al*., 1988). Acute exposure to ethylamine produced severe irritation to the eyes and skin of laboratory animals (Fasset, 1963; Brieger and Hodes, 1951). There are no data reported on the irritation potential of ethylamine in humans. Although animal toxicity data for other ethyl-amines are similar (diethylamine and triethylamine), the TLV-TWA for triethylamine (1ppm) has been established to prevent acute symptoms in humans (visual disturbances) ... No reports of this manifestation have been reported to date with ethylamine.
>
> "There are no human data for skin absorption; however, considering that the lethal dose to rabbits following dermal exposure was 390mg/kg, a **Skin** notation for this chemical is recommended." (references cited in ACGIH®, 2013).

The ACGIH® found there was insufficient data available to recommend DSEN, RSEN or carcinogenicity notations for ethylamine (ACGIH®, 2013).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of ethylamine recommended an 8-hour TWA of 5ppm (9.4mg/m^3), based on a **LOAEL** of 48ppm for lung damage in rabbits reported by Brieger and Hodes (1951). The SEG noted that no "skin" notation was considered necessary, while there was insufficient basis to propose a STEL (SEG, 1994).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, ACGIH® and SEG reviews, WorkSafe considers its current WES-TWA of 10ppm (18mg/m^3) for ethylamine with a *skin* notation, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for ethylamine that a WES-TWA of 5ppm (9mg/m^3) and a WES-STEL of 15ppm (28mg/m^3) are adopted, to protect against upper respiratory tract irritation, and eye and lung damage from acute exposures, based on the ACGIH® recommendations. The *skin* notation should be maintained.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/ETHYLAMINE#section=Chemical-and-Physical-Properties
CAS Number	75-04-7
Conversion factors	1mg/m³ = 0.54ppm (25°C; 101.3**kPa**) 1ppm = 1.84mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Ethanamine, anhydrous (ethylamine) www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/815E0EDF-D7A8-4AFB-AE73-7F98E7AFC76B Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Ethylamine."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2019. *"Ethylamine."* MAK Value Documentation, 2019; The MAK Collection for Occupational Health and Safety; pp 2045-2053. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7504e6619

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

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Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Ethylamine*. https://engage.swa.gov.au/51516/widgets/269929/documents/123275

Scientific Expert Group on Occupational Exposure Limits (SEG), 1994. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for Ethylamine."* SEG/SUM/33

ETHYLENE GLYCOL

CAS NO: 107-21-1

Summary

Workplace Exposure Standards for ethylene glycol vapour (CAS: 107-21-1)

	CURRENT	PROPOSED
WES-TWA	–	25**ppm** (64**mg/m³**)
WES-STEL	–	50ppm (127mg/m³)
WES-Ceiling	vapour and mist: 50ppm (127mg/m³)	–
Notations	–	***ifv***; the WES recommendations for vapor and aerosol should be applied separately, and they are not intended to be additive

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for ethylene glycol vapour

Workplace Exposure Standards for ethylene glycol particulate (CAS: 107-21-1)

	CURRENT	PROPOSED
WES-TWA	–	–
WES-STEL	–	10mg/m³
WES-Ceiling	–	–
Notations	–	*ifv*; the WES recommendations for vapor and aerosol should be applied separately, and they are not intended to be additive

TABLE 2: Current and proposed Workplace Exposure Standards (**WES**) for ethylene glycol particulate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for ethylene glycol vapour of 25ppm (64mg/m³)
2. adopt a WES-STEL for ethylene glycol vapour of 50ppm (127mg/m³)
3. adopt a WES-STEL for ethylene glycol particulate of 10mg/m³
4. adopt an ifv notation, and
5. remove the WES-Ceiling for ethylene glycol vapour and mist.

To protect for eye and upper respiratory tract irritation.

Discussion

Ethylene glycol is used as an antifreeze, as a chemical intermediate (for polyester fibres, films and resins), and as a substitute for glycerine in a range of commercial products (**Safe Work Australia**, 2020; **ACGIH®**, 2017).

Ethylene glycol is reported to be odourless, with a sweet or bitter-sweet taste (PubChem, 2022; ACGIH®, 2017).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of ethylene glycol noted that the critical effects were upper respiratory tract irritation (ACGIH®, 2017).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 25ppm and a **TLV-STEL** of 50ppm (both as vapor fraction) are recommended to minimize the potential for respiratory and eye irritation. In addition, a TLV-STEL of 10mg/m^3, as inhalable particulate matter (aerosol only), is also recommended to prevent particulate concentrations known to be irritating in the presence of vapors. Wills *et al*. (1974) exposed human volunteers to continuous aerosolized ethylene glycol for 20 to 22 hours/day in exposure chambers for 4 weeks at mean daily concentrations of 3-67mg/m^3 (1-26ppm). Mean weekly concentrations ranged from 17-49mg/m^3 (6.6-19ppm). The most common complaint was irritation of the upper respiratory tract, which appeared to correlate well with the exposure concentration. Irritation of the upper respiratory tract became more common at 140mg/m^3 (55ppm). Although data from oral toxicity studies in mice and rats showed evidence of renal toxicity, with no-observed-adverse-effect-levels (**NOAEL**s) ranging from 150-227mg/kg (Cruzan *et al*., 2004; Robinson *et al*., 1990), inhalation studies in rats, rabbits, dogs, monkeys, and guinea pigs showed no significant renal changes following exposures up to 22ppm for 8 hours/day, 5 days/week for 6 weeks (Coon eta al., 1970). Physiologically-based pharmacokinetic (**PBPK**) modeling showed that, following inhalation, humans are unlikely to achieve blood levels required to produce the renal effects reported in animals (Corley *et al*., 2005). The controlled human exposure studies also supported a TLV-STEL of 50ppm. Wills *et al*. (1974) reported that a concentration of 188mg/m^3 could only be tolerated for 15 minutes, and at 244mg/m^3, respiratory irritation could not be tolerated after a minute or two. Exposure at 308mg/m^3 was intolerable, even for a brief period. These conditions are possible during spraying operations (e.g. de-icing aircraft). A STEL of 10mg/m^3, as an aerosol, will also limit the amount of mist produced if the saturated vapor concentration is exceeded. Exposures above the saturated vapor concentration include both vapor and mist, the latter of which is expected to be irritating to mucous membranes at the site of deposition based on surrogate data showing ethylene glycol is irritating to the eyes of rabbits (McDonald *et al*., 1972). Limiting the aerosols to this concentration is also consistent with good industrial hygiene practice by improving housekeeping for a slippery material that can represent a safety concern (e.g., visual impairment, slips and falls). Air monitoring methods should reflect the possible presence of both aerosol and vapor when levels exceed the saturated vapor concentration. The TLV recommendations for vapor and aerosol should be applied separately, and they are not intended to be additive."
>
> "Data from animal (U.S. NTP, 1991; DePass *et al*., 1986a, 1986b; Dunkelberg, 1987) and human studies (Bond *et al*., 1985) to date do not provide evidence that exposures to ethylene glycol has carcinogenic properties. Therefore, an **A4**, **Not Classifiable as a Human Carcinogen**, notation is assigned.
>
> "Given the low percutaneous absorption found in controlled studies, a **Skin** notation is not appropriate (Frantz *et al*., 1989, 1991)." (references cited in ACGIH®, 2017).

The ACGIH® noted that there was insufficient data to assign **RSEN** or **DSEN** notations for ethylene glycol (ACGIH®, 2017).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of ethylene glycol noted that the critical effects were irritation of the mucous membranes (DFG MAK, 1992).

The DFG noted that the **MAK** value of 10ppm (26mg/m^3) for ethylene glycol, **peak limitation Category I** with an excursion factor of 2, were based on controlled studies in human volunteers that reported pronounced irritation at aerosol-vapor concentrations above 140mg/m^3 (DFG MAK, 1992), but in a second study exposure to 25ppm was tolerated (DFG MAK, 2000).

The DFG also noted that an **"H"** notation was warranted for ethylene glycol, due to reports of toxicity after dermal exposure (DFG MAK, 1992).

"Sa" or **"Sh"** notations were not assigned for ethylene glycol (DFG MAK, 1992).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of ethylene glycol recommendation concluded:

> "The study of Wills *et al* (1974), establishing a NOAEL of 67mg/m^3, for irritation of the mucosae in human volunteers, was considered to be the best available basis for proposing occupational exposure limits. Because this study involved exposure for 20-22h/d, and large differences in response were seen with continuous exposure compared with exposure for 8h/d in the studies of Coon *et al*. (1970), an uncertainty factor of 2 was considered adequate to allow for interindividual variation and for the absence of long term human data. Taking into account the preferred value approach, the recommended 8-hour TWA is 20ppm (52mg/m^3). This is supported by the repeated exposure study of Coon *et al*. (1970). A STEL (15 mins) of 40ppm (104mg/m^3) was proposed to limit peaks of exposure which could result in irritation. A "skin" notation was recommended as dermal absorption could contribute substantially to the total body burden." (references cited in SEG, 1995).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SEG reviews, WorkSafe considers its current WES-Ceiling of 50ppm (127mg/m^3) for ethylene glycol (vapour and mist) to be inadequate to manage health risks from possible workplace exposure.

It is recommended for ethylene glycol vapour that a WES-TWA of 25ppm (64mg/m^3) and a WES-STEL of 50ppm (127mg/m^3), and for ethylene glycol particulate that a WES-STEL of 10mg/m^3 are adopted, to protect against eye and upper respiratory tract irritation, based on the ACGIH®recommendations. It is further recommended that the WES-Ceiling for ethylene glycol vapour and mist is removed.

It is further recommended that an inhalable fraction and vapour (*ifv*) notation be adopted in recognition of the potential for ethylene glycol to be present in both particle and vapour phases, with each contributing to a significant portion of exposure.

Reported acute dermal toxicity and dermal absorption data indicated that a *skin* notation was not warranted for ethylene glycol (ACGIH®, 2017).

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/174#section=Chemical-and-Physical-Properties
CAS Number	107-21-1
Conversion factors	1ppm = 2.mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.39ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 1,2-Ethanediol (ethylene glycol) www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/0203248B-BD21-4F1A-88FF-A351B2CC5CC9 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Ethylene glycol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1992. *"Ethylene glycol."* MAK Value Documentation, 1992; The MAK Collection for Occupational Health and Safety, Vol. 4; pp 225-245. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10721e0004

Deutsche Forschungsgemeinschaft (DFG), 2000. *"Ethylenglykol."* MAK Value Documentation in German language, 2000; The MAK Collection for Occupational Health and Safety; pp 1-2. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10721d0030

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National Center for Biotechnology Information. PubChem Database. Accessed January 2022. *1,2-Ethanediol*, CID: 174. https://pubchem.ncbi.nlm.nih.gov/compound/174

Safe Work Australia (2020). Safe Work Australia Draft Evaluation Report and Recommendations – *Ethylene glycol (vapour and particulate)*. https://engage.swa.gov.au/65429/widgets/323765/documents/192153 [Word document]

Scientific Expert Group on Occupational Exposure Limits (SEG), 1995. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for Ethylene glycol."* SEG/SUM/40

ETHYLENE GLYCOL ISOPROPYL ETHER

CAS NO: 109-59-1

Summary

Workplace Exposure Standards for ethylene glycol isopropyl ether (CAS: 109-59-1)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (106**mg/m³**)	10ppm (43mg/m³)
WES-STEL	–	20ppm (85mg/m³)
WES-Ceiling	–	–
Notations	–	***skin***

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for ethylene glycol isopropyl ether

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for ethylene glycol isopropyl ether of 10ppm (43mg/m³)
2. adopt a WES-STEL for ethylene glycol isopropyl ether of 20ppm (85mg/m³), and
3. adopt a *skin* notation for ethylene glycol isopropyl ether.

To protect for respiratory tract irritation and haemolytic effects.

Discussion

Ethylene glycol isopropyl ether is used as a component of latex paints, lacquers and other coatings; and, as a solvent for resins, textile dyes, coalescing aids, and coupling agents (**Safe Work Australia**, 2019; **ACGIH**®, 2001).

Ethylene glycol isopropyl ether has a mild, ethereal odour (PubChem, 2021; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of ethylene glycol isopropyl ether (2-isopropoxyethanol) noted that the critical effects were eye and skin irritation reported in rabbits, with the assumption that respiratory tract irritation would be expected in humans; and, haemolytic anaemia in rats with humans showing less sensitivity (DFG MAK, 2018).

The DFG noted that the **MAK** value of 10ppm, **peak limitation Category I** with an excursion factor of 2, were based on studies with the more extensively studied analogue, 2-butoxyethanol with a **LOAEC** of 31ppm for nasal irritation from a 2-year inhalation study in rats. A 28-day inhalation study with ethylene glycol isopropyl ether induced concentration-dependent haemolytic anaemia in female rats at 100ppm and above, which when adjusted to the workplace confirms the MAK value (DFG MAK, 2018).

The DFG noted that ethylene glycol isopropyl ether was readily absorbed through the skin, and warranted an **"H"** notation (DFG MAK, 2018).

The DFG also noted that there was no robust data available to evaluate **"Sa"** or **"Sh"** notations (DFG MAK, 2018).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of ethylene glycol isopropyl ether (2-isopropoxyethanol) noted that the potential critical effects were induced blood anomalies (ACGIH®, 2001).

The ACGIH® review concluded that:

> "While the rat seems more susceptible than other animals and humans to the action of these hemolytic agents, anemia is not an uncommon condition in the human population. It seems prudent not to expose workers to chemicals at levels that definitely affect the blood of any animal species (Carpenter *et al*., 1956; Moffett *et al*., 1976). Therefore, a **TLV-TWA** of 25ppm is recommended for **IPE**. By analogy with 2-butoxyethanol, a **Skin** notation is recommended." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **DSEN**, **RSEN** or carcinogenicity notations, or a **TLV-STEL** for ethylene glycol isopropyl ether (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 25ppm (106mg/m^3) for ethylene glycol isopropyl ether, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for ethylene glycol isopropyl ether that a WES-TWA of 10ppm (43mg/m^3) and a WES-STEL of 20ppm (85mg/m^3) with a *skin* notation are adopted, to protect against respiratory tract irritation and haemolytic effects, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/2-Isopropoxyethanol#section=Chemical-and-Physical-Properties
CAS Number	109-59-1
Conversion factors	1mg/m^3 = 0.235ppm (25°C; 101.3**kPa**) 1ppm = 4.25mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Ethanol, 2-(1-methylethoxy) www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/6FF92AD8-B71C-4F94-923B-8825D93F9741 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"2-Isopropoxyethanol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2018. *"2-Isopropoxyethanol."* MAK Value Documentation, 2018; The MAK Collection for Occupational Health and Safety 2019, Vol 4, No 3; pp 1130-1145. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10959e6519

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National Center for Biotechnology Information. PubChem Database. Accessed July 2021. *2-Isopropoxyethanol*, CID: 7996. https://pubchem.ncbi.nlm.nih.gov/compound/2-Isopropoxyethanol

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Isopropxyethanol*. https://engage.swa.gov.au/52508/widgets/273797/documents/127287

FLOUR DUST

CAS NO: N/A

Summary

Workplace Exposure Standards for flour dust (CAS: N/A)

	CURRENT	PROPOSED
WES-TWA	1**mg/m³**	0.2mg/m³
WES-STEL	–	–
WES-Ceiling	–	–
Notations	***rsen***	*rsen*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for flour dust

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA of 0.2mg/m³ for flour dust, and
2. maintain the *rsen* notation for flour dust.

To protect for sensitisation, changes in lung function, chronic bronchitis, and respiratory and asthmatic symptoms.

Discussion

Flour dust is a complex organic dust of finely ground particles arising from the milling of cereals or pulses; for example wheat, rye, millet, barley, oats or corn cereals, or a combination of these (ACGIH®, 2014). Flour is used to make foods for human or animal consumption (**Safe Work Australia**, 2019; **ACGIH®**, 2014).

DECOS

The Dutch Expert Committee on Occupational Standards (**DECOS**) proposed an 8-hour **TWA** health-based recommended occupational exposure limit (**HBROEL**) for inhalable wheat and other cereal dust of 0.2mg/m³. The HBROEL was based on calculated exposures from two study data sets from Dutch worker populations that corresponded to an 1% extra risk of sensitisation by occupational exposure to wheat flour dust compared to the general population (DECOS, 2017). The DECOS noted that it was not possible to determine a threshold for sensitisation by allergens in flour dusts, and a risk-based approach must be adopted (DECOS, 2017).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of flour dust noted that the critical effects were sensitisation, changes in lung function, chronic bronchitis, and respiratory and asthmatic symptoms (ACGIH®, 2014).

The ACGIH® review concluded that:

> "In a review of exposure-response relationships for occupational allergens Baur *et al*. (1998) note the difficulties in identifying dose-response relationships, because the only exposure usually measured is dust, which "may contain different levels of allergenic and nonallergenic substances" (Baur *et al*., 1998). However, despite these difficulties, "in general an increased exposure to dust is related to an increased exposure to allergen." For flour, they note that a number of investigators have found that dust concentrations of 1 to 2.4mg/m^3 to be associated with a significantly elevated risk of sensitization to wheat antigens."
>
> "The studies by Hartmann *et al*., (1985), Hartmann, (1986) Awa del Karim *et al*., (1986) Musk *et al*., (1989) De Zotti *et al*., (1994) Cullinan *et al*., (1994; Ehrlich, 1994) Bohadana *et al*., (1994) Massin *et al*., (1995) Shamssain, (1995) Gimenez *et al*., (1995) Zuskin *et al*., (1998) and Houba *et al*. (1998) offer support that flour-dust exposed workers are more likely than controls to exhibit respiratory symptoms and sensitization; many of these studies also offer strong support for a dose-response relationship between both flour dust and aeroallergen exposures and both symptoms and sensitization. In particular, the studies by Musk *et al*., (1989) Cullinan *et al*., (1994) and Houba *et al*. (1998; 1995) suggest that an airborne concentration of less than 1mg/m^3 flour dust marks the level below which no symptoms or sensitization will occur.
>
> "It appears that exposure to flour dust can lead to both irritation, resulting in inflammatory responses throughout the respiratory system, and sensitization, resulting eventually in asthma. There is also, apparently, a long latency for the development of sensitization, which is affected by whether an individual has allergies to other common allergens (demonstrates atopy). The presence of respiratory symptoms, therefore, will not always be associated with sensitization. It is also clear from the literature, however, that the prevention of sensitization should be of over-riding concern, because it occurs at lower exposures than does irritation and its accompanying symptoms. The prevention of sensitization for atopic individuals should be of greatest concern.
>
> "Therefore, ACGIH recommends a **TLV-TWA** of 0.5mg/m^3, inhalable particulate matter, for occupational exposure to inhalable flour dust to protect against both sensitization (in both atopic and nonatopic workers) and symptoms resulting from both sensitization and irritation. While wheat flour aeroallergens and sensitization have been most frequently studied, numerous investigators have shown that other flours result in similar prevalences of sensitization. Therefore, this TLV covers all types of flour. ... because several authors have demonstrated considerable cross-reactivity between different cereal grains, including wheat, rye, corn, and barley (Comes *et al*., 1935; Bjorksten *et al*., 1977). The **RSEN** notation is justified by data from numerous studies cited ... ." (references cited in ACGIH®, 2014).

The ACGIH® noted that there was insufficient data to assign a **DSEN** notation (ACGIH®, 2014).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of flour dust noted that the critical effects were symptoms from the respiratory tract and the eyes, such as rhinitis, conjunctivitis and asthma (SCOEL, 2008).

The SCOEL review summarised:

"The symptoms may be induced immunologically, mostly mediated by IgE-type antibodies, or by irritation. Symptoms induced by irritation are reversible, whereas immunologically induced sensitization is persistent. Allergic symptoms may thus continue even after cessation of occupational exposure to flour dusts.

"The available literature does not demonstrate a trustworthy threshold for any of the flour dust-induced effects.

"Sensitization signifies the development of specific IgE antibodies to any of several flour dust allergens. The vast majority of studies on flour dust have been done on wheat.

"Sensitization to wheat allergen occurs in the general population not occupationally exposed at a prevalence rate of about 2-4%. In tasks associated with exposure to wheat flour, there is an excess risk of sensitization that becomes clearly dose-dependent at a time-weighted average of about 1mg/m^3 of inhalable flour dust. The dose-response curve was linear in the range 1–3mg/m^3 (Heederik & Houba 2001; Peretz *et al* 2003; DECOS 2004). Based on advanced analyses of dose-response data (Houba *et al* 1998, Heederik and Houba 2001), it has been calculated that a person who starts working in the bakery industry for the first time, would have an additional risk of 10% to ever becoming sensitized to flour dust over a working life of forty years, if occupationally exposed to an average of 1.2mg/m^3 inhalable dust (DECOS 2004). Sensitization causes an about four-fold risk of developing respiratory symptoms (De Zotti and Bovenzi 2000). Sensitization as such should be considered a sentinel event that warrants preventive action at the work place. Sensitized workers ought to be subjected to intensified health surveillance. Due to the clearly increased risk of sensitized workers of developing symptoms, measures to reduce exposure should be taken.

"A retrospective incidence study suggests that the risk of nasal symptoms starts to increase at concentrations exceeding 1mg/m^3 inhalable flour dust in all bakery job tasks; the risk of asthma increases at levels above 3mg/m^3, respectively (Brisman *et al* 2000). This is in rather good concordance with other studies (Cullinan *et al* 1994; 2001; Houba *et al* 1998). Studies on dose-response indicate that symptoms, especially symptoms from the lower respiratory tract, asthma, as well as sensitization, are rare in the range of 0.5-1.0mg/m^3 inhalable dust, which thus gives a range for a **LOEL**. (Houba *et al* 1998; Heederik and Houba 2001; Brisman *et al* 2000).

"As a general rule, the SCOEL committee does not recommend health-based **OEL**s for sensitizers, as no threshold can be identified. However, in view of the large number of workers exposed and the relatively large data base, SCOEL recognizes that exposures ≤1mg/m^3 of inhalable flour dust would protect the majority of exposed workers from the onset of disease and that the envisaged symptoms would be mild. However, concentrations <1mg/m^3 may trigger symptoms in already sensitized workers. As an OEL that protects all workers cannot be identified, it would be advisable to routinely apply good practices and health surveillance systems to bakery and mill environments.

"Peak exposures of short duration occur frequently in certain, easily specified, tasks within the bakery and flour mill industries. The importance of peak exposure of short duration for the development of sensitization and symptoms is likely to be considerable. Although a scientifically based STEL for flour dust cannot be established, efforts should be made to control peak exposures." (references cited in SCOEL, 2008).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DECOS, ACGIH® and SCOEL reviews, WorkSafe considers its current WES-TWA of 1mg/m^3 for flour dust to be inadequate to manage health risks from possible workplace exposure.

It is recommended for flour dust that a WES-TWA of 0.2mg/m^3 is adopted, while maintaining the *rsen* notation, to protect against sensitisation, changes in lung function, chronic bronchitis, and respiratory and asthmatic symptoms, based on the DECOS recommendations. It should be noted that due the potential of flour dust for sensitisation, exposure at the recommended WES-TWA may not eliminate all risk, as no thresholds have been established, and exposures should be kept as low as possible.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: None

References: **IFA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Flour dust."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Flour dust (cereal)*. https://engage.swa.gov.au/52508/widgets/273797/documents/127206

Scientific Committee on Occupational Exposure Limits (SCOEL), 2008. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for Flour Dust."* SCOEL/SUM/123

FLUORIDES, as F

CAS NO: N/A

Summary

Workplace Exposure Standards for fluorides (CAS: N/A)

	CURRENT	PROPOSED
WES-TWA	2.5**mg/m³**	1mg/m³
WES-STEL	–	–
WES-Ceiling	–	–
Notations	***bio***	*bio*
BEI	prior to shift: 2**mg/L** urine; end of shift: 3mg/L urine	prior to shift: 2mg/L urine; end of shift: 3mg/L urine

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) and Biological Exposure Index (**BEI**) for fluorides, as **F**

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for fluorides of 1mg/m³ as F, and
2. maintain the BEI of 2mg F/L urine, prior to shift; and, 3mg F/L urine, end of shift for fluorides.

To protect for skeletal fluorosis.

Discussion

Fluorides are a range of simple to complex compounds of fluorine with other chemical elements, and as such have a large range of uses in many workplaces (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Hydrogen fluoride (CAS No.: 7664-39-3) is subject to its own WES (see draft WES Review for Hydrogen fluoride, 2022).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of fluorides noted that the critical effects were skeletal fluorosis (DFG MAK, 2006).

The DFG noted that the **MAK** value of 1mg/m³ for fluorides, **peak limitation Category II** with an excursion factor of 4, were based on findings that clinical stage III skeletal fluorosis can occur after 20 years exposure to >20mg/day, and accounting for fluoride intake through food and drink, was adjusted to the workplace. The MAK value was supported by a study indicating intakes equivalent to 1.5mg/m³ over 20 years resulted in more bone fractures, while intakes equivalent to 1mg/m³ did not (DFG MAK, 2006). Based on analogy with hydrogen fluoride, DFG noted that the MAK value should be protective against respiratory tract irritation (DFG MAK, 2006). Studies in volunteers reported upper respiratory tract irritation at inhalation exposures of 3ppm and above for one hour, but not at 2.84ppm and below; and, at average concentrations of 2.59ppm for 6 hours/day for 25 days, but not at 1.42ppm (DFG MAK, 2001).

The DFG noted that an **"H"** notation was warranted for water soluble fluorides, as the dermal **LD_{50}** in mice was low and significant dermal exposures could not be discounted. No data indicated that **"Sh"** and **"Sa"** notations were warranted for fluorides (DFG MAK, 2006).

The DFG review of the Biologische Arbeitsstoff-Toleranzwerte (Biological Tolerance Value, **BAT**) for hydrogen fluoride and inorganic fluoride compounds concluded that a BAT of 4mg fluoride/L urine, collected at the end of exposure or at the end of the shift, would provide protection of the individual with occupational exposure (DFG BAT, 2014). The BAT value was based on several long-term studies indicating 4mg fluoride/L urine could be tolerated without skeletal fluorosis (DFG BAT, 2014).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of fluorides noted that the critical effects were skeletal fluorosis (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Fluorides cause irritation of the eyes and respiratory tract. Long-term absorption of excessive amounts of fluorides has caused fluorosis. Based on the study in which the threshold for a minimum increase in bone density was 3.38mg F/m^3 (Derryberry *et al*., 1963), a **TLV-TWA** of 2.5mg/m^3 is recommended to minimize the potential for irritant effects and disabling bone changes. Some data indicated this value, if strictly observed, would protect against almost any degree of fluorosis. Hodge and Smith (1977), in a review of the U.S. National Institute for Occupational Safety and Health (**NIOSH**) Criteria Document on inorganic fluorides (NIOSH, 1997), concluded that the NIOSH recommended exposure limit (**REL**) and the **TLV** were supported by the available data. Hodge and Smith (1977) believed that occupational exposure below the TLV would have no adverse effects on pregnant women and their offspring. They (Hodge and Smith, 1977) noted that effects reported on the respiratory system resulted from heavier exposures than were required to cause fluorosis.
>
> "Based on the essentially negative animal studies (US NTP, 1990), a carcinogenicity notation of **A4**, **Not Classifiable as a Human Carcinogen**, is assigned to fluorides." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **Skin** or **SEN** notations, or a **TLV-STEL** for fluorides (ACGIH®, 2001).

The ACGIH® review of the BEI® for fluorides recommended:

> "ACGIH recommends a BEI of 2mg/L for urine samples collected prior to the shift and a BEI of 3mg/L for samples collected at the end of the shift. Both sampling times should be considered for health preventative measures and in occupational hygiene. Measurements in post-shift urine samples are an indicator of exposure during shift. The use of post-shift samples for biological monitoring is a strong health preventative measure in order to identify and eliminate potential sources of occupational exposures to fluoride and to prevent long-term accumulation of fluoride in exposed persons. Measurements in pre-shift samples are an indicator of long-term exposure to fluoride and may or may not be significantly affected by environmental exposure depending on the area of living. The use of pre-shift urine samples is a strong health preventative measure in order to protect from stage II skeletal fluorosis later in life." (ACGIH®, 2012).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 2.5mg/m³ for fluorides as F to be inadequate to manage health risks from possible workplace exposure.

It is recommended for fluorides as F that a WES-TWA of 1mg/m³ is adopted to protect against skeletal fluorosis, based on the DFG recommendations.

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current BEI of 2mg/L urine, prior to shift; and, 3mg/L urine, end of shift will protect against skeletal fluorosis.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Fluoride-ion#section=Chemical-and-Physical-Properties
CAS Number	N/A
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: None

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Fluorides."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2001. *"Hydrogen fluoride."* MAK Value Documentation, 2001; The MAK Collection for Occupational Health and Safety; pp 1-24. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb766439e3214

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Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Fluorides (as F)*. https://engage.swa.gov.au/52961/widgets/275459/documents/128650

FLUOROTRICHLOROMETHANE

CAS NO: 75-69-4

Summary

Workplace Exposure Standards for fluorotrichloromethane (CAS: 75-69-4)

	CURRENT	PROPOSED
WES-TWA		
WES-STEL		
WES-Ceiling	1,000**ppm** (5,620**mg/m³**)	1,000ppm (5,620mg/m³)
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for fluorotrichloromethane

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-Ceiling of 1,000ppm (5,620mg/m³) for fluorotrichloromethane.

To protect for acute cardiac sensitisation and systemic toxicity (including fluorosis).

Discussion

Fluorotrichloromethane is used as a blowing agent in the production of polyurethane foams, refrigerant, heat transfer medium, solvent, and as an aerosol propellant for asthma treatments (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Fluorotrichloromethane has a faint, sweet, ether-like odour, with a threshold reported at 5ppm (PubChem, 2022; ACGIH®, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of fluorotrichloromethane noted that the critical effects were acute cardiac sensitisation and systemic toxicity (including fluorosis) (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Following inhalation of extremely high concentrations, **CFC-11** has caused acute narcosis and death from respiratory depression. Instantaneous deaths have occurred following sensitization of the heart to the arrythmogenic actions of adrenaline (Garriott and Petty, 1980). Following inhalation of CFC-11, the compound is promptly absorbed and rapidly eliminated (Blake and Mergner, 1974; Azar *et al*., 1973; Mergner *et al*., 1975). No acute or chronic toxicities were reported in either animals or humans exposed to concentrations of CFC-11 normally encountered in household or industrial use of the compound (Marier *et al*., 1974).
>
> "Based on a no-observed-adverse effect concentration in animals inhaling CFC-11 24 hours/day for 90 days at 1,000ppm (Jenkins *et al*., 1970), a **TLV-Ceiling** of 1,000ppm is recommended for CFC-11. This value should provide a substantial margin of safety to minimize the potential for systemic toxicity (including fluorosis) and incorporates a wide margin of safety to preclude acute cardiac sensitization. There was no evidence of carcinogenicity in mice

treated subcutaneously with CFC-11; there also was no significant increase in tumor incidence in rats of mice treated with CFC-11 by gavage (U.S. NCI, 1978; Epstein *et al*., 1967). Accordingly, an A4, Not Classifiable as a Human Carcinogen, notation is assigned to CFC-11." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was no evidence of carcinogenicity and insufficient data to assign **Skin** or **SEN** notations for fluorotrichloromethane (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of fluorotrichloromethane noted that the critical effects were heart and lung toxicity at very high concentrations (DFG MAK, 1990).

The DFG noted that the **MAK** value of 1,000ppm for fluorotrichloromethane, **peak limitation Category II** with an excursion factor of 2, were not based on a toxicity threshold from available data, but from a basic occupational hygiene object to limit inhaled impurities (DFG MAK, 1990; DFG MAK, 2002).

"H", **"Sa"**, **"Sh"** and carcinogenicity notations were not assigned for fluorotrichloromethane (DFG MAK, 2002; DFG MAK, 1990).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-Ceiling of 1,000ppm (5,620mg/m³) for fluorotrichloromethane to be adequate to manage health risks from possible workplace exposure.

It is recommended for fluorotrichloromethane that the WES-Ceiling of 1,000ppm (5,620mg/m³) is maintained to protect against acute cardiac sensitisation and systemic toxicity (including fluorosis), based on the ACGIH® and DFG recommendations. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/6389#section=Chemical-and-Physical-Properties
CAS Number	75-69-4
Conversion factors	1ppm = 5.60mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.179ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: None

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Trichlorofluoromethane."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1990. *"Trichlorofluoromethane."* MAK Value Documentation, 1990. The MAK-Collection for Occupational Health and Safety, Vol 1; pp 335-346. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7569e0001

Deutsche Forschungsgemeinschaft (DFG), 2002. *"Trichlorfluormethan."* MAK Value Documentation in German language, 2002. The MAK-Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7569d0034

Environmental Protection Authority (EPA), 2022. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2022. GESTIS International Limit Values. Accessed February 2022. http://limitvalue.ifa.dguv.de

National Center for Biotechnology Information. PubChem Database. Accessed February 2022. *Trichlorofluoromethane*, CID: 6389. https://pubchem.ncbi.nlm.nih.gov/compound/6389

Safe Work Australia (2020). Safe Work Australia Draft Evaluation Report and Recommendations – *Trichlorofluoromethane*. https://engage.swa.gov.au/65429/widgets/323765/documents/191984

HEXANE, OTHER ISOMERS (2,2-DIMETHYLBUTANE, 2,3-DIMETHYLBUTANE, 2-METHYLYPENTANE, 3-METHYLPENTANE)

CAS NO: 75-83-2; 79-29-8; 107-83-5; 96-14-0

Summary

Workplace Exposure Standards for hexane, other isomers

	CURRENT	PROPOSED
WES-TWA	500**ppm** (1,760**mg/m³**)	500ppm (1,760mg/m³)
WES-STEL	1,000ppm (3,500mg/m³)	1,000ppm (3,500mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hexane, other isomers

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA for hexane, other isomers of 500ppm (1,760mg/m³), and,
2. maintain the WES-STEL for hexane, other isomers of 1,000ppm (3,500mg/m³).

To protect for sensory irritation and narcotic effects.

Discussion

The hexane isomers, other than n-hexane (**CAS No.**: 110-54-3), include: 2-dimethyl-butane (CAS No.: 75-83-2); 2,3-dimethylbutane (CAS No.: 79-29-8); 2-methylpentane (CAS No.: 107-83-5); and, 3-methylpentane (CAS No.: 96-14-0). Commercial hexanes are used as solvents for vegetable oils, glues, coatings, and paints; and, found in petroleum fuels (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Hexane isomers have mild, petroleum-like odours (PubChem, 2022; ACGIH®, 2001).

n-Hexane (CAS No.: 110-54-3) is subject to its own WES.

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hexane isomers, other than *n*-hexane noted that the critical effects were sensory irritation and narcotic effects (DFG MAK, 2009).

The DFG noted that the **MAK** value of 500ppm for hexane isomers, except *n*-hexane, **peak limitation Category II** with an excursion factor of 2, were based on the results of studies in animals and humans with n-hexane, hexane isomers, *n*-pentane, and *n*-heptane. The MAK value was supported by a LOAEC of >1,000ppm for pre-narcotic effects in humans exposed to *n*-hexane (DFG MAK, 2009).

The DFG noted that an **"H"** notation was not warranted for hexane isomers, as the dermal absorption of 2-methylpentane through rat skin was very low, and by analogy significant dermal exposures could be discounted. No data indicated that **"Sh"** and **"Sa"** notations were warranted for hexane isomers (DFG MAK, 2009).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of hexane isomers, other than *n*-hexane noted that the critical effects were eye and mucous membrane irritation, dizziness, and central nervous system depression (ACGIH®, 2001).

The ACGIH® review concluded that:

> "It is the opinion of ACGIH that the metabolites of n-hexane (primarily 5-hydroxy-2-hexanone and 2,5-hexanedione) are responsible for its neurotoxicity (Nomiyama *et al*., 1973; Spencer *et al*., 1978). This conclusion is supported by the similar production of these metabolites after exposure to methyl n-butyl ketone, a compound which can induce an identical syndrome (Schaumburg & Spencer, 1976; Spencer & Schaumburg, 1977; Couri *et al*., 1978). Based on known patterns of hepatic microsomal oxidation and marked variations in structures of the hexane isomers considered here, it is considered unlikely that all hexanes would follow the same metabolic route in the body.
>
> "A **TLV-TWA** of 500ppm is recommended for isomers of hexane and mixtures of hexanes containing no n-hexane, based on the above metabolic data and in the absence of adverse effects from exposure to concentrations at or below 500ppm (Nelson *et al*., 1943; Elkins, 1959). It is further recommended that the n-hexane TLV-TWA (50ppm) would apply not only to n-hexane itself but also to commercial hexane which contains greater than 5% n-hexane.
>
> "A **TLV-STEL** of 1,000ppm is recommended in order to minimize objective depression of the **CNS**. For hexane isomers containing less than 5% n-hexane, a TLV-TWA of 500ppm should provide adequate protection from nausea, headache, ocular and upper respiratory tract irritation, and CNS depression associated with hexane inhalation in the absence of additional organic compounds with narcotic or neurotoxic characteristics." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations for hexane isomers (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 500ppm (1,760mg/m^3) and WES-STEL of 1,000ppm (3,500mg/m^3) for hexane isomers other than *n*-hexane to be adequate to manage health risks from possible workplace exposure.

It is recommended for hexane isomers other than *n*-hexane that the WES-TWA of 500ppm (1,760mg/m^3) and WES-STEL of 1,000ppm (3,500mg/m^3) are maintained to protect against sensory irritation and narcotic effects, based on the DFG and ACGIH® recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	2,2-Dimethyl-butane https://pubchem.ncbi.nlm.nih.gov/compound/6403#section=Chemical-and-Physical-Properties 2,3-Dimethylbutane https://pubchem.ncbi.nlm.nih.gov/compound/6589#section=Chemical-and-Physical-Properties 2-Methylpentane https://pubchem.ncbi.nlm.nih.gov/compound/7892#section=Chemical-and-Physical-Properties 3-Methylpentane https://pubchem.ncbi.nlm.nih.gov/compound/7282#section=Chemical-and-Physical-Properties
CAS Number	75-83-2; 79-29-8; 107-83-5; 96-14-0
Conversion factors	1ppm = 3.58mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.28ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 2,2-Dimethyl-butane www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/C78496D3-8614-43DA-AF72-A9F891865A3D 2,3-Dimethylbutane www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/04924AC6-F1BA-4E7C-B54B-5425034B0FD9 2-Methylpentane www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/98AC7AE7-0BC3-46DA-8A23-9741400ED3F1 3-Methylpentane www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/53A95180-47EF-4E3B-B9A4-7894E9E6076E

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

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Deutsche Forschungsgemeinschaft (DFG), 2009. *"Hexan-Isomeren (außer n-Hexan) und Methylcyclopentan."* MAK Value Documentation in German language, 2009; The MAK Collection for Occupational Health and Safety; pp 1-9. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb11054ismd0047

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HEXONE

CAS NO: 108-10-1

Summary

Workplace Exposure Standards for hexone (CAS: 108-10-1)

	CURRENT	PROPOSED
WES-TWA	50**ppm** (205**mg/m³**)	20ppm (82mg/m³)
WES-STEL	75ppm (307mg/m³)	75ppm (307mg/m³)
WES-Ceiling	–	–
Notations	–	***skin***

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hexone

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for hexone of 20ppm (82mg/m³)
2. adopt a *skin* notation for hexone, and
3. maintain the WES-STEL for hexone of 75ppm (307mg/m³).

To protect for **CNS** effects and mucous membrane irritation.

Discussion

Hexone is used in cellulose and polyurethane lacquers and paint solvents; as an extraction solvent; in the manufacture of methyl amyl alcohol; and, to denature ethanol (**Safe Work Australia**, 2019; **ACGIH®**, 2010).

Hexone has a fruity, ethereal, sweet odour, with odour thresholds reported at 0.3 and 0.7ppm (PubChem, 2021; ACGIH®, 2010).

Cancer risks

The International Agency for Research on Cancer (**IARC**) evaluation of hexone (methyl isobutyl ketone) concluded that:

> There were no data in humans for the carcinogenicity of methyl isobutyl ketone.
>
> There is ***sufficient evidence in experimental animals*** for the carcinogenicity of methyl isobutyl ketone.

With an overall evaluation that:

> Methyl isobutyl ketone is *possibly carcinogenic to humans* (**Group 2B**). (IARC, 2012).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of hexone noted that the critical effects were central nervous system effects and irritation of mucous membranes (ACGIH®, 2010).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 20ppm (82mg/m^3) is recommended to protect against human central nervous system (CNS) symptoms as reported on a 17-item questionnaire associated with 90 to 120 minutes exposure at 200mg/m^3 (49ppm) (Wigaeus-Hjelm *et al*., 1990; Iregren *et al*., 1993). A **TLV-STEL** of 75ppm (307mg/m^3) is recommended to protect against irritation of the mucous membranes associated with short-term exposures (Silverman *et al*., 1946). Both limits should protect against irritation, CNS, and gastro-intestinal symptoms observed in occupational populations (Linari *et al*., 1964; Armeli *et al*., 1968). **MIBK** is assigned the **A3 notation**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, because elevated rates of renal tubule adenomas and mononuclear cell leukemia were found in male rats exposed to 1800ppm MIBK, and elevated rates of hepatocellular adenoma were significantly increased in male and female mice exposed at 1800ppm (U.S. NTP, 2006). However, no human cancer data were available." (references cited in ACGIH®, 2010).

The ACGIH® noted that there was insufficient data to recommend **DSEN**, **RSEN** or **Skin** notations for hexone (ACGIH®, 2010).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hexone (4-methylpentan-2-on) noted that the critical effects were mucous membrane irritation and CNS effects (DFG MAK, 1999).

The DFG noted that the **MAK** value of 20ppm, **peak limitation Category I** with an excursion factor of 2, were based on workplace studies and NOEL from animal studies. In human studies, no important differences in subjective symptoms were found when comparing the effects of 100ppm with those of 25ppm administered for 2 hours, and when comparing 25 and 50 with 2.4ppm. However, the severity of the symptoms increased with increasing concentration, the irritative more so than the central nervous system symptoms. No long-term sequelae of the irritation were apparent from observations after exposure ended, and the re-adaptation of the sense of smell. 90-day studies in rats and mice demonstrated NOELs of 50ppm for systemic toxicity, 7-day continuous exposure at 50ppm caused first reaction time effects in baboons (DFG MAK, 1999).

The DFG noted that an **"H"** notation was warranted for hexone, as dermal exposure could potentially significantly contribute to systemic toxicity (DFG MAK, 1999).

"Sa" and **"Sh"** notations were not considered necessary, based on the available data (DFG MAK, 1999).

The DFG noted that the MAK value of 20ppm corresponded to a **BAT** value of 0.7mg hexone/L urine (end of shift), based on a good linear correlation between hexone in air and hexone in urine from workplace studies (DFG BAT, 2014).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 50ppm (205mg/m^3) for hexone, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for hexone that a WES-TWA of 20ppm (82mg/m^3) with a *skin* notation are adopted, while the WES-STEL of 75ppm (307mg/m^3) is maintained to protect against CNS effects and mucous membrane irritation, based on the ACGIH® and DFG recommendations.

[Hexone (MIBK) is the primary metabolite of methyl amyl alcohol (methyl isobutyl carbinol, **MIBC**). See WorkSafe WES review for methyl amyl alcohol, 2024].

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Methyl-isobutyl-ketone#section=Chemical-and-Physical-Properties
CAS Number	108-10-1
Conversion factors	1mg/m^3 = 0.245ppm (25°C; 101.3**kPa**) 1ppm = 4.09mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 2-Pentanone, 4-methyl www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/DE0DC087-9B15-49F0-9249-33B369B4B115 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methyl Isobutyl Ketone."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1999. *"Hexone."* MAK Value Documentation, 1999; The MAK Collection for Occupational Health and Safety; pp 169-180. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10810e0013

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HEXYLENE GLYCOL

CAS NO: 107-41-5

Summary

Workplace Exposure Standards for hexylene glycol, vapour (CAS: 107-41-5)

	CURRENT	PROPOSED
WES-TWA	–	25**ppm** (121**mg/m³**)
WES-STEL	–	50ppm (242mg/m³)
WES-Ceiling	25**ppm** (121**mg/m³**)	–
Notations	–	***ifv***; the WES recommendations for vapor and aerosol should be applied separately, and they are not intended to be additive

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hexylene glycol, vapour

Workplace Exposure Standards for hexylene glycol, particulate (CAS: 107-41-5)

	CURRENT	PROPOSED
WES-TWA	–	–
WES-STEL	–	10mg/m³
WES-Ceiling	–	–
Notations	–	*ifv*; the WES recommendations for vapor and aerosol should be applied separately, and they are not intended to be additive

TABLE 2: Current and proposed Workplace Exposure Standards (WES) for hexylene glycol, particulate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for hexylene glycol, vapour of 25ppm (121mg/m³)
2. adopt a WES-STEL for hexylene glycol, vapour of 50ppm (242mg/m³)
3. adopt a WES-STEL for hexylene glycol, particulate of 10mg/m³, and
4. remove the WES-Ceiling for hexylene glycol.

To protect for eye and upper respiratory tract irritation.

Discussion

Hexylene glycol is used as a solvent plasticiser, chemical intermediate, selective solvent, and lubricant/moistening/softening agent (**Safe Work Australia**, 2019; **ACGIH®**, 2017).

Hexylene glycol has a mild, sweetish odour, with an odour threshold reported at 3.93ppm (PubChem, 2022; ACGIH®, 2017).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of hexylene glycol noted that the critical effects were upper respiratory tract and eye irritation (ACGIH®, 2017).

The ACGIH® review concluded that:

"A **TLV-TWA** of 25ppm and a **TLV-STEL** of 50ppm (both as vapor fraction) are recommended to minimize the potential for respiratory and eye irritation. In addition, a TLV-STEL of 10mg/m^3, as inhalable particulate matter (aerosol only), is also recommended to prevent particulate concentrations known to be irritating in the presence of vapors. Microscopic evidence of mild respiratory irritation (e.g., congestion, hyperplasia) was observed in the tracheas of 10 rats and 1 rabbit exposed 7 hours/day for 9 days to 0.7mg/L of an aerosol of hexylene glycol with a mean droplet size of 1**µm**; some vapor was likely present (Union Carbide Corp., 1976). In a 90-day oral study in rats, hepatocellular hypertrophy, species and gender-specific renal changes, and inflammation-induced hyperplastic changes in the forestomach and stomach were observed. The lowest-observed-adverse-effect level (**LOAEL**) was 150**mg/kg/day** (Fabreguettes, 1999b as cited in OECD, 2001). The equivalent dose for humans is 17-fold higher than that at the recommended TLV-TWA. Hexylene glycol exposure at 50ppm for 15 minutes produced a slight odor with a few volunteer subjects noticing slight eye irritation. At higher (unspecified) concentrations, nose and throat irritation was reported (Silverman *et al*., 1946). Some volunteers exposed to hexylene glycol at 100ppm for 5 minutes, involving exposure to saturated vapor and mist, reported slight nasal irritation and one individual reported slight pulmonary discomfort (Hine *et al*., 1955 as cited in OECD, 2001). For a similar compound, ethylene glycol, irritation of the upper respiratory tract was observed at 55ppm (Wills *et al*., 1974). Collectively, these data support a TLV-STEL of 50ppm. Exposures above the saturated vapor concentration of 66ppm (317mg/m^3) include both vapor and mist. Based on data showing that hexylene glycol was irritating to the eyes of rabbits (Gardner, 1996c as cited in OECD, 2001), the mist is expected to be irritating to mucous membranes at the site of deposition where the concentration in the local microenvironment is high. Because of its low vapor pressure and hygroscopicity, industrial use of hexylene glycol at normal room temperature should not create a significant vapor hazard. At higher temperatures, the irritant effects become more pronounced due to the generation of irritating mists from condensed vapors. The 10mg/m^3 TLV-STEL, as an aerosol, approximates the incremental increase in air concentration that corresponds to the observation of increased irritation above the saturated vapor concentration for hexylene glycol. Limiting the aerosol concentration is also consistent with good industrial hygiene practice by improving housekeeping for a slippery material that can represent a safety concern … The TLV recommendations for vapor and aerosol should be applied separately, and they are not intended to be additive.

"Several cases of narcosis, renal impairment, possible liver damage, coma and death were reported in children exposed to hexylene glycol impregnated burn dressings (Procter, 1966). A similar case was reported in an adult following application of hexylene glycol impregnated burn dressings, producing delirium and ataxia, but he recovered within 12 hours following removal of the dressings (Fischer *et al*., 1968). These cases highlight the potential for toxicity following dermal contact with burned skin; however, a **Skin** notation was not considered necessary under normal handling conditions." (references cited in ACGIH®, 2017).

The ACGIH® noted that there were insufficient data to assign **RSEN**, **DSEN** or carcinogenicity notations for hexylene glycol (ACGIH®, 2017).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hexylene glycol noted that the critical effect was eye irritation (DFG MAK, 2001).

The DFG noted that the **MAK** value of 10ppm (49mg/m³) for hexylene glycol, **peak limitation Category I** with an excursion factor of 2, were based on reports of eye irritation (not severe) in volunteers exposed to 50ppm for 15 minutes. The DFG noted that 50ppm hexylene glycol is approximately equivalent to the saturation concentration at 25°C (DFG MAK, 2001).

The DFG also noted that **"H"** and **"Sh"** notations were not assigned for hexylene glycol as the available data indicated that the potential for dermal toxicity or sensitisation were low (DFG MAK, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-Ceiling of 25ppm (121mg/m³) for hexylene glycol to be inadequate to manage health risks from possible workplace exposure.

It is recommended for hexylene glycol vapour, that a WES-TWA of 25ppm (121mg/m³) and a WES-STEL of 50ppm (242mg/m³), and for hexylene glycol particulate, that a WES-STEL of 10mg/m³ are adopted, to protect against eye and upper respiratory tract irritation, based on the ACGIH® recommendations. Noting the limited database for hexylene glycol.

It is further recommended that an inhalable fraction and vapour (ifv) notation be adopted in recognition of the potential for hexylene glycol to be present in both particle and vapour phases, with each contributing to a significant portion of exposure.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Hexylene-glycol#section=Chemical-and-Physical-Properties
CAS Number	107-41-5
Conversion factors	1ppm = 4.83mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.207ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Hexylene glycol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2001. *"Hexylene glycol."* MAK Value Documentation, 2001; The MAK Collection for Occupational Health and Safety, Vol. 16; pp 233-246. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10741kske0016

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2022. GESTIS International Limit Values. Accessed January 2022. http://limitvalue.ifa.dguv.de

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Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Hexylene glycol*. https://engage.swa.gov.au/52508/widgets/273797/documents/127244

HYDROGEN BROMIDE

CAS NO: 10035-10-6

Summary

Workplace Exposure Standards for hydrogen bromide (CAS: 10035-10-6)

	CURRENT	PROPOSED
WES-TWA	–	–
WES-STEL	–	–
WES-Ceiling	3**ppm** (9.9**mg/m³**)	2ppm (6.6mg/m³)
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hydrogen bromide

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-Ceiling for hydrogen bromide of 2ppm (6.6mg/m³).

To protect for irritation and corrosion of the skin and mucous membranes of the eyes, nose and respiratory tract.

Discussion

Hydrogen bromide is used in organic synthesis, for dissolving certain ores, bromide manufacture, and as an alkylation catalyst (**Safe Work Australia**, 2019; **ACGIH®**, 2004).

Hydrogen bromide has an acrid, irritating odour, with an odour threshold reported at 2ppm (PubChem, 2022; ACGIH®, 2004).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hydrogen bromide noted that the critical effects were irritation and corrosion of the skin and mucous membranes of the eyes, nose and respiratory tract (DFG MAK, 2010a).

The DFG noted that the **MAK** value of 2ppm for hydrogen bromide, **peak limitation Category I** with an excursion factor of 1, were based on the results of exposures of several minutes that indicated that concentrations of 3ppm and above induced irritation of the nose and throat in volunteers (DFG MAK, 2010a; 2012).

The DFG also noted that **“H”**, **“Sa”** or **“Sh”** notations were not assigned for hydrogen bromide (DFG MAK, 2012).

ACGIH®

The American Conference of Governmental Industrial Hygienists’ (ACGIH®) review of hydrogen bromide noted that the critical effects were irritation (ACGIH®, 2004).

The ACGIH® review concluded that:

> "ACGIH® considers hydrogen bromide a primary irritant and believes that primary irritants with no known chronic effects should have **ceiling TLV**s rather than **TWA** or **STEL** values. The animal studies by Stavert *et al*. (1991) found that hydrogen bromide was quantitatively similar to hydrogen chloride, whose TLV is a ceiling limit of 2ppm. Therefore, a TLV-Ceiling of 2ppm (reduced from 3ppm) is recommended for hydrogen bromide, based upon irritation effects. A report on the responses of six human subjects who inhaled hydrogen bromide at concentrations ranging from 2 to 6ppm formed part of the basis of the previous TLV recommendation, but this 1955 report (Connecticut State Department of Health) is not available from the agency that supported the study and was, therefore, not considered in the present recommendation. Maintaining workplace air concentration below the TLV-Ceiling should minimize even transient irritation and complaints. There is no implication that brief, small excursions above the 2ppm ceiling are life-threatening or have the potential for creating permanent harm." (references cited in ACGIH®, 2004).

The ACGIH® noted that there was insufficient data to assign **Skin**, **SEN** or carcinogenicity notations for hydrogen bromide (ACGIH®, 2004).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-Ceiling of 3ppm (9.9mg/m³) for hydrogen bromide to be inadequate to manage health risks from possible workplace exposure.

It is recommended for hydrogen bromide that a WES-Ceiling of 2ppm (6.6mg/m³) is adopted, to protect against irritation and corrosion of the skin and mucous membranes of the eyes, nose and respiratory tract, based on ACGIH® recommendations. [Noting the limited database for hydrogen bromide.]

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/hydrogen-bromide#section=Chemical-and-Physical-Properties
CAS Number	10035-10-6
Conversion factors	1ppm = 3.37mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.3ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/BE2040CE-8863-4C8E-AA03-030ABA4A5E08

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Hydrogen bromide."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2012. *"Hydrogen bromide."* MAK Value Documentation, 1999; The MAK Collection for Occupational Health and Safety, Vol 13; pp 187-191. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1003510e0013

Deutsche Forschungsgemeinschaft (DFG), 2010a. *"Hydrogen bromide."* MAK Value Documentation, 2010a; The MAK Collection-Part 1; pp 1-2. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1003510e0026a

Deutsche Forschungsgemeinschaft (DFG), 2010b. *"Hydrogen bromide."* MAK Value Documentation, 2010b; The MAK Collection-Part 1; pp 1-2. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1003510e0026b

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National Center for Biotechnology Information. PubChem Database. Accessed January 2022. *Hydrogen bromide*, CID: 260. https://pubchem.ncbi.nlm.nih.gov/compound/hydrogen-bromide

Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Hydrogen bromide*. https://engage.swa.gov.au/52508/widgets/273797/documents/127249

HYDROGEN CHLORIDE

CAS NO: 7647-01-0

Summary

Workplace Exposure Standards for hydrogen chloride (CAS: 7647-01-0)

	CURRENT	PROPOSED
WES-TWA	–	–
WES-STEL	–	–
WES-Ceiling	5**ppm** (7.5**mg/m³**)	2ppm (2.98mg/m³)
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hydrogen chloride

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-Ceiling for hydrogen chloride of 2ppm (2.98mg/m³).

To protect for irritation and corrosion of the skin and mucous membranes of the eyes, nose and respiratory tract.

Discussion

Hydrogen chloride is used in chemical manufacture, and where strong acids are required (**ACGIH®**, 2003). Hydrogen chloride is released when polyvinyl chloride burns (ACGIH®, 2003).

Hydrogen chloride has a characteristic suffocating, pungent odour, with an odour threshold reported at 0.77ppm (PubChem, 2022; ACGIH®, 2003).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hydrogen chloride noted that the critical effects were local irritation of the nose and respiratory tract (DFG MAK, 2007).

The DFG noted that the **MAK** value of 2ppm for hydrogen chloride, **peak limitation Category I** with an excursion factor of 2, were based on the results of a 2-year inhalation study in rats reporting hyperplasia in the larynx and trachea at 10ppm. A linear interpolation back to the control incidences indicated 2ppm would not be statistically significantly different. The MAK value was supported by a workplace study reporting very slight mucosa irritation at concentrations up to 3.4ppm hydrogen chloride, and slight irritation at 5ppm which rapidly regressed (DFG MAK, 2007).

The DFG also noted that **"H"**, **"Sa"** and **"Sh"** notations were not assigned for hydrogen chloride, as no evidence was available to show significant dermal absorption, while dermal sensitisation studies in humans and guinea pigs were negative (DFG MAK, 2007).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of hydrogen chloride noted that the critical effects were irritation and corrosion (ACGIH®, 2003).

The ACGIH® review concluded that:

> "Hydrogen chloride is a strong irritant of the eyes, mucous membranes, and the skin. Chronic exposure to hydrogen chloride has an acknowledged corrosive action on the teeth. Based on the reports of respiratory irritation from short-term exposures to hydrogen chloride and a **NOAEL** of 1.8ppm (Stevens *et al*., 1992), a **TLV-Ceiling** of 2ppm is recommended to minimize the acute irritation associated with exposure to hydrogen chloride vapor. Occupational exposure to hydrogen chloride occurs primarily via exposure to vapor. In environments in which aerosols of hydrogen chloride are encountered, the TLV should be converted to mg/m³. Although direct skin contact can cause severe burns if the acid is not quickly rinsed away with copious amounts of water, there was no indication that skin contact with hydrogen chloride can elicit systemic poisoning; hence, the Skin notation was not applied to this compound. The **A4**, **Not Classifiable as a Human Carcinogen**, notation is based on the **IARC** (1992) review and the Bond *et al*. (1991) study." (references cited in ACGIH®, 2003).

The ACGIH® noted that there was insufficient data to assign **SEN** or **Skin** notations for hydrogen chloride (ACGIH®, 2003).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-Ceiling of 5ppm (7.5mg/m³) for hydrogen chloride to be inadequate to manage health risks from possible workplace exposure.

It is recommended for hydrogen chloride that a WES-Ceiling of 2ppm (2.98mg/m³) is adopted, to protect against irritation and corrosion of the skin and mucous membranes of the eyes, nose and respiratory tract, based on the ACGIH® recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Hydrochloric-acid#section=Chemical-and-Physical-Properties
CAS Number	7647-01-0
Conversion factors	1ppm = 1.49mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.67ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/E23ED1EE-D257-498A-96DC-AE04F2C29AC5

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Hydrogen chloride."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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HYDROGEN FLUORIDE, as F

CAS NO: 7664-39-3

Summary

Workplace Exposure Standards for hydrogen fluoride, as F (CAS: 7664-39-3)

	CURRENT	PROPOSED
WES-TWA	–	1ppm (0.8mg/m³)
WES-STEL	–	2ppm (1.6mg/m³)
WES-Ceiling	3**ppm** (2.6**mg/m³**)	–
Notations	***bio***	*bio*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hydrogen fluoride, as F

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for hydrogen fluoride of 1ppm (0.8mg/m³), and
2. adopt a WES-STEL for hydrogen fluoride of 2ppm (1.6mg/m³).

To protect for respiratory tract irritation and skeletal fluorosis.

Discussion

Hydrogen fluoride is used as a catalyst in chemical syntheses, a fluorination agent, to etch glass, in pickling stainless steel, and other uses (**Safe Work Australia**, 2019; **ACGIH®**, 2005).

Hydrogen fluoride has an irritating, pungent odour, with an odour threshold reported at 0.042ppm (PubChem, 2022; ACGIH®, 2005).

A current Biological Exposure Index (**BEI**) of 2mg fluoride/L urine, prior to shift; and, 3mg fluoride/L urine, end of shift is established to protect against skeletal fluorosis (WorkSafe, 2022; see draft WES Review for Fluorides as F, 2023).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hydrogen fluoride noted that the critical effects were respiratory tract irritation and skeletal fluorosis (DFG MAK, 2001; 2006a; 2006b).

The DFG noted that the **MAK** value of 1ppm for hydrogen fluoride, **peak limitation Category I** with an excursion factor of 2, were based on both local respiratory tract irritation and systemic skeletal fluorosis (DFG MAK, 2006a). Studies in volunteers reported upper respiratory tract irritation at inhalation exposures of 3ppm and above for one hour, but not at 2.84ppm and below; and, at average concentrations of 2.59ppm for 6 hours/day for 25 days, but not at 1.42ppm (DFG MAK, 2001). Clinical stage III skeletal fluorosis has been reported to occur after 20 years exposure to >20mg fluoride/day. Accounting for fluoride intake through food and drink, this result was adjusted to the workplace to give a MAK value of 1ppm. The MAK value was supported by a study indicating intakes equivalent to 1.5mg/m³ over 20 years resulted in more bone fractures, while intakes equivalent to 1mg/m3 did not (DFG MAK, 2006b).

The DFG also noted that **"H"**, **"Sa"** and **"Sh"** notations were not assigned for hydrogen fluoride, as the strong irritant induces skin damage precluding assessment of dermal absorption or sensitisation (DFG MAK, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of hydrogen fluoride noted that the critical effects were pulmonary inflammation and lung damage (ACGIH®, 2005).

The ACGIH® review concluded that:

> "Hydrogen fluoride, as a gas, is a severe respiratory irritant, and in solution, it causes severe and painful burns of the skin and eyes. ACGIH® considers hydrogen fluoride a primary irritant. Based upon the results of controlled inhalation studies in healthy human volunteers (Lund *et al*., 1997; 1999), which showed symptom increases and bronchoalveolar lavage fluid changes in the 0.6 to 2.4mg/m³ group (0.9 to 2.9ppm), a **TLV-TWA** of 0.5ppm, measured as **F**, is recommended. This limit should minimize cellular changes and adverse symptoms such as irritation due to exposure to hydrogen fluoride. This limit should also minimize the potential for occurrence of dental and osteofluorosis associated with occupational exposure to hydrogen fluoride. Similar to hydrogen chloride and hydrogen bromide, there is concern regarding the corrosive nature of hydrogen fluoride vapors; therefore, a **TLV-Ceiling** of 2ppm is also recommended. Because of this concern for the corrosive and skin-penetrating properties of hydrogen fluoride, a **Skin** notation is recommended." (references cited in ACGIH®, 2005).

The ACGIH® noted that there was insufficient data to assign **SEN** or carcinogenicity notations for hydrogen fluoride (ACGIH®, 2005).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-Ceiling of 3ppm (2.6mg/m³) for hydrogen fluoride to be inadequate to manage health risks from possible workplace exposure.

It is recommended for hydrogen fluoride that a WES-TWA of 1ppm (0.8mg/m³) and a WES-STEL of 2ppm (1.6mg/m³) are adopted, to protect against respiratory tract irritation and skeletal fluorosis, based on the DFG recommendations.

It is noted that biological monitoring for fluorides in urine remains an option for assessing worker exposure to hydrogen fluoride.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Hydrofluoric-acid#section=Chemical-and-Physical-Properties
CAS Number	7664-39-3
Conversion factors	1ppm = 0.82mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 1.22ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Hydrofluoric acid, >60% www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/47332E67-DE24-45C9-85A7-5807D43E69A8

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Hydrogen fluoride."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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HYDROGEN PEROXIDE

CAS NO: 7722-84-1

Summary

Workplace Exposure Standards for hydrogen peroxide (CAS: 7722-84-1)

	CURRENT	PROPOSED
WES-TWA	1**ppm** (1.4**mg/m³**)	0.5ppm (0.71mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for hydrogen peroxide

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for hydrogen peroxide of 0.5ppm (0.71mg/m³).

To protect for irritation of the eyes, mucous membranes, and respiratory tract.

Discussion

Hydrogen peroxide, as a common oxidising agent, is used for bleaching or deodorising; in the treatment of water and sewage; as a disinfectant; as a component of rocket fuels; and, in chemical manufacturing (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Hydrogen peroxide has a slightly sharp odour resembling that of ozone (PubChem, 2021).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of hydrogen peroxide noted that the critical effects were local irritation of the respiratory tract and eyes (DFG MAK, 2019).

The DFG noted that the **MAK** value of 0.5ppm for hydrogen peroxide, **peak limitation Category I** with an excursion factor of 1, were based on a **NOAEC** of 0.5ppm from human studies after 2-hour exposures with slight irritation reported at 2.2ppm. The MAK value was supported by other studies reporting no unusual lung function test results after exposures up to 0.56ppm and 0.67ppm, or no adverse effects at the workplace after average 8-hour values of up to 0.5ppm. A 28-day inhalation study in rats reported a NOAEC of 2ppm with histological changes in the anterior region of the nasal cavity and respiratory epithelium at 10ppm and above. While a 90-day inhalation study revealed no adverse effects up to 7ppm (DFG MAK, 2019).

The DFG concluded that an **"H"** notation was not required for hydrogen peroxide, based on the absence of data indicating systemic effects after dermal exposure (DFG MAK, 2010).

The DFG concluded that **"Sh"** or **"Sa"** notations were not required for hydrogen peroxide due to the limited reports of sensitisation in spite of the widespread use, and the negative results in animal studies (DFG MAK, 2010).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of hydrogen peroxide noted that the critical effects were irritation of the eyes, mucous membranes, lungs, and skin (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Hydrogen peroxide is an irritant of the eyes, mucous membranes, lungs, and skin. The vapor of 90% hydrogen peroxide has caused skin, eye, and pulmonary irritation and hair bleaching in dogs at 7ppm (Oberst *et al*., 1954). A **TLV-TWA** of 1ppm of hydrogen peroxide vapor is recommended to minimize the likelihood of dermal, ocular, and pulmonary irritation, and bleaching of the hair. Based on the carcinogenicity data reviewed by **IARC** (1987), there exists limited evidence for the carcinogenicity of hydrogen peroxide. Accordingly, a carcinogenicity notation of **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, is assigned to hydrogen peroxide." (references cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin** or **SEN** notations or a **TLV-STEL** for hydrogen peroxide (ACGIH®, 2001).

Conclusions

Based on the documentation cited and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 1ppm (1.4mg/m^3) for hydrogen peroxide, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for hydrogen peroxide that a WES-TWA of 0.5ppm (0.71mg/m^3) is adopted, to protect against irritation of the eyes, mucous membranes, and respiratory tract, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Hydrogen-peroxide#section=Chemical-and-Physical-Properties
CAS Number	7722-84-1
Conversion factors	1mg/m^3 = 0.719ppm (25°C; 101.3**kPa**) 1ppm = 1.39mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Hydrogen peroxide, > 60% aqueous solution www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/8BCD973C-534A-4576-AD13-B833FB15DF13 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

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ISOPHORONE

CAS NO: 78-59-1

Summary

Workplace Exposure Standards for isophorone (CAS: 78-59-1)

	CURRENT	PROPOSED
WES-TWA	–	–
WES-STEL	–	–
WES-Ceiling	5**ppm** (28**mg/m³**)	5ppm (28mg/m³)
Notations	***carcinogen category 2***	carcinogen category 2

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for isophorone

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-Ceiling for isophorone of 5ppm (28mg/m³), and
2. maintain the *carcinogen category 2* notation.

To protect for irritation of the eyes, nose and respiratory tract.

Discussion

Isophorone is used as a solvent for resins and polyacrylates, as a chemical intermediate, and in pesticides (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Isophorone has a peppermint- or camphor-like odour, with an odour threshold reported at 0.20ppm (PubChem, 2022; ACGIH®, 2001).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of isophorone noted that the critical effects were irritation and narcosis (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Based on the report by Silverman *et al*. (1946) and other information (Ware, 1973) that workplace air **TWA** concentrations of 5 to 8ppm were associated with fatigue and malaise, and that reduction of ambient concentrations of isophorone to 1 to 4ppm eliminated the complaints of irritation, a **TLV-Ceiling** of 5ppm is recommended for isophorone. Although the **NTP** report (Bucher *et al*., 1986) concluded "some" or equivocal" evidence of carcinogenicity in male rats and male mice, ACGIH considers these data of minimal weight in assessing workplace hazards because the resulting male rat kidney tumors are viewed as a manifestation of the well-known α-2-μ-globin-induced nephropathy. In a strain of rat (NCI-Black-Reiter) that cannot synthesize the hepatic form of this low-molecular-weight protein, agents that produce neuropathy [*sic.*] in male F344 rats were inactive (Dietrich and Swenberg, 1991). The authors (Dietrich and Swenberg, 1991) concluded that the presence of α-2-μ-globulin was "causal to the development of the renal disease in rats

exposed to isophorone," and this process was specific to the male rat. Little weight was also given to the findings of marginal increases in certain mouse tumors; the high and variable incidence of such tumors in the NTP historical database and the absence of such tumors in female mice and male and female rats suggested that the occurrence of such tumors (Bucher *et al*., 1986) was unrelated to the administration of isophorone. This conclusion is consistent with that published by an expert group in Europe reviewing the same data set (ECETOC, 1989). The almost complete absence of genotoxic activity associated with isophorone indicated that it is unlikely to be a direct-acting carcinogen and any potential carcinogenicity would be mediated through promotion, mitogenesis, or other, presumably threshold, mechanisms. Accordingly, an **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, notation is recommended for isophorone." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to assign **Skin** or **SEN** notations for isophorone (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of isophorone noted that the critical effects were local irritation of the eyes, nose and respiratory tract (DFG MAK, 2000; DFG MAK, 1995).

The DFG noted that the **MAK** value of 2ppm for isophorone, **peak limitation Category I** with an excursion factor of 2, were based on the results of studies in volunteers that reported irritation of the eyes, nose and throat immediately after inhalation exposure to 25ppm, while 15 minutes exposure to 10ppm was tolerated by most volunteers. The MAK value was supported by reports that 1-4ppm was tolerated without symptoms during industrial handling (DFG MAK, 2000; DFG MAK, 1995).

"H", **"Sa"** and **"Sh"** notations were not assigned for isophorone (DFG MAK, 2000).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DGF reviews, WorkSafe considers its current WES-Ceiling of 5ppm (28mg/m^3) for isophorone to be adequate to manage health risks from possible workplace exposure.

It is recommended for isophorone that the WES-Ceiling of 5ppm (28mg/m^3) is maintained, to protect against irritation of the eyes, nose and respiratory tract, based on the ACGIH® recommendations. The carcinogen category 2 notation should be maintained, as the available evidence suggests that isophorone is a carcinogen in rodents, although at least one of the putative mechanisms is not relevant to humans.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/isophorone#section=Chemical-and-Physical-Properties
CAS Number	78-59-1
Conversion factors	1ppm = 5.71mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.175ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 2-Cyclohexen-1-one, 3,5,5-trimethyl www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/F988818C-56EF-499C-97C9-63BE5ADD0E1F

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Isophorone."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Deutsche Forschungsgemeinschaft (DFG), 2000. *"3,5,5-Trimethyl-2-cyclohexen-1-on (Isophoron)"* MAK Value Documentation in German language, 2000. The MAK-Collection for Occupational Health and Safety; pp 1-2. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7859d0030

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ISOPROPYL ALCOHOL

CAS NO: 67-63-0

Summary

Workplace Exposure Standards for isopropyl alcohol (CAS: 67-63-0)

	CURRENT	PROPOSED
WES-TWA	400**ppm** (983**mg/m³**)	200ppm (491mg/m³)
WES-STEL	500ppm (1,230mg/m³)	400ppm (983mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for isopropyl alcohol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for isopropyl alcohol of 200ppm (491mg/m³), and
2. adopt a WES-STEL for isopropyl alcohol of 400ppm (983mg/m³).

To protect for eye and upper respiratory tract irritation and acute nasal irritation.

Discussion

Isopropyl alcohol is used as a solvent, a disinfectant, a major component of rubbing alcohol and as a raw material in chemical synthesis. (Safe Work Australia, 2019; ACGIH®, 2006).

Isopropyl alcohol has an odour resembling a mixture of ethanol and acetone, with an odour threshold reported at 22ppm (ACGIH®, 2001; PubChem, 2021).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of isopropyl alcohol noted that the critical effects were narcotic effect at high concentrations (DFG MAK, 2018).

The DFG noted that the **MAK** value of 200ppm for isopropyl alcohol, **peak limitation Category II** with an excursion factor of 2, were based on a **LOAEC** of 2,500ppm for narcotic effects in rats and mice exposed for 2 years and was scaled to account for the lack of a **NOAEC**, interspecies variation, and increased respiratory rate (workers *cf*. resting animals). The MAK value was supported by the MAK of 500ppm for acetone, the main metabolite of isopropyl alcohol (DFG MAK, 2018).

The DFG noted that **"H"** and **"S"** notations were not warranted for isopropyl alcohol, based on available data (DFG MAK, 2013).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of isopropyl alcohol (2-propanol) noted that the critical effects were eye, nose and upper respiratory tract irritation (ACGIH®, 2006).

The ACGIH® review concluded that:

> "The **TLV** is set on the basis of avoidance of ocular and upper respiratory tract irritation. Few human studies have been completed and sample sizes were relatively small; available human studies have suggested a **LOAEL** of 400ppm resulting in mild irritation of the eyes, nose, and throat (Nelson *et al*., 1943) or subtle changes in postural sway (Sethre *et al*., 2000), although other authors have concluded that the irritation threshold is above 400ppm (Smeets *et al*., 2001; Smeets and Dalton, 2001). The lowest chronic NOAEL in rodents is 500ppm (Burleigh-Flayer *et al*., 1997). The lowest applicable subchronic LOAEL in rodents is 500ppm, based on obvious upper respiratory tract irritation, with a NOAEL of 100ppm (Burleigh-Flayer *et al*., 1994).
>
> "A **TLV-TWA** of 200ppm and a **STEL** of 400ppm are recommended for 2-propanol. The TLV-TWA recommendations should minimize the potential for objective narcotic effects, significant irritation of the eyes or upper respiratory tract, or systemic toxicity.
>
> "Although dermal absorption can occur, the rate of absorption is considered too low to warrant a skin notation." (ACGIH®, 2006). (references cited in ACGIH®, 2006).

The ACGIH® found there was insufficient data available to recommend **DSEN** or **RSEN** notations for isopropyl alcohol (ACGIH®, 2006).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 400ppm (983mg/m^3) and WES-STEL of 500ppm (1,230mg/m^3) for isopropyl alcohol, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for isopropyl alcohol that a WES-TWA of 200ppm (491mg/m^3) and a WES-STEL of 400ppm (983mg/m^3) are adopted, to protect against eye and upper respiratory tract irritation and acute nasal irritation, based on the DFG and ACGIH® recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Isopropyl-alcohol#section=Chemical-and-Physical-Properties
CAS Number	67-63-0
Conversion factors	1mg/m^3 = 0.4ppm (25°C; 101.3**kPa**) 1ppm = 2.46mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 2-Propanol www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/68524AA6-C3BC-45AA-A946-C16CC5D241DB Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"2-Propanol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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ISOPROPYL ETHER

CAS NO: 108-20-3

Summary

Workplace Exposure Standards for isopropyl ether (CAS: 108-20-3)

	CURRENT	PROPOSED
WES-TWA	250**ppm** (1,040**mg/m³**)	250ppm (1,040mg/m³)
WES-STEL	310ppm (1,300mg/m³)	310ppm (1,300mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for isopropyl ether

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA for isopropyl ether of 250ppm (1,040mg/m³), and
2. maintain the WES-STEL for isopropyl ether of 310ppm (1,300mg/m³).

To protect for mucous membrane and eye irritation, and CNS effects.

Discussion

Isopropyl ether is used as a solvent for oils, waxes, resins, dyes, paints, and varnish removers (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Isopropyl ether has a sharp, sweet, ether-like odour, with an odour threshold reported at 0.07mg/m³ (PubChem, 2021; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of isopropyl ether (diisopropyl ether) noted that the critical effects were mucous membrane irritation and central nervous depression in humans (DFG MAK, 2005).

The DFG noted that the **MAK** value of 200ppm, **peak limitation Category I** with an excursion factor of 2, were based on complaints of an unpleasant odour after short-term exposures to 300ppm, and a NOEL of 480ppm from a 90-day inhalation study in rats with systemic toxicity reported at 3,300ppm (DFG MAK, 2005).

The DFG noted that an **"H"** notation was not warranted for isopropyl ether, based on results from acute dermal toxicity studies (DFG MAK, 2005).

No data was available to evaluate **"Sa"** or **"Sh"** notations (DFG MAK, 2005).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of isopropyl ether noted that the critical effects were mucous membrane and eye irritation (ACGIH®, 2001).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 250ppm (1,040mg/m³) and a **TLV-STEL** of 310ppm (1,300mg/m³) are recommended for occupational exposure to isopropyl ether. Toxicity data are extremely limited. The most significant response from exposure of human volunteers at concentrations above 300ppm were sensory in the form of unpleasant odor and irritation of the eyes and mucous membranes of the nose." (ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **Skin**, **DSEN**, **RSEN** or carcinogenicity notations for isopropyl ether (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 250ppm (1,040mg/m³) and WES-STEL of 310ppm (1,300mg/m³) for isopropyl ether, to be adequate to manage health risks from possible workplace exposure.

The toxicological database appeared limited, particularly relating to long-term exposures.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Diisopropyl-ether#section=Chemical-and-Physical-Properties
CAS Number	108-20-3
Conversion factors	1mg/m³ = 0.240ppm (25°C; 101.3**kPa**) 1ppm = 4.17mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Propane, 2,2'-oxybis www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/81CCEDEF-DD2D-4CDC-B060-B16AE4089B1D Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Isopropyl ether."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2005. *"Diisopropyl ether."* MAK Value Documentation, 2005; The MAK Collection for Occupational Health and Safety; pp 187-193. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10820e0021

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MAGNESIUM OXIDE

CAS NO: 1309-48-4

Summary

Workplace Exposure Standards for magnesium oxide (fume) (CAS: 1309-48-4)

	CURRENT	PROPOSED
WES-TWA	10**mg/m³**	1mg/m³ **(r)**
WES-STEL	–	5mg/m³ (r)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for magnesium oxide (fume)

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for magnesium oxide (fume) of 1mg/m³ for **respirable fraction**, and
2. adopt a WES-STEL for magnesium oxide (fume) of 5mg/m³ for respirable fraction.

To protect for the effects of biopersistent granular particles in the lungs.

Discussion

Magnesium oxide fume is produced when magnesium is burnt in high-temperature processes (**ACGIH**®, 2001). Magnesium oxide powder is used in ceramics, firebricks, pharmaceuticals, food additives, and in enteric acid-neutralising agents (**Safe Work Australia**, 2019; **DECOS**, 2004; ACGIH®, 2003).

Magnesium oxide is reported to be odourless (PubChem, 2021; ACGIH®, 2003).

Magnesium oxide is hydrated to magnesium hydroxide in physiological solutions (ACGIH®, 2003).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of magnesium oxide noted that the critical effects were due to the substance consisting of biopersistent granular particles (DFG MAK, 2018).

The DFG noted that the **MAK** value of 1mg/m³ for the respirable fraction of magnesium oxide [0.3mg/m³ x material density of 3.58kg/m³], **peak limitation Category II** with an excursion factor of 8, were confirmed by results from a controlled clinical study that found no adverse effects after exposure to 133mg/m³ fume for 45 minutes (DFG MAK, 2018). The particles in the fume were characterised as >98% with a diameter of <2.5µm (DFG MAK, 2018). Linear extrapolation from this experimental result to the MAK value indicated that no effects in the bronchoalveolar lavage (BAL) should be detected after exposure to the MAK value for 8 hours/day for 10 days. The DFG noted that the MAK value of 4mg/m³ for the inhalable fraction should be retained (DFG MAK, 2018).

In analogy with other biopersistent granular dusts, DFG noted that **"H"**, **"Sa"** or **"Sh"** notations were not warranted for magnesium oxide (DFG MAK, 2018).

DECOS

The Dutch Expert Committee on Occupational Standards Committee (DECOS) noted that the 8-hour TWA of 10mg/m^3 was suitable for an inert dust, and may be suitable for magnesium powder or dusts. However, DECOS noted that evidence suggested that magnesium oxide fume, particularly if freshly generated, was not inert and the TWA of 10mg/m^3 may be too high (DECOS, 2004).

The DECOS review noted:

> "In the hazard assessment, a difference should be made between magnesium oxide fumes and magnesium oxide powder or dusts. Fumes consist of freshly generated particles of magnesium oxide, formed at high temperatures, with smaller dimensions than powder or dusts. Hartmann *et al*. (Har83) reported diameters between 0.01 and 1.0**µm** for the fumes, which can be classified as respirable particles reaching the alveolar spaces of the lungs. Uptake takes place only by inhalation, with the respiratory system as the target organ.
>
> "Human case reports showed that exposure to magnesium oxide fumes, comparable to exposure to zinc oxide fumes, may induce symptoms consistent with metal fume fever, although no such symptoms were found in volunteers exposed to fume levels of ca. 145 and 230mg mg/m^3, for 45 and 15 minutes, respectively. However, the committee did not find valid data from studies on effects in man or experimental animals following repeated inhalation exposure or from studies on the potential carcinogenicity or reproduction toxicity.
>
> "Magnesium oxide was negative in an *in vitro* mutation assay in *S, typhimurium* strain TA102 and in a poorly reported *in vivo* chromosome aberration mouse bone marrow assay.
>
> "The committee considers the toxicological database on magnesium oxide fumes too poor to justify recommendation of a health-based occupational exposure limit." (reference cited in DECOS, 2004).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of magnesium oxide noted that the critical effects were mild eye and nose irritation, and metal fume fever at high concentrations of fresh substance (ACGIH®, 2003).

The ACGIH® review concluded that:

> "Magnesium oxide fume is reported to be a mild irritant of the eyes and nose. Volunteers exposed to high concentrations of fresh magnesium oxide can develop metal fume fever (Drinker *et al*., 1927). These observations have occurred at either very high concentrations (Drinker *et al*., 1927; Elkins, 1963; Kuschner *et al*., 1997) or at unspecified exposure levels (Stokinger, 1981; Hartmann *et al*., 1983). Kuschner and colleagues (1997) observed a no-observed-adverse-effect level of approximately 100mg/m^3 for human subjects exposed to magnesium oxide for less than 1 hour. To account for the uncertainties associated with this short-term study, a **TLV-TWA** of 10mg/m^3, inhalable particulate matter, is recommended for occupational exposure to magnesium oxide. Although there is experimental evidence suggesting a potential for carcinogenic properties, these studies were not performed rigorously, had confounding issues, and have not been replicated (Stenback *et al*., 1973, 1975; Heldaas *et al*., 1989). Therefore, a carcinogenicity notation of **A4**, **Not Classifiable as a Human Carcinogen**, is assigned." (references cited in ACGIH®, 2003).

The ACGIH® noted that there was insufficient data available to recommend **Skin** or **SEN** notations, or a TLV-STEL for magnesium oxide (ACGIH®, 2003).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, DECOS and ACGIH® reviews, WorkSafe considers its current WES-TWA of 10mg/m^3 for magnesium oxide (fume), to be inadequate to manage health risks from possible workplace exposure.

It is recommended for magnesium oxide (fume) a WES-TWA of 1mg/m^3 and a WES-STEL of 3mg/m^3 is adopted for respirable fraction, to protect against the effects of biopersistent granular particles in the lungs, based on the DFG recommendation. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Magnesium-oxide#section=Chemical-and-Physical-Properties
CAS Number	1309-48-4
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Magnesium oxide, >26% in a non hazardous diluent www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/588A0667-0C46-4463-A66A-3B2E1C152052

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Magnesium oxide."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Dutch Expert Committee on Occupational Safety (DECOS), 2004. *"Magnesium oxide (fume)(CAS No: 1309-48-4): Health-based Reassessment of Administrative Occupational Exposure Limits."* No. 2000/15OSH/123, The Hague. www.healthcouncil.nl/binaries/healthcouncil/documenten/advisory-reports/2004/06/08/magnesium-oxide-fume/advisory-report-health-based-reassessment-of-administrative-occupational-exposure-limits-magnesium-oxide-fume.pdf

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METHYL ACETATE

CAS NO: 79-20-9

Summary

Workplace Exposure Standards for methyl acetate (CAS: 79-20-9)

	CURRENT	PROPOSED
WES-TWA	200**ppm** (606**mg/m³**)	100ppm (303mg/m³)
WES-STEL	250ppm (757mg/m³)	250ppm (757mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for methyl acetate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for methyl acetate of 100ppm (303mg/m³), and
2. maintain the WES-STEL for methyl acetate of 250ppm (757mg/m³).

To protect for respiratory tract irritation, headache, dizziness, nausea, and eye damage.

Discussion

Methyl acetate is used as a solvent, a paint remover; as an imitation fruit flavour; in the manufacture of perfume, colouring agents, lacquers, plastics and artificial leather; and, as a catalyst for the biodegradation of organic matter (**Safe Work Australia**, 2019; **ACGIH®**, 2013).

Methyl acetate has a fragrant, fruity odour, with an odour threshold of 610mg/m³ reported (PubChem, 2021; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of methyl acetate noted that the critical effects were local irritation of the olfactory epithelium of the rat (DFG MAK, 2016).

The DFG noted that the **MAK** value of 100ppm for methyl acetate, **peak limitation Category I** with an excursion factor of 4, were based on a **NOAEC** of 350ppm from a 28-day inhalation study in rats where degeneration and necrosis of the olfactory epithelium were reported at 2,000ppm. The DFG noted that methyl acetate and vinyl acetate have a common mode of action, cleavage of the ester group by carboxylesterases releasing acetic acid, and the severity of the toxicity is governed more by the enzyme activity than the concentration of the methyl or vinyl acetate. The level of carboxylesterases was stated to be similar in the olfactory epithelia of rats and humans, and the NOAEC was adjusted accordingly to give a workplace air **NAEC** of 63 to 84ppm (DFG MAK, 2016).

The DFG noted that there was no reason to assign an **"H"** notation to methyl acetate, based on a dermal **LD_{50}** greater than 5,000**mg/kg/bw**; and, the high volatility of methyl acetate that would limit any dermal exposure (DFG MAK, 2002).

The DFG also noted that there was no data available to assess **"Sh"** or **"Sa"** notations for methyl acetate (DFG MAK, 2002).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of methyl acetate noted that the critical effects were headache, dizziness, nausea, and eye damage (ACGIH®, 2013).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 200ppm (606mg/m³) and a **TLV-STEL** of 250ppm (757mg/m³) are recommended for occupational exposure to methyl acetate. This is based on the TLV for its metabolite, methanol. Methyl acetate is rapidly and proportionally metabolized to methanol in the body.
>
> "Methanol causes sensory irritation, headaches, nausea and visual disturbances, as well as optic neuropathy, metabolic acidosis, narcosis, and respiratory depression at high exposure levels (1,000 to 10,000ppm from chronic studies) (U.S. NIOSH, 1997; Gosselin *et al*., 1984; McNally, 1937; Browning, 1965; Henson, 1960).
>
> "These values should protect against the upper respiratory tract irritation observed in animals where the authors identified a no-observed-adverse-effect level (NOAEL) of 350ppm (1,057mg/m³) (Hofmann, 1999) and in exposed workers (Schmid, 1956)." (references cited in ACGIH®, 2013).

The ACGIH® found there was insufficient data available to recommend **Skin**, **DSEN** or **RSEN** notations, or a carcinogenicity designation for methyl acetate (ACGIH®, 2013).

Conclusions

Based on the documentation cited and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 200ppm (606mg/m³) and WES-STEL of 250ppm (757mg/m³) for methyl acetate, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for methyl acetate that a WES-TWA of 100ppm (303mg/m³) is adopted, and a WES-STEL of 250ppm (757mg/m³) is maintained, to protect against respiratory tract irritation, headache, dizziness, nausea, and eye damage, resulting from metabolic products acetic acid and methanol, based on DFG and ACGIH® recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/methyl-acetate#section=Chemical-and-Physical-Properties
CAS Number	79-20-9
Conversion factors	1mg/m³ = 0.33ppm (25°C; 101.3**kPa**) 1ppm = 3.03mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Acetic acid, methyl ester www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/253726DA-40E4-446E-B180-C8CEFB7E04F1 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methyl acetate."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Deutsche Forschungsgemeinschaft (DFG), 2016. *"Methyl acetate."* MAK Value Documentation, 2016; The MAK Collection for Occupational Health and Safety; pp 1918-1922. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb7920e6018

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Safe Work Australia (2019). Safe Work Australia Draft Evaluation Report and Recommendations – *Methyl acetate*. https://engage.swa.gov.au/52961/widgets/275459/documents/128686

METHYL AMYL ALCOHOL

CAS NO: 108-11-2

Summary

Workplace Exposure Standards for methyl amyl alcohol (CAS: 108-11-2)

	CURRENT	PROPOSED
WES-TWA	25**ppm** (104**mg/m³**)	20ppm (85mg/m³)
WES-STEL	40ppm (167mg/m³)	40ppm (167mg/m³)
WES-Ceiling	–	–
Notations	***skin***	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for methyl amyl alcohol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for methyl amyl alcohol of 20ppm (85mg/m³)
2. maintain the WES-STEL for methyl amyl alcohol of 40ppm (167mg/m³), and
3. remove the *skin* notation for methyl amyl alcohol.

To protect for CNS effects, and eye and mucous membrane irritation.

Discussion

Methyl amyl alcohol is used in the production of oil additives; as a flotation agent; a component of surface coatings; and, as a solvent (**Safe Work Australia**, 2019; **ACGIH®**, 2020).

Methyl amyl alcohol has a mild alcohol odour, with an odour threshold reported at 0.07ppm (PubChem, 2021; ACGIH®, 2020).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of methyl amyl alcohol (methyl isobutyl carbinol) noted that the critical effects were central nervous system effects, and upper respiratory tract and eye irritation (ACGIH®, 2020).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 20ppm is recommended to minimize the potential for central nervous system (**CNS**) symptoms. The primary metabolite of methyl isobutyl carbinol (**MIBC**) is methyl isobutyl ketone (**MIBK**) that, in a study of human volunteers exposed to 48ppm MIBK for 90 to 120 minutes, produced reports of a variety of CNS symptoms on a 17-item questionnaire (Wigaeus-Hjem *et al*., 1990; Iregren *et al*., 1993). Metabolism data in animals demonstrate that at least 73% of administered MIBC is rapidly converted to MIBK (Guillaumat, 2002; Gingell *et al*., 2003); therefore, the MIBK TLV-TWA that is protective for MIBK neurological symptoms is recommended for MIBC. The TLV-TWA is substantially below 886ppm, the concentration of MIBC that produced increases in ketone bodies, kidney weight differences and blood chemistry values in subchronically exposed animals (Shell, 1982; OECD, 2005). Human evidence of systemic toxicity from MIBK exposure has been observed at lower concentrations of MIBK than humans or animal effects reported for MIBC.

Thus, the MIBK data should be a protective basis for the MIBC TLV-TWA. A **TLV-STEL** of 40ppm is recommended to protect against eye and mucous membrane irritation observed in humans that received short-term exposures to MIBC (Silverman *et al*., 1946).

"No animal cancer data are available for MIBC or human cancer data available for MIBC or MIBK. MIBK has been assigned the **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, notation; however, the MIBK exposure concentrations that produced animal tumors (U.S. NTP, 2006) would require concentrations of MIBC that are known to produce significant signs of central nervous system depression (anesthesia) and deaths in animals (Smyth *et al*., 1951; Shell, 1981) and are therefore not appropriate to attribute to MIBC. Thus a cancer notation for MIBC is not recommended." (references cited in ACGIH®, 2020).

A **Skin** notation was not warranted for methyl amyl alcohol, based on existing data indicating that dermal absorption was not a significant route for systemic toxicity. A **DSEN** notation was not warranted for methyl amyl alcohol, based on a negative guinea pig maximisation study (ACGIH®, 2020).

The ACGIH® noted that there was insufficient data to recommend a **RSEN** notation for methyl amyl alcohol (ACGIH®, 2020).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of methyl amyl alcohol (4-methylpentan-2-ol) noted that the critical effects were mucous membrane irritation in humans (DFG MAK, 2002).

The DFG noted that the **MAK** value of 20ppm, **peak limitation Category I** with an excursion factor of 1, were based on studies of irritative effects on the mucous membranes of test subjects, who reported eye irritation at 50ppm for 15 minutes, but reported that 25ppm was tolerable for 8-hour exposures by most individuals (DFG MAK, 2002).

The DFG noted that an **"H"** notation was not warranted for methyl amyl alcohol, as dermal exposure would be unlikely to contribute significantly to systemic toxicity (DFG MAK, 2002).

No data was available to evaluate **"Sa"** or **"Sh"** notations (DFG MAK, 2002).

[Note: in the DFG re-evaluation of ethyl amyl ketone (5-methylheptan-3-on) (2001), cross-reference was made to: ethyl butyl ketone (CAS: 106-35-4); methyl isoamyl ketone (CAS: 110-12-3); and, methyl amyl alcohol (CAS: 108-11-2).

See WorkSafe draft WES Reviews for:

- ethyl butyl ketone (CAS: 106-35-4), 2021: WES-TWA of 10ppm (47mg/m^3) and a WES-STEL of 20ppm (93mg/m^3)
- methyl isoamyl ketone (CAS: 110-12-3), 2021: WES-TWA of 20ppm (93mg/m^3) and a WES-STEL of 50ppm (233mg/m^3), and
- ethyl amyl ketone (CAS: 541-85-5), 2022: WES-TWA of 10ppm (53mg/m^3) and a WES-STEL of 20ppm (107mg/m^3)].

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 25ppm (104mg/m^3) with a *skin* notation for methyl amyl alcohol, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for methyl amyl alcohol that a WES-TWA of 20ppm (85mg/m^3) is adopted and a WES-STEL of 40ppm (167mg/m^3) is maintained to protect against CNS effects, and eye and mucous membrane irritation, based on the ACGIH® recommendations. The *skin* notation can be removed for methyl amyl alcohol, as evidence indicates that the dermal route is unlikely to be a significant contributor to systemic toxicity.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/4-methyl-2-pentanol#section=Chemical-and-Physical-Properties
CAS Number	108-11-2
Conversion factors	1mg/m^3 = 0.24ppm (25°C; 101.3**kPa**) 1ppm = 4.17mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 2-Pentanol, 4-methyl- www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/066910A9-C102-4433-AE7C-EAEAAB32DE34 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methyl isobutyl carbinol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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METHYL FORMATE

CAS NO: 107-31-3

Summary

Workplace Exposure Standards for methyl formate (CAS: 107-31-3)

	CURRENT	PROPOSED
WES-TWA	100**ppm** (246**mg/m³**)	50ppm (123mg/m³)
WES-STEL	150ppm (368mg/m³)	100ppm (245mg/m³)
WES-Ceiling	–	–
Notations	–	***skin***

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for methyl formate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for methyl formate of 50ppm (123mg/m³)
2. adopt a WES-STEL for methyl formate of 100ppm (245mg/m³), and
3. adopt a *skin* notation for methyl formate.

To protect for upper respiratory tract irritation, CNS effects and eye damage.

Discussion

Methyl formate is used as a fumigant and larvicide; solvent; blowing agent; refrigeration solvent; and, in organic chemistry syntheses (**Safe Work Australia**, 2019; **ACGIH®**, 2015).

Methyl formate has an ethereal odour, with a wide range of odour thresholds reported from 500 to 5,000mg/m³ and olfactory fatigue at 1,500ppm (PubChem, 2021; ACGIH®, 2015; **SCOEL**, 2004).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of methyl formate noted that the critical effects were upper respiratory tract irritation, central nervous system effects and eye damage due to the formation of formic acid (ACGIH®, 2015).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 50ppm (123mg/m³) and a **TLV-STEL** of 100ppm (245mg/m³) are recommended for occupational exposure to methyl formate to protect workers from upper respiratory tract irritation, central nervous system effects and eye damage (through the formation of the metabolite formic acid).
>
> "End of shift fatigue was increased as reported by subjects exposed to 100ppm in chamber studies when compared to controls not exposed (Sethre *et al*., 2000a). At a lower mean exposure of 36ppm, detrimental neurobehavioral effects were not apparent in a study of foundry workers (Sethre *et al*., 2000b). Methyl formate is quickly broken down to methanol and formic acid. Based on a toxicokinetic model, an exposure of no higher than 50ppm will limit the formation of the metabolite formic acid to a level equivalent to that caused by a methanol exposure at the TLV (**TWA_{8hr}** of

200ppm) (Nihlen and Droz, 2000). Formic acid is believed to cause optic neuropathy in methanol intoxication. An incident involving a mixture containing 30% methyl formate resulted in temporary blindness (Duquenois and Revel, 1935).

"A TLV-STEL of 100ppm (245mg/m3) is recommended to prevent predicted sensory irritation as seen in mice ($\mathbf{RD_0}$ of 184ppm and $\mathbf{RD_{50}}$ of 1,109ppm) (Larsen and Nielsen, 2012) and nasal irritation in guinea pigs exposed to 1,500ppm for 5 minutes (Schrenk *et al*., 1936).

"A **Skin** notation is warranted due to the ability of methyl formate to be absorbed through skin, resulting in toxic effects as noted in a case report of a 19-month-old child (Gettler, 1940) and a rat dermal study (BASF AG, 1979)." (references cited in ACGIH®, 2015).

The ACGIH® noted that there was insufficient data to recommend **DSEN**, **RSEN** or Carcinogenicity notations for methyl formate (ACGIH®, 2015).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of methyl formate (formic acid methyl ester) noted that the critical effects were neuropsychological effects in human volunteers (DFG MAK, 2013).

The DFG noted that the **MAK** value of 50ppm, **peak limitation Category II** with an excursion factor of 4, were based on studies of neuropsychological effects (subjective tiredness and neuropsychological tests) in small groups of human volunteers. The three workers with the highest exposures (maximum concentration of 136ppm methyl formate and 73ppm isopropanol) were reported not to have performed as well in 3 of 15 psychological behaviour tests as the three workers with the lowest exposures (median concentrations for the 21 workers were 68ppm methyl formate and 28ppm isopropanol). This experimental data supported the previous provisional MAK value of 50ppm that was based on analogy to methanol with a MAK value of 100ppm, noting that methyl formate forms twice as much formic acid as methanol (DFG MAK, 2013). [See WorkSafe WES draft review for methanol, 2021].

The DFG noted that an **"H"** notation was warranted for methyl formate, as dermal exposure could potentially significantly contribute to systemic toxicity (DFG MAK, 2013).

No data was available to evaluate **"Sa"** or **"Sh"** notations (DFG MAK, 2013).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of methyl formate recommended an 8-hour TWA of 50ppm (120mg/m^3) and a 15-minute STEL of 100ppm (240mg/m^3), based on minimal subjective effects in volunteers exposed to 100ppm methyl formate for 8 hours and no effects in workers exposed to 36ppm methyl formate and 44ppm isopropanol. The TWA for methyl formate was supported by analogy to methanol, TWA of 200ppm, and toxicokinetic modelling (SCOEL, 2004).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SCOEL reviews, WorkSafe considers its current WES-TWA of 100ppm (246mg/m^3) and WES-STEL of 150ppm (368mg/m^3) for methyl formate, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for methyl formate that a WES-TWA of 50ppm (123mg/m^3) and a WES-STEL of 100ppm (245mg/m^3) with a skin notation are adopted to protect against upper respiratory tract irritation, CNS effects and eye damage, based on the ACGIH® recommendation.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Methyl-formate#section=Chemical-and-Physical-Properties
CAS Number	107-31-3
Conversion factors	1mg/m^3 = 0.408ppm (25°C; 101.3**kPa**) 1ppm = 2.55mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Formic acid, methyl ester www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/5AED690D-8467-4030-8BF4-8B7B2BEE0287 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methyl formate."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2013. *"Formic acid methyl ester."* MAK Value Documentation, 2013; The MAK Collection for Occupational Health and Safety; pp 1-11. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10731e3613

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Scientific Committee on Occupational Exposure Limits (SCOEL), 2004. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for methyl formate."* SCOEL/SUM/59

METHYL METHACRYLATE

CAS NO: 80-62-6

Summary

Workplace Exposure Standards for methyl methacrylate (CAS: 80-62-6)

	CURRENT	PROPOSED
WES-TWA	50**ppm** (208**mg/m³**)	50ppm (208mg/m³)
WES-STEL	100ppm (416mg/m³)	100ppm (416mg/m³)
WES-Ceiling	-	-
Notations	***skin***, ***dsen***	*dsen*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for methyl methacrylate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA for methyl methacrylate of 50ppm (208mg/m³)
2. maintain the WES-STEL for methyl methacrylate of 100ppm (416mg/m³), and
3. remove the *skin* notation for methyl methacrylate.

To protect for nasal irritation.

Discussion

Methyl methacrylate is used as polymers or copolymers in the manufacture of acrylic sheet, moulding, clear plastics, extrusion powder, surface and paper coatings, latex paint, adhesive cements, dental restorations and surgical implants, and concrete impregnation (**Safe Work Australia**, 2019; **ACGIH®**, 2015).

Methyl methacrylate has a distinctive, fruity, pungent odour, with odour thresholds of 0.05ppm to 0.34ppm reported (PubChem, 2021; ACGIH®, 2015).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of methyl methacrylate noted that the critical effects were upper respiratory tract and eye irritation, and pulmonary oedema (ACGIH®, 2015).

The ACGIH® review concluded that:

> "**MMA** is an ocular and upper respiratory tract irritant, and it is a skin sensitizer and a suspected respiratory sensitizer. In view of the lack of oncogenic response in animals (Stringer (Ed.), 1995; US NTP, 1986; Chan *et al*., 1988) and the limited epidemiological investigations published to date among workers chronically exposed to airborne MMA, the **A4**, **Not Classifiable as a Human Carcinogen**, notation is appropriate. Adverse effects on olfactory epithelium (rodent **NOEL** 25ppm (Stringer (Ed.), 1995)) and human olfactory ability (Schwartz *et al*., 1989) are recognized. While there are no controlled inhalation trials in volunteers and the mouse **RD_{50}** results (Stadler, 1993) are such that ACGIH cannot define rigorously the airborne MMA concentrations associated with irritation, published reports indicate a concentration-related increase in complaints. Therefore, based on the rat inhalation subchronic **LOAEL** (116ppm (Tansy *et al*., 1980a; 1980b)), the rat chronic **NOAEL** (25ppm (Stringer (Ed.), 1995; Chan *et al*., 1988), the reports of impaired human olfactory function (Schwartz *et al*., 1989), and human

pulmonary deficits after repeated exposures at concentrations greater than 50ppm (Mizunuma *et al*., 1993; Karpov, 1954; US NIOSH, 1997; Marez *et al*., 1993; Jedrychowski, 1982; Schwartz *et al*., 1989), a **TLV-TWA**of 50ppm is recommended. A **TLV-STEL** of 100ppm takes into account the rapid elimination kinetics of this material from the body (Svartling *et al*., 1986) and is intended to reduce complaints of objectionable ocular and upper respiratory tract irritation reported after exposures in excess of 100ppm (Cromer & Kronoveter, 1976; Colman, 1963; Mizunuma *et al*., 1993). Available data on sensitization from exposure to MMA warrant the addition of a **DSEN** notation. MMA is assigned a DSEN sensitizer notation based on human allergic dermatitis, erythema, and edema associated with cutaneous exposure. The evidence that airborne MMA can act as a respiratory sensitizer is not overwhelming, but it does appear to have caused delayed asthmatic responses in at least some subjects, suggesting a mechanism involving a host response in addition to simple direct irritancy caused by the agent itself (Savonius *et al*., 1993; Pickering *et al*., 1986; Wittczak *et al*., 1996)." (references cited in ACGIH®, 2015).

The ACGIH® noted that there was insufficient data available to recommend a **Skin** notation for methyl methacrylate (ACGIH®, 2015).

The ACGIH® also noted that *the recommended TLV may not necessarily protect susceptible workers from possible sensitization or an allergic reaction in previously sensitized individuals; accordingly, exposures should be kept as low as possible below the recommended TLV* (ACGIH®, 2015).

DECOS

The Dutch Expert Committee on Occupational Standards Committee (**DECOS**) proposed an 8-hour **TWA** health-based recommended occupational exposure limit (**HBROEL**) for methyl methacrylate of 160mg/m^3 (38ppm). The HBROEL was based on a $BMDL_{10}$ of 482mg/m^3 (116ppm) for irritation of nasal epithelium in rats with an uncertainty factor of 3 to account for inter-individual differences. The DECOS considered the susceptibility for nasal irritation to be similar between rodents and humans (DECOS, 2011). The DECOS noted several epidemiological studies that indicated slight nasal irritation in workers at exposure levels below 100mg/m^3 (24ppm), but the data was not robust enough for an HBROEL (DECOS, 2011).

The DECOS also noted that there was inadequate data to set a limit on peak exposures for methyl methacrylate; and that a *skin* notation was not warranted, based on calculations that dermal absorption would not contribute significantly to total body burden (DECOS, 2011).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of methyl methacrylate noted that the critical effects were nasal irritation (DFG MAK, 2010).

The DFG noted that the **MAK** value of 50ppm for methyl methacrylate, **peak limitation Category I** with an excursion factor of 2, were based on studies of workers reporting no rhinologically detectable irritant effects or impairment of the sense of smell after an average 8.8 years of employment with 8-hour mean exposure values for methyl methacrylate of up to 40ppm; while sensory irritation was reported after short-term exposure peaks of 100ppm or more (DFG MAK, 2010).

The DFG concluded that an **"H"** notation was not warranted for methyl methacrylate, based on data indicating that dermal absorption would not contribute significantly to systemic toxicity (DFG MAK, 2010).

The DFG also noted that the **"Sh"** notation should be maintained for methyl methacrylate, based on human and animal data, but there was insufficient data to justify a **"Sa"** notation (DFG MAK, 2010).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of methyl methacrylate noted that the critical effects were focal lesions of the olfactory region of the nasal epithelium reported in rodents (SCOEL, 2006).

The SCOEL review summarised:

> "A reliable NOAEL of 25ppm has been established in a 2-year inhalation study in rats, with slight effects on the nasal olfactory epithelium being evident at the next higher dose of 100ppm. Extensive PBPK modelling work has predicted that on kinetic grounds, for a given level of exposure to MMA, human nasal olfactory epithelium will be at least 3 times less sensitive than that of rats to the toxicity of MMA.
>
> "Studies of workforces have provided reassuring evidence that workers exposed to MMA levels of up to approximately 50ppm (8-hr TWA) have not suffered any respiratory ill-health consequences related to their long-term exposure; the occasional respiratory symptoms reported seem to be clearly connected with short-term peak exposures and the sensory irritant potential of MMA which starts to be expressed at concentrations somewhere in excess of 100ppm. The few reports in the literature of asthmatic reactions arising from MMA exposure also seem most likely to be (in the majority of cases at least) as a consequence of this sensory irritancy.
>
> "Overall, SCOEL recommends an occupational exposure limit of 50ppm (8h TWA) as being the highest level of exposure at which one can be confident of avoiding any ill-health consequences.
>
> "Control of short-term peak exposures is also needed, in view of the sensory irritancy of MMA. There are no data to clearly indicate the threshold concentration above which such irritancy begins to be expressed in humans. However, irritant concentrations clearly lie above 100ppm. Hence a STEL of 100ppm is recommended.
>
> "A "Sk" notation is not appropriate; absorption through the skin is relatively low and there is no concern for systemic toxicity arising as a consequence. Although a skin sensitiser, there is no convincing evidence that methyl methacrylate is a significant inducer of asthma in humans and therefore the "Sen" notation is not appropriate. There are no grounds for recommending a biological monitoring limit value for methyl methacrylate." (SCOEL, 2006).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DECOS, DFG and SCOEL reviews, WorkSafe considers its current WES-TWA of 50ppm (208mg/m^3) and WES-STEL of 100ppm (416mg/m^3) with a *skin* and *dsen* notation for methyl methacrylate, to be adequate to manage health risks from possible workplace exposure.

It is recommended for methyl methacrylate that a WES-TWA of 50ppm (208mg/m^3) and WES-STEL of 100ppm (416mg/m^3) with dsen notation are maintained, to protect against nasal irritation, based on the ACGIH®, DFG and SCOEL recommendations. The skin notation can be removed, based on the ACGIH®, DECOS, DFG and SCOEL recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Methyl-methacrylate#section=Chemical-and-Physical-Properties
CAS Number	80-62-6
Conversion factors	1mg/m³ = 0.24ppm (25°C; 101.3**kPa**) 1ppm = 4.1mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: 2-Propenoic acid, 2-methyl-, methyl ester www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/E3C4B0F7-2028-49B0-87EA-22A00CD57C94 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methyl methacrylate."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2010. *"Methyl methacrylate."* MAK Value Documentation, 2010; The MAK Collection for Occupational Health and Safety; pp 229-256. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb8062e0026

Dutch Expert Committee on Occupational Safety (DECOS), 2011. *"Methyl methacrylate: Health-based recommended occupational exposure limit."* No. 2011/38, The Hague. www.healthcouncil.nl/documents/advisory-reports/2011/12/16/methyl-methacrylate-health-based-recommended-occupational-exposure-limit

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Scientific Committee on Occupational Exposure Limits (SCOEL), 2006. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for methyl methacrylate."* SCOEL/SUM/126

METHYLCYCLOHEXANE

CAS NO: 108-87-2

Summary

Workplace Exposure Standards for methylcyclohexane (CAS: 108-87-2)

	CURRENT	PROPOSED
WES-TWA	400**ppm** (1,610**mg/m³**)	50ppm (200mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for methylcyclohexane

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for methylcyclohexane of 50ppm (200mg/m³).

To protect for kidney effects.

Discussion

Methylcyclohexane is used in organic synthesis; as a solvent for cellulose ethers; and, as a component of jet fuel (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Methylcyclohexane has a faint benzene-like odour, with odour thresholds reported at 480 and 630ppm (PubChem, 2021; **DECOS**, 2005; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of methylcyclohexane (methylcyclohexan) noted that the critical effects were kidney toxicity reported in male rats (DFG MAK, 2000; DFG MAK, 2007).

The DFG noted that the MAK value of 200ppm, **peak limitation Category II** with an excursion factor of 2, were based on a **NOEL** of 400ppm from a 1-year inhalation study (with a 1-year follow-up) in rats with kidney toxicity reported in males at 2,000ppm (DFG MAK, 2000). The DFG 2007 review noted that the kidney toxicity was probably α2u-globulin-mediated, and thus species- and sex-specific and not relevant for humans, but the available evidence was not adequate to confirm the α2u-globulin mechanism (DFG MAK, 2007).

The DFG noted that there was no data available to evaluate **"H"**, **"Sa"** or **"Sh"** notations (DFG MAK, 2000).

DECOS

The Dutch Expert Committee on Occupational Standards Committee (**DECOS**) proposed an 8-hour **TWA** health-based recommended occupational exposure limit (**HBROEL**) for methylcyclohexane of 200mg/m³ (48ppm). The HBROEL was based on a **NOAEL** of 1,636mg/m³ (400ppm) for kidney effects in rats and body weight effects in rats and hamsters, as no suitable human studies were available, and modified by uncertainty factors to account for intra-species variation and confidence in the database (DECOS, 2005).

The DECOS noted that no data was available on the irritation and sensitisation properties of methylcyclohexane in humans, and was only slightly irritating to the skin and eyes of rabbits (DECOS, 2005).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of methylcyclohexane noted that the potential critical effects were irritation; narcosis; and, liver, kidney or vascular injury as reported in animals (ACGIH®, 2001).

The ACGIH® review concluded that:

> "At high concentrations, methylcyclohexane caused narcosis in animals. No systemic poisonings have been reported in humans; however, vascular, renal, and hepatic degeneration have been reported after high repeated inhalation exposures in animals (Gosselin *et al*., 1984). Prolonged exposure at 370ppm failed to cause any adverse health effects in monkeys (Treon *et al*., 1943). Accordingly, a **TLV-TWA** for methylcyclohexane of 400ppm is recommended, based on analogy with the comparable acute toxicity of heptane." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **Skin**, **DSEN**, **RSEN** or carcinogenicity notations for methylcyclohexane (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, DECOS and ACGIH® reviews, WorkSafe considers its current WES-TWA of 400ppm (1,610mg/m^3) for methylcyclohexane, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for methylcyclohexane that a WES-TWA of 50ppm (200mg/m^3) is adopted to protect against kidney effects, based on the DECOS recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/methylcyclohexane#section=Chemical-and-Physical-Properties
CAS Number	108-87-2
Conversion factors	1mg/m^3 = 0.250ppm (25°C; 101.3**kPa**) 1ppm = 4.01mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Cyclohexane, methyl- www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/C3F766BF-ECC0-4346-80BA-81ECEA8D9228 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Methylcyclohexane."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2000. *"Methylcyclohexan."* MAK Value Documentation in German language, 2000; The MAK Collection for Occupational Health and Safety; pp 1-6. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb10887d0030

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MORPHOLINE

CAS NO: 110-91-8

Summary

Workplace Exposure Standards for morpholine (CAS: 110-91-8)

	CURRENT	PROPOSED
WES-TWA	20**ppm** (71**mg/m³**)	10ppm (36mg/m³)
WES-STEL	–	20ppm (71mg/m³)
WES-Ceiling	–	–
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for morpholine

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for morpholine of 10ppm (36mg/m³)
2. adopt a WES-STEL for morpholine of 20ppm (71mg/m³), and
3. maintain the *skin* notation for morpholine.

To protect for nose and eye irritation.

Discussion

Morpholine is used as a chemical intermediate in the rubber industry; in corrosion control; in the synthesis of a large number of drugs, crop protection agents, dyes and optical brighteners; and, as a solvent in a wide number of organic materials, including resins, dyes and waxes (**Safe Work Australia**, 2019; **SCOEL**, 1999).

Morpholine has an ammonia-like, or fish-like odour, with a reported odour threshold of 0.01ppm (PubChem, 2021).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (**ACGIH®**) review of morpholine noted that the critical effects were eye, skin and upper respiratory tract irritation, and transient corneal oedema reported from exposed workers (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Morpholine vapor is an irritant of eyes, nose, and throat (Shea, 1939; API, 1948; Conaway *et al*., 1984; Haworth *et al*., 1983). It has caused eye, skin, and mucous membrane irritation in rats exposed repeatedly at 25ppm (Harbison *et al*., 1989). Accordingly, a **TLV-TWA** of 20ppm is recommended to minimize the potential for irritation and toxicity in the upper respiratory tract and eye. A **Skin** notation is assigned based on a report of human dermal penetration (Jefferson Chemical Co., 1961) and a dermal **LD_{50}** for 24-hour skin contact of 0.5ml/kg in rats (Smyth *et al*., 1954). Based on the negative findings from the long-term inhalation study, where male and female rats were exposed 6 hours/day, 5 days/week for 104 weeks at 10, 50, or 150ppm (Harbison *et al*., 1989), a carcinogenicity notation of **A4**, **Not Classifiable as a Human Carcinogen**, is assigned to morpholine." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **RSEN** or **DSEN** notations, or **TLV-STEL** for morpholine (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of morpholine (morpholin) noted that the critical effects were eye, skin and upper respiratory tract irritation (DFG MAK, 2000).

The DFG noted that the **MAK** value of 10ppm, **peak limitation Category I** with an excursion factor of 2, were based on a **NOEL** of 25ppm from a 13-week inhalation study in rats, and a NOEL of 10ppm from a 2-year study in the same strain with necrosis of the nasal turbinates reported at 50ppm (DFG MAK, 2000).

The DFG noted the corrosive effect of morpholine, so an **"H"** notation was not warranted (DFG MAK, 1996).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of morpholine noted that the critical effects were irritation and corrosion due the basicity of morpholine (SCOEL, 1999).

The SCOEL review concluded that:

> "2-year study of Harbison *et al*. (1989) and its 13-week dose-finding study (Conaway *et al*., 1984) were considered to be the best available bases for setting occupational exposure limits for morpholine. Overall assessment of these studies indicates a NOAEL of 36mg/m³ morpholine. The **NOAEL** is based on an extensive long-term exposure inhalation study in rats. The SCOEL considers the use of an uncertainty factor of 1 justifiable because of the low incidence of histopathological nasal changes seen at 181mg/m³ in the long-term study and at 360mg/m³ in the 13-week study, and the absence of histopathological nasal changes and the very mild nature of the effects (occasional rapid breathing) at 90mg/m³ in the 13-week study. Although the negative results obtained in *in vivo* mutagenicity and carcinogenicity studies indicate that these endpoints are not of concern for exposure to morpholine, the possibility of nitrosation, forming N-nitrosomorpholine, cannot be excluded from the information available. The recommended 8-hour **TWA** for morpholine is 36mg/m³ (10ppm). A **STEL** (15 mins) of 72mg/m³ (20ppm) was proposed to limit peaks in exposure which could result in irritation.
>
> Observations on skin uptake are mostly due to the corrosive properties of morpholine, so no "skin" notation was considered necessary."
>
> "Because of the potential for nitrosation of morpholine to form nitrosamines under some workplace conditions, monitoring of ambient nitrous oxides is highly recommended." (reference cited in SCOEL, 1999).

NIOSH

National Institute for Occupational Safety and Health (**NIOSH**) Skin Notation Profile for cyclohexanone summarised:

> "No toxicokinetic data were identified to evaluate the potential of morpholine to be absorbed through the skin. However, data from an acute dermal toxicity study in rabbits [Smyth *et al*. 1954] and from a short-term dermal toxicity study in guinea pigs and rabbits [Shea 1939] are sufficient to indicate that morpholine has the potential to be absorbed through the skin, be systemically

available and toxic, and cause liver, kidney, and spleen effects following repeated exposure. Available studies in animals indicate that undiluted morpholine is corrosive to the skin [Shea 1939; Smyth 1954]. Results from a modified Buehler test suggest that morpholine is not likely to cause skin sensitization but can cross-react with structurally similar chemicals. Therefore, on the basis of these assessments, morpholine is assigned a composite skin notation of **SK: SYS-DIR (COR)**." (references cited in NIOSH, 2017).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SCOEL reviews, WorkSafe considers its current WES-TWA of 20ppm (71mg/m³) for morpholine, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for morpholine that a WES-TWA of 10ppm (36mg/m³) and a WES-STEL of 20ppm (71mg/m³) are adopted, to protect against nose and eye irritation, based on the DFG and SCOEL recommendations.

It is also recommended to maintain the *skin* notation as morpholine has the potential to be absorbed through the skin and to become available systemically following dermal exposure.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/morpholine#section=Chemical-and-Physical-Properties
CAS Number	110-91-8
Conversion factors	1mg/m³ = 0.281ppm (25°C; 101.3**kPa**) 1ppm = 3.56mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/E3D2089C-2B17-4F66-B6D3-AD8AA873BB6E Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Morpholine."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Scientific Committee on Occupational Exposure Limits (SCOEL), 1999. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for morpholine."* SCOEL/SUM/81

n-BUTYL ALCOHOL

CAS NO: 71-36-3

Summary

Workplace Exposure Standards for *n*-butyl alcohol (CAS: 71-36-3)

	CURRENT	PROPOSED
WES-TWA	–	20**ppm** (61**mg/m³**)
WES-STEL	–	–
WES-Ceiling	50ppm (150mg/m³)	–
Notations	***skin***	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for *n*-butyl alcohol

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for *n*-butyl alcohol of 20ppm (61mg/m³)
2. remove the WES-Ceiling for *n*-butyl alcohol, and
3. remove the *skin* notation for *n*-butyl alcohol.

To protect for eye irritation.

Discussion

n-Butyl alcohol is widely used as a solvent in a number of industries, and as a flavouring agent (**Safe Work Australia**, 2019; **ACGIH®**, 2002). *n*-Butyl alcohol is produced during the selective fermentation of carbohydrates and is a common product of mould metabolism (ACGIH®, 2002).

n-Butyl alcohol has a rancid, sweet, wine-like odour, with a threshold reported at 0.17ppm (PubChem, 2022; ACGIH®, 2002).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of *n*-butyl alcohol noted that the critical effect was eye irritation (DFG MAK, 2003).

The DFG noted that the **MAK** value of 100ppm for *n*-butyl alcohol, **peak limitation Category I** with an excursion factor of 1, were based on a workplace study that indicated eye irritation in workers at average concentrations around 200ppm, but not when reduced to 100ppm. The MAK value was supported by other human study results. A 90-day oral study in rats reported central nervous system depression at 250**mg/kg b.w./day**, but not at 125mg/kg b.w./day, estimated to be ten times the amount absorbed during an 8-hour shift exposed to 100ppm (DFG MAK, 2003).

An **"H"** notation was not assigned to *n*-butyl alcohol, as dermal absorption studies indicated that skin exposure would not significantly impact total body burden (DFG MAK, 2015). **"Sa"** and **"Sh"** notations were not assigned for *n*-butyl alcohol, based on reports of mainly negative reactions (DFG MAK, 2003).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of *n*-butyl alcohol noted that the critical effects were eye and upper respiratory tract irritation (ACGIH®, 2002).

The ACGIH® review concluded that:

> "The systemic toxicity of *n*-butanol is low, although it may potentiate the hepatic toxicity of other inhaled compounds, such as carbon tetrachloride (Cornish and Adefuin, 1967). *N*-Butanol, in the liquid or vapor phase, can cause skin, eye, and upper respiratory tract irritation in humans. Several early 1940s reports indicate that ocular irritation is the primary adverse effect consistently reported following occupational exposure to n-butanol. Thus, eye irritation is the endpoint upon which control of occupational exposure to *n*-butanol can most reliably be based.
>
> "Reports describing ocular irritant effects of n-butanol in humans were for the most part based on occupational and volunteer studies published in the 1940s. In the most comprehensive of these studies, Sterner *et al*. (1949) conducted a 10-year study in workers and reported "new or no complaints" of irritation among workers exposed at an average n-butanol breathing zone concentration of 100ppm, and further noted that even in those complainants short-run exposures likely exceeded 100ppm. However, blurred vision, lacrimation, photophobia, burning, moderate corneal edema and edematous conjunctiva were noted at average breathing zone concentrations of 200ppm. These early findings were consistent with recent controlled human studies of the ocular-specific effects of *n*-butanol that indicated 1 hour exposures at 990ppm, but not at 314ppm, resulted in conjunctival hyperemia (Hempel-Jorgensen *et al*., 1998). In several more limited and earlier studies of workers in raincoat manufacturing plants (Tabershaw *et al*., 1944; Cogan and Grant, 1945), eye irritation was reported in workers where *n*-butanol concentrations (area samples) ranged from 15 to 115ppm. Although in some reports the reported exposures were to *n*-butanol alone (Tabershaw *et al*., 1944), the nature of the manufacturing process indicated that short-term personal exposures likely exceeded the reported values. Nelson *et al*. (1943) conducted a blind, controlled chamber test with exposure-naïve human volunteers and found that exposure at 50ppm n-butanol caused ocular irritation. However, Sterner *et al*. (1949) observed that plant employees readily accepted *n*-butanol concentrations that were initially irritating and objectionable to the casual visitor or office worker. Given these reports, a **TLV-TWA** of 20ppm should be protective of *n*-butanol ocular irritancy. Importantly, a 20ppm TLV-TWA will prevent the possibility of attaining n-butanol exposures greater than 100ppm, the concentration at which the most reliable worker study (Sterner *et al*., 1949) suggested was the threshold for initiation of eye irritation.
>
> "Unacclimatized workers may perceive the odor of *n*-butanol to be irritating at levels below the TLV; however, this response diminishes with time. In addition, specialized human volunteer studies indicated that the lowest upper respiratory irritation threshold was 289 ppm, as compared to an estimated odor thresh-old (*sic*) of 0.17ppm (Wysocki and Dalton, 1996). The low respiratory tract irritation potential of n-butanol was affirmed in animal **RD_{50}** studies, in which a value of 1,286ppm was reported (de Ceaurriz *et al*., 1981).
>
> "Although n-butanol can enter the circulation after topical application (Anon, 1987), the absorbed dose is insignificant by percutaneous uptake through intact skin compared to that from other routes; therefore, no **Skin** notation is required." (references cited in ACGIH®, 2002).

The ACGIH® noted that there was insufficient data to assign **SEN** or carcinogenicity notations for *n*-butyl alcohol (ACGIH®, 2002).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-Ceiling of 50ppm (150mg/m³) for n-butyl alcohol to be inadequate to manage health risks from possible workplace exposure.

It is recommended for n-butyl alcohol that a WES-TWA of 20ppm (61mg/m³) is adopted, to protect against eye irritation, based on the ACGIH® recommendations. The *skin* notation can be removed, as available data indicates that dermal absorption is unlikely to add significantly to total body burden.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/1-butanol#section=Chemical-and-Physical-Properties
CAS Number	71-36-3
Conversion factors	1ppm = 3.03mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.33ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/E70DF4D8-1672-4F5D-ACB6-88AA9CB0D5F3

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"n-Butanol."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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NITRIC ACID

CAS NO: 7697-37-2

Summary

Workplace Exposure Standards for nitric acid (CAS: 7697-37-2)

	CURRENT	PROPOSED
WES-TWA	2**ppm** (5.2**mg/m³**)	2ppm (5.2mg/m³)
WES-STEL	4ppm (10mg/m³)	4ppm (10mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for nitric acid

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA for nitric acid of 2ppm (5.2mg/m³), and
2. maintain the WES-STEL for nitric acid of 4ppm (10mg/m³).

To protect for irritation, corrosion and lung function effects.

Discussion

Nitric acid is used to dissolve noble metals, for etching and cleaning metals, and to make nitrates (predominantly ammonium nitrate fertiliser) and nitro-compounds (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Nitric acid has a characteristic, sweet to acrid choking odour, with an odour threshold reported at 0.75mg/m³ (PubChem, 2022; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of nitric acid noted that the critical effects were on lung function, as a result of inflammation (DFG MAK, 2008).

The DFG noted that the provisional **MAK** value of 2ppm should be withdrawn due to the lack of robust data from either human experience [Sackner and Ford, 1981 cited] or animal studies (DFG MAK, 2008).

The DFG also noted that **"H"**, **"Sa"** or **"Sh"** notations could not be assessed due to lack of data for nitric acid (DFG MAK, 2008).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of nitric acid noted that the critical effects were irritation and corrosion (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Occupational exposure to nitric acid can cause corrosion of the skin, teeth, and other tissues. It is a potent irritant to the eyes and mucous membranes (NIOSH, 1997; McAdams & Krop, 1955; Ask, 1925; Fairhall, 1957; Desgranges, 1804; Darke & Warrack, 1958). Acute pulmonary edema or chronic obstructive lung disease may occur from inhalation of the vapors of nitric acid (Hall & Cooper, 1905; Treiger & Przypyszny, 1947). The irritation from nitric acid alone would be expected to be equal to that of other strong acids.
>
> "Accordingly, a **TLV-TWA** of 2ppm and the **TLV-STEL** of 4ppm are recommended for nitric acid. The TLV-TWA of 2ppm for nitric acid is intermediate between the TLV for hydrogen chloride (5ppm TLV-Ceiling) and that for sulfuric acid (1mg/m³ or 0.25ppm). The TLV-TWA and the TLV-STEL are considered sufficiently low to prevent ocular and upper respiratory tract irritation and should prevent dental corrosion. It is not clear whether the TLV-TWA and TLV-STEL values will prevent potentiation of the toxicity of inhaled nitrogen dioxide." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations for nitric acid (ACGIH®, 2001).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of nitric acid noted that the critical effects were irritation, corrosion and lung function effects (SCOEL, 2001).

The SCOEL review summarised:

> "There are no data from which to derive an 8-h **TWA** limit value.
>
> "The study of Sackner and Ford (1981) indicates a **NOAEL** of 1.6ppm (4.2mg/m³) for effects of nitric acid on pulmonary function in volunteers over a 10min period. Only one concentration was tested in a small number (5) of individuals and therefore this study offers only a limited basis for deriving health-based limit values. However, it is considered to provide a basis for proposing a **STEL** (15mins). Based on the NOAEL of 1.6ppm for local short-term (10min) effects of nitric acid on the airways a STEL of 1.0ppm (2.6mg/m³) is recommended. Although SCOEL could not recommend a specific 8-h TWA limit, the committee felt that 8-h TWA exposures should be appreciably below the STEL. No "**Skin**" notation was considered to be necessary." (reference cited in SCOEL, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, ACGIH® and SCOEL reviews, WorkSafe considers its current WES-TWA of 2ppm (5.2mg/m³) and WES-STEL of 4ppm (10mg/m³) for nitric acid to be adequate to manage health risks from possible workplace exposure.

It is recommended for nitric acid that the WES-TWA of 2ppm (5.2mg/m³) and WES-STEL of 4ppm (10mg/m³) are maintained, to protect against irritation, corrosion and lung function effects, based on the ACGIH® and SCOEL recommendations. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Nitric-acid#section=Chemical-and-Physical-Properties
CAS Number	7697-37-2
Conversion factors	1ppm = 2.58mg/m³ (25°C; 101.3**kPa**) 1mg/m³ = 0.38ppm (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Nitric acid, red fuming www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/BD5A1D13-9562-4221-AE70-F638A9000C5F

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Nitric acid."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2008. *"Salpetersäure."* MAK Value Documentation in German language, 2008; The MAK Collection for Occupational Health and Safety; pp 1-2. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb769737d0045

Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (IFA), 2022. GESTIS International Limit Values. Accessed January 2022. http://limitvalue.ifa.dguv.de

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Scientific Committee on Occupational Exposure Limits (SCOEL), 2001. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for nitric acid."* SCOEL/SUM/61

NITROGEN DIOXIDE

CAS NO: 10102-44-0

Summary

Workplace Exposure Standards for nitrogen dioxide (CAS: 10102-44-0)

	CURRENT	PROPOSED
WES-TWA	1**ppm** (1.9**mg/m³**)	0.2ppm (0.38mg/m³)
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for nitrogen dioxide

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for nitrogen dioxide of 0.2ppm (0.38mg/m³).

To protect for irritative effects in the lower respiratory tract.

Discussion

Nitrogen dioxide is used as a chemical intermediate. However, the majority of occupational exposures to nitrogen dioxide result from fuel combustion (exhausts); metal working with nitric acid; acetylene use; electric cutting and welding; explosives use (mining); and, fermentation of agricultural silage (silos) (**Safe Work Australia**, 2020; **SCOEL**, 2014; **ACGIH®**, 2012).

Nitrogen dioxide has an irritating, acrid odour, with an odour threshold reported at 2.0mg/m³ (PubChem, 2022).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of nitrogen dioxide noted that the critical effects were in the deep respiratory tract (SCOEL, 2014).

The SCOEL noted that the **OEL** (8-h **TWA**) of 0.5ppm was based on a **NOAEC** of 0.5ppm for lung function effects in exposed workers; and, the STEL of 1.0ppm was based on reports of increased bronchial reactivity in volunteers exposed to 1.5ppm for more than 3 hours, and increased airways resistance after exposure to 2ppm for 4 hours for 4 days, with both displaying marked changes in bronchoalveolar lavage fluid (**BALF**) (SCOEL, 2014).

The SCOEL noted that there was no evidence indicating significant skin absorption, so a "skin" notation was not required.

The SCOEL also noted that there were no human studies on the effects of nitrogen dioxide on asthmatics in the workplace, but considered that the recommended OEL would be protective of asthmatics.

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of nitrogen dioxide noted that the critical effects were lower respiratory tract irritation (ACGIH®, 2012).

The ACGIH® review concluded that:

> "Based on respiratory system irritant effects during controlled human exposure studies to nitrogen dioxide (NO_2), a **TLV-TWA** of 0.2ppm (0.38mg/m^3) is recommended. This value should protect both non-asthmatic and asthmatic workers from respiratory system effects. Asthmatic workers require a lower TLV-TWA than would be needed by non-asthmatic workers. Based on equivocal human studies, an **A4**, **Not Classifiable as a Human Carcinogen**, designation is assigned.
>
> "Controlled human exposure studies of mild asthmatics and non-asthmatic subjects to NO_2 have demonstrated levels of exposure to NO_2 at which no short-term respiratory irritant effects are observed in either asthmatics or non-asthmatics, and levels at which short-term adverse respiratory effects are seen first in mild asthmatics (at lower levels) and in non-asthmatics (at higher levels). ... No effects were seen for non-asthmatics and mild asthmatics exposed at 0.1ppm at rest (Hazucha *et al*., 1983), and no statistically significant increase on bronchial reactivity was seen in asthmatics exposed to 0.2ppm with light intermittent exercise (Kleinman *et al*., 1983). In mild asthmatics, subclinical effects on bronchoalveolar lavaged cells could be seen after exposure at 0.26ppm (Barck *et al*., 2002). Mild asthmatics experienced no symptoms or lung function effects after 75 minutes of exposure with intermittent exercise at 0.6ppm (Roger *et al*., 1990). However, after three hours at 0.4ppm, mild asthmatics showed increased airway reactivity to inhalation challenge with house mite antigen (Jenkins *et al*., 1999). A one-hour exposure of non-asthmatics at rest to 2ppm resulted in increased methacholine airway reactivity (Mohsenin, 1988), and other effects were seen in non-asthmatics at this concentration ... ." (references cited in ACGIH®, 2012).

The ACGIH® noted that there was insufficient data to recommend a **TLV-STEL**, or skin or sensitiser notations for nitrogen dioxide (ACGIH®, 2012).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of nitrogen dioxide noted that the critical effects were local oxidative damage in the terminal airways of the lungs (DFG MAK, 2005).

The DFG noted that the **MAK** value of 0.5ppm for nitrogen dioxide, **peak limitation Category I** with an excursion factor of 1, were based on the results of studies in rats (**LOAEC** of 5ppm after 6 hours/day for 5 days; and, NOAEC of 2.14ppm after 6 hours/day for 13 weeks), and BALF changes in volunteers after 3-hour exposures to 1.5 or 2.0ppm (DFG MAK, 2010).

The DFG estimated dermal absorption would not contribute significantly to total body burden, so an **"H"** notation was not assigned to nitrogen dioxide (DFG MAK, 2010).

"Sh" and **"Sa"** notations were not assigned for nitrogen dioxide due to lack of evidence (DFG MAK, 2010).

Conclusions

Based on the documentation cited, and informed by the conclusions of the SCOEL, ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 1ppm (1.9mg/m^3) for nitrogen dioxide to be inadequate to manage health risks from possible workplace exposure.

It is recommended for nitrogen dioxide that a WES-TWA of 0.2ppm (0.38mg/m^3) is adopted, to protect against irritative effects in the lower respiratory tract, based on the ACGIH® recommendations. Noting that the recommended WES-TWA for nitrogen dioxide should protect both non-asthmatic and asthmatic workers.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Nitrogen-dioxide#section=Chemical-and-Physical-Properties
CAS Number	10102-44-0
Conversion factors	1mg/m^3 = 0.532ppm (25°C; 101.3**kPa**) 1ppm = 1.88mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/678AD5B7-97F1-4B24-9437-DFA6BE406B8C

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Nitrogen dioxide."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Deutsche Forschungsgemeinschaft (DFG), 2010. *"Nitrogen dioxide."* MAK Value Documentation, 2010. The MAK-Collection for Occupational Health and Safety; pp 1-10. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1010244e4914

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n-METHYL ANILINE

CAS NO: 100-61-8

Summary

Workplace Exposure Standards for *n*-methyl aniline (CAS: 100-61-8)

	CURRENT	PROPOSED
WES-TWA	0.5**ppm** (2.2**mg/m³**)	0.5ppm (2.2mg/m³)
WES-STEL	–	1ppm (4.4mg/m³)
WES-Ceiling	–	–
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for *n*-methyl aniline

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain a WES-TWA for n-methyl aniline of 0.5ppm (2.2mg/m³)
2. adopt a WES-STEL for n-methyl aniline of 1ppm (4.4mg/m³), and
3. maintain the ***skin*** notation for n-methyl aniline.

To protect for methaemoglobin formation and sequelae (anoxia and cyanosis).

Discussion

n-Methyl aniline is used as an acid acceptor; as a solvent; and, in organic syntheses (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

n-Methyl aniline has a weak, ammonia-like odour, with an odour threshold reported at 1.7ppm (PubChem, 2021; ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of *n*-methyl aniline noted that the critical effects were methaemoglobin formation in humans (DFG MAK, 2017).

The DFG noted that the **MAK** value of 0.5ppm, **peak limitation Category II** with an excursion factor of 2, were based on analogy with aniline where methaemoglobin formation is also the critical effect in exposed humans. No adequate human studies with *n*-methyl aniline were available, and animal data was unsuitable due to marked differences in the significance of methaemoglobin formation in species. 28- and 14-day inhalation studies in rats indicated that *n*-methyl aniline was about 2.7 times as effective as aniline in methaemoglobin induction. Aniline has a MAK value of 2ppm (DFG MAK, 2017). [See WorkSafe WES draft review for aniline and homologues, 2019].

An **"H"** notation was warranted for *n*-methyl aniline, based on the potential for dermal absorption to contribute significantly to systemic dose (DFG MAK, 2017).

"Sa" or **"Sh"** notations were not warranted for *n*-methyl aniline, based on a negative local lymph node assay in mice (DFG MAK, 2017).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of *n*-methyl aniline recommended:

"For the evaluation of the toxicity of **NMA**, the following effects must be taken into account:

- methaemoglobin (MetHb) formation
- toxic effects on the haematopoietic system with erythrocytotoxicity and effects on the spleen

"Information is insufficient to assess the carcinogenic and reprotoxic capacity of NMA.

"No human data were available regarding the haematological effects of NMA. In experimental animals, the critical effect of NMA (acute and chronic) is the formation of MetHb but the available database does not allow directly deriving a clear point of departure in studies conducted with NMA. Animal data indicate, however, that NMA is twice more potent at inducing MetHb than aniline, and this analogy may help to recommend an **OEL**. SCOEL proposed for aniline an 8-hour **TWA** OEL and a **STEL** of 0.5 and 1ppm, respectively (SCOEL 2010). An *8-hour TWA OEL and a STEL of 0.2 and 0.5ppm*, respectively, are therefore proposed for NMA.

"Aniline is at worst considered as a very weak *in vivo* genotoxicant and no carcinogenic activity or reproductive toxicity can be expected at exposure levels that do not cause increased MetHb formation (SCOEL 2010). It can, therefore, be expected by analogy that the OEL proposed for NMA also protects against carcinogenicity and reproductive toxicity, if any.

"Animal studies clearly indicate that NMA is well absorbed through the intact skin. Therefore, assignment of a "skin" notation is recommended. Data regarding sensitisation were not available." (reference cited in SCOEL, 2012).

Note that SCOEL re-assessed aniline in 2016 and recommended an 8-hour OEL of 2ppm with a 15-minute STEL of 5ppm for occupational exposure to aniline, based in part on a recent experimental human exposure study by Käfferlein *et al*. (2014) (SCOEL, 2016).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review *n*-methyl aniline noted that the critical effects were anoxia and cyanosis due to methaemoglobinaemia (ACGIH®, 2001).

The ACGIH® review concluded that:

"A **TLV-TWA** of 0.5ppm (2.2mg/m^3) is recommended for occupational exposure to N-methylaniline to minimize the potential for the induction of anoxia and cyanosis due to the formation of methemoglobinemia. Dizziness, weakness, and headache are accompanying sequela. The clinical toxicology of N-methylaniline resembles that of aniline. N-Methylaniline is readily absorbed through the skin in amounts that can contribute substantially to systemic poisoning; therefore, a **Skin** notation is appropriate. In addition to workplace air monitoring, **BEI**s are recommended for aniline to provide an additional means of assessing the total body burden of that chemical. These BEIs are also considered applicable for exposure to N-methylaniline and its metabolites." (ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to recommend **DSEN**, **RSEN** or Carcinogenicity notations, or **TLV-STEL** for *n*-methyl aniline (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, SCOEL and ACGIH® reviews, WorkSafe considers its current WES-TWA of 0.5ppm (2.2mg/m³) for *n*-methyl aniline with a *skin* notation, to be adequate to manage health risks from possible workplace exposure.

It is recommended for *n*-methyl aniline that a WES-STEL of 1ppm (4.4mg/m³) is adopted to protect against methaemoglobin formation and sequelae (anoxia and cyanosis) during peak concentrations, based on the DFG recommendations.

Extra care should be exercised if co-exposure with other methaemoglobin inducers, such as aniline, is suspected.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/n-methylaniline#section=Chemical-and-Physical-Properties
CAS Number	100-61-8
Conversion factors	1mg/m³ = 0.229ppm (25°C; 101.3**kPa**) 1ppm = 4.38mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/F22A7520-31D7-4913-BADB-E4C007143995 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"*N-*Methylaniline."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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PENTYL ACETATE (ALL ISOMERS)

CAS NO: *n*-amyl acetate 628-63-7; sec-amyl acetate 626-38-0; iso-amyl acetate 123-92-2; tert-amyl acetate 625-16-1; 2-methylbutyl acetate 624-41-9; 3-pentyl acetate 620-11-1

Summary

Workplace Exposure Standards for pentyl acetate (all isomers)

	CURRENT	PROPOSED
***n*-amyl acetate (CAS: 628-63-7)**		
WES-TWA	100**ppm** (532**mg/m³**)	50ppm (270mg/m³)
WES-STEL	–	50ppm (270mg/m³)
WES-Ceiling	–	–
Notations	–	–
sec-amyl acetate (CAS: 626-38-0)		
WES-TWA	125ppm (665mg/m³)	50ppm (270mg/m³)
WES-STEL	–	50ppm (270mg/m³)
WES-Ceiling	–	–
Notations	–	–
isoamyl acetate (CAS: 123-92-2)		
WES-TWA	100ppm (532mg/m³)	50ppm (270mg/m³)
WES-STEL	–	50ppm (270mg/m³)
WES-Ceiling	–	–
Notations	–	–
tert-amyl acetate (CAS: 625-16-1)		
WES-TWA	–	50ppm (270mg/m³)
WES-STEL	–	50ppm (270mg/m³)
WES-Ceiling	–	–
Notations	–	–
2-methylbutyl acetate (CAS: 624-41-9)		
WES-TWA	–	50ppm (270mg/m³)
WES-STEL	–	50ppm (270mg/m³)
WES-Ceiling	–	–
Notations	–	–
3-pentyl acetate (CAS: 620-11-1)		
WES-TWA	–	50ppm (270mg/m³)
WES-STEL	–	50ppm (270mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1:
Current and proposed Workplace Exposure Standards (**WES**) for pentyl acetate (all isomers)

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for pentyl acetate (all isomers) of 50ppm (270mg/m^3), and
2. adopt a WES-STEL for pentyl acetate (all isomers) of 50ppm (270mg/m^3).

To protect for eye and mucous membrane irritation.

Discussion

Pentyl acetates are used as a solvent; flavouring agent; and, insecticide (**Safe Work Australia**, 2019; **ACGIH®**, 2001).

Pentyl acetates have a fruit-like odour, with an odour threshold reported at 0.18ppm (ACGIH®, 2001; PubChem, 2021).

OEL evaluations by Safe Work Australia (2019) considered *n*-, *sec*- and *iso*-amyl acetate isomers together. ACGIH® (2001), **DFG MAK** (2000) and **SEG** (1991) considered all amyl acetate isomers together, due to the commonalities in structure and critical effects, recommending one standard for the group: *n*-, CAS: 628-63-7; *sec*-, CAS: 626-38-0; and, *iso*-amyl acetate, CAS: 123-92-2 (Safe Work Australia, 2019). Commercial amyl acetates are often mixtures of isomers (ACGIH®, 2001). Therefore, WorkSafe proposes to set a group WES for all pentyl acetates.

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of amyl acetate (pentyl acetate) all isomers noted that the critical effects were eye and mucous membrane irritation, and at higher concentrations: narcosis, hepatotoxicity and developmental effects (ACGIH®, 2001).

The ACGIH® review concluded that:

> "The pentyl acetates are irritating to the eyes and mucous membranes; at higher concentrations they are narcotic (Mackinson *et al*., 1978). Subjects exposed to 100ppm pentyl acetate reported mild throat discomfort, while at 200ppm throat irritation was severe (Nelson *et al*., 1943); exposure at 300ppm resulted in conjunctival hyperemia (Dahl *et al*., 1988). Based on these data and the **RD_{50}** values, which correlate with suggested occupational exposure values between 43 and 47ppm (Schaper, 1993), a **TLV-TWA** of 50ppm and a **TLV-STEL** of 100ppm are recommended to protect against the irritating effects of pentyl acetate."
>
> "Irritation of the mucous membranes and eyes is generally considered to be the critical effect of exposure to pentyl acetate (Anon, 1988; DFG, 1997; Nelson *et al*., 1943). Because pentyl acetates are metabolized to their corresponding alcohol and acetic acid, there is little chance of significant bioaccumulation (Anon, 1988; DFG, 1997). Systemic effects, including narcosis, hepatotoxicity, and developmental toxicity, occur at exposure levels well above those that result in irritation (DFG, 1997). The low dermal toxicity of 1-pentyl acetate in rabbits (**LD_{50}** > 20**ml/kg**) (Smyth *et al*., 1962) suggests that this route of exposure is of minor importance (DFG, 1997); thus, a **Skin** notation is not considered appropriate. Human patch testing studies provided no evidence of skin sensitization, phototoxicity, or photoallergy (Anon, 1988)." (ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend Skin, **DSEN**, **RSEN** or carcinogenicity notations for n-amyl acetate (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of amyl acetate (pentyl acetate) isomers noted that the critical effects were irritation (DFG MAK, 1998).

The DFG noted that the **MAK** value of 50ppm for amyl acetate isomers, **peak limitation Category I** with an excursion factor of 1, were based on studies with volunteers that reported mild irritation at 100ppm and severe irritation at 200ppm after 3-5 minutes exposure to "amyl acetate". Other studies with volunteers reported throat and tracheal irritation after exposure to 185ppm 3-methylbutyl acetate for 5 minutes, while animal studies suggested the irritation threshold lay between 200 and 300ppm (DFG MAK, 1998; DFG MAK, 2000).

The DFG noted that there was no data available to assess an **"H"** notation (DFG MAK, 1998).

The DFG also noted that **"S"** notations were not warranted, based on negative results in humans and animals (DFG MAK, 1998).

SCOEL

The Scientific Committee on Occupational Exposure Limits' (**SCOEL**, formerly the Scientific Expert Group on Occupational Exposure Limits (**SEG**)) evaluation of amyl acetate isomers recommended an 8-hour TWA of 50ppm (270mg/m^3) and a 15-minute STEL of 100ppm (540mg/m^3), based on the irritant properties of pentyl acetate in humans and RD50 investigations in mice (SEG, 1991).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SEG reviews, WorkSafe considers its current WES-TWA of 100ppm (532mg/m^3) for *n-*, *sec-*, and isoamyl acetates, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for pentyl acetate (all isomers) that a WES-TWA of 50ppm (270mg/m^3) and a WES-STEL of 50ppm (270mg/m^3) are adopted, to protect against eye and mucous membrane irritation, based on the DFG recommendations, and noting the potential additive effects of co-exposure with other amyl acetate isomers. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	Pentyl acetate https://pubchem.ncbi.nlm.nih.gov/compound/Pentyl-acetate#section=Chemical-and-Physical-Properties 1-Methylbutyl acetate https://pubchem.ncbi.nlm.nih.gov/compound/12278#section=Chemical-and-Physical-Properties Isoamyl acetate https://pubchem.ncbi.nlm.nih.gov/compound/31276#section=Chemical-and-Physical-Properties tert-Amyl acetate https://pubchem.ncbi.nlm.nih.gov/compound/12238#section=Chemical-and-Physical-Properties 2-Methylbutyl acetate https://pubchem.ncbi.nlm.nih.gov/compound/12209#section=Chemical-and-Physical-Properties 3-Pentyl acetate https://pubchem.ncbi.nlm.nih.gov/compound/69279#section=Chemical-and-Physical-Properties
CAS Number	n-amyl acetate 628-63-7 sec-amyl acetate 626-38-0 iso-amyl acetate 123-92-2 tert-amyl acetate 625-16-1 2-methylbutyl acetate 624-41-9 3-pentyl acetate 620-11-1
Conversion factors	1mg/m³ = 0.188ppm (25°C; 101.3**kPa**) 1ppm = 5.325mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Acetic acid, pentyl ester www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/4479A254-A02E-478D-80D1-4BDCBE20300D 2-Pentanol, acetate www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/8D31BE59-3F7A-4A6E-A0CE-5DC12FAE094A 1-Butanol, 3-methyl-, acetate www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/C53F1D4B-BD17-43FA-8562-2EFA00805979 Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Pentyl acetate, all isomers."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Deutsche Forschungsgemeinschaft (DFG), 2000. *"Pentylacetat (alle Isomeren)."* [MAK Value Documentation in German language, 2000]. In The MAK-Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb0222ismd0030

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Scientific Expert Group on Occupational Exposure Limits (SEG), 1991. *"Recommendation from the Scientific Expert Group on Occupational Exposure Limits for Pentyl Acetate and its Isomers."* SEG/SUM/3

PHOSPHORUS TRICHLORIDE

CAS NO: 7719-12-2

Summary

Workplace Exposure Standards for phosphorus trichloride (CAS: 7719-12-2)

	CURRENT	PROPOSED
WES-TWA	0.2**ppm** (1.1**mg/m³**)	0.2ppm (1.1mg/m³)
WES-STEL	0.5ppm (2.8mg/m³)	0.5ppm (2.8mg/m³)
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for phosphorus trichloride

Recommendation and basis for WES

It is proposed that WorkSafe:

1. maintain the WES-TWA for phosphorus trichloride of 0.2ppm (1.1mg/m³), and
2. maintain the WES-STEL for phosphorus trichloride of 0.5ppm (2.8mg/m³).

To protect for irritation of the eyes, skin, mucous membranes, and respiratory tract.

Discussion

Phosphorus trichloride is used as an intermediate in the production of pesticides, surfactants, gasoline additives, plasticisers, and dyestuffs; as a chlorinating agent and catalyst; and, in textile-finishing agents (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Phosphorus trichloride has a pungent odour, with an odour threshold reported at 0.5mg/m³ (PubChem, 2021).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of phosphorus trichloride noted that the critical effects were local irritation of the respiratory epithelium of the nose of rats (DFG MAK, 2016).

The DFG noted that the **MAK** value of 0.1ppm for phosphorus trichloride, **peak limitation Category I** with an excursion factor of 1, were based on a **NOAEC** of 3ppm from a 28-day inhalation study in rats and modified to extrapolate to the workplace. The DFG noted that there was no human data to derive a MAK value or modify the excursion factor of 1 (DFG MAK, 2016).

No data was reported to evaluate **"H"** or **"S"** notations for phosphorus trichloride (DFG MAK, 2016).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of phosphorus trichloride noted that the critical effects were irritation of the eyes, skin, mucous membranes, and respiratory tract (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Phosphorus trichloride is a severe irritant of the eyes, mucous membranes, and the skin. Based on the work of Butjagin (1904), Henderson and Haggard (1943) recommended that a maximum allowable concentration for prolonged exposure to phosphorus trichloride should be less than 0.7ppm. A **TLV-TWA** of 0.5ppm was recommended from 1948 to 1981. On the basis of the animal (Butjagin, 1904; Weeks *et al*., 1964) and human (Sassi, 1952) data and the comparison with the effects produced from exposure to hydrogen chloride (ILO, 1934), a TLV-TWA of 0.2ppm and a **TLV-STEL** of 0.5ppm are currently recommended for phosphorus trichloride." (references cited in ACGIH®, 2001).

The ACGIH® found there was insufficient data available to recommend **Skin**, **SEN** or carcinogenicity notations for phosphorus trichloride (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 0.2ppm (1.1mg/m³) and WES-STEL of 0.5ppm (2.8mg/m³) for phosphorus trichloride, to be adequate to manage health risks from possible workplace exposure.

It is recommended for phosphorus trichloride that the WES-TWA of 0.2ppm (1.1mg/m³) and WES-STEL of 0.5ppm (2.8mg/m³) are maintained, to protect against irritation of the eyes, skin, mucous membranes, and respiratory tract, based on the DFG and ACGIH® recommendations. Noting the limited database.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Phosphorus-trichloride#section=Chemical-and-Physical-Properties
CAS Number	7719-12-2
Conversion factors	1mg/m³ = 0.179ppm (25°C; 101.3**kPa**) 1ppm = 5.60mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/A6D5E0E2-7BCE-4DB6-A52C-3369ED354B4B Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Phosphorus trichloride."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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SODIUM AZIDE

CAS NO: 26628-22-8

Summary

Workplace Exposure Standards for sodium azide (CAS: 26628-22-8)

	CURRENT	PROPOSED
WES-TWA	–	0.04**ppm** (0.1**mg/m³**)
WES-STEL	–	–
WES-Ceiling	0.11ppm (0.29mg/m³)	
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for sodium azide

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for sodium azide of 0.1mg/m³ (0.04ppm), and
2. remove the WES-Ceiling for sodium azide.

To protect for hypotension and the onset of acute symptoms, and irritating effects of hydrazoic acid that form when sodium azide is handled.

Discussion

Sodium azide is used in organic syntheses, as a propellant (vehicle airbags), in explosives and pesticides, and in rubber and beer production (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Sodium azide is odourless, but on forming hydrazoic acid in the presence of water has a faint fishy smell (PubChem, 2022).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of sodium azide noted that the critical effects were local irritation and acute systemic toxicity (DFG MAK, 2003,).

The DFG noted that the **MAK** value of 0.2mg/m³ for sodium azide, **peak limitation Category I** with an excursion factor of 2, were based on inhalation studies with hydrazoic acid vapour and oral studies with sodium azide in animals, as there were no suitable human study data to derive a MAK value (DFG MAK, 2003). The DFG noted reports of 0.5ppm (0.9mg/m³) or more of hydrazoic acid vapour causing nasal mucosa irritation and headaches in exposed workers (DFG MAK, 2003). The MAK value was supported by a **LOAEL** for sodium azide of 1.25**mg/kg b.w./day** for liver toxicity from a 13-week study in F344/N rats (DFG MAK, 2003), and observations in cancer patients that doses of 3.9mg/day for periods of 5 days to 2 years did not cause toxicity (equivalent to 0.39mg/m³ when adjusted to an 8-hour workplace air concentration) (DFG MAK, 2003).

An **"H"** notation was not assigned to sodium azide (DFG MAK, 2003). **"Sa"** and **"Sh"** notations were not assigned for sodium azide, based on lack of data to make an assessment (DFG MAK, 2003).

The DFG has a separate MAK value of 0.1ppm (0.18mg/m³) for hydrazoic acid (Stickstoffwasserstoffsäure), peak limitation Category I with an excursion factor of 2 (DFG MAK, 2000).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of sodium azide noted that the critical effects were acute cardiovascular collapse and central respiratory paralysis (ACGIH®, 2001).

The ACGIH® review concluded that:

> "Sodium azide can cause death by acute cardiovascular collapse and central respiratory paralysis (U.S. NTP, 1991; Mettler and Sax, 1972; Hicks, 1950). Inhalation or ingestion can cause dizziness, weakness, blurred vision, slight dyspnea, tachypnea, hypotension, tachycardia, acidosis, abdominal pain, and spasms (Graham, 1949; Burger and Bauer, 1965; Black *et al*., 1954; Richardson *et al*., 1975). Serious cases of exposure may result in polydipsia, leukocytosis, pulmonary edema, bronchitis, convulsions, unconsciousness, and death (Graham, 1949; Burger and Bauer, 1965; Emmett and Ricking, 1975). Hydrazoic acid is released from solutions of sodium azide, and the acid has the same degree of acute toxicity as does the salt (Graham *et al*., 1948; Fairhall *et al*., 1943).
>
> "It is apparent from the medicinal uses (Black *et al*., 1954) of sodium azide that exposures must be controlled to very low levels if hypotension is to be avoided. Estimation of a maximal intake of sodium azide for a daily 8-hour work shift, assuming 10m^3 of air inhaled and a 75% retention for a daily pulmonary absorption of 0.75mg results in an ambient air concentration of about 0.1mg/m^3 (0.04ppm). This value is consistent with the value estimated by Haas and Marsh (Haas and Marsh, 1970).
>
> "In order that the permissible limits of exposure to sodium and hydrogen azides incorporate a reasonable margin of safety against headache and other symptoms of systemic discomfort and to minimize the potential for significant changes in electrocardiogram readings and hypotension, **TLV-Ceilings** of 0.29mg/m^3, as sodium azide, and 0.11ppm, as hydrazoic acid vapor, are recommended. There was no evidence of carcinogenicity seen in rats fed sodium azide in the diet for 18 months or in rats administered sodium azide in water by gavage for 2 years (U.S. NTP, 1991; Weisburger *et al*., 1981). Accordingly, an **A4**, **Not Classifiable as a Human Carcinogen**, notation is assigned to sodium azide." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data to assign **Skin** or **SEN** notations for sodium azide (ACGIH®, 2001).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) noted that the critical systemic endpoints of sodium azide exposure at the workplace are the direct vasodilatory effect and effects on the central nervous system, related to the cytotoxic effects of sodium azide or its metabolites (SCOEL, 2009).

SCOEL considered a LOAEL of 0.3mg/m^3 for mean blood pressure decrease in workers at a group level and a **LOAEL** of 0.5 mg/m^3 for the occurrence of acute hypotensive episodes as the basis for recommending an 8-hour TWA of 0.1mg/m^3 to prevent hypotension and the onset of acute symptoms. This recommended exposure limit was also considered protective of the irritating effects of hydrazoic acid that may be present in the workplace air where sodium azide is handled (SCOEL, 2009).

Conclusions

Based on the documentation cited, and informed by the conclusions of the SCOEL, DGF and ACGIH® reviews, WorkSafe considers its current WES-Ceiling of 0.11ppm (0.29mg/m^3) for sodium azide to be inadequate to manage health risks from possible workplace exposure.

It is recommended for sodium azide that a WES-TWA of 0.1mg/m^3 (0.04ppm) is adopted to protect against hypotension and the onset of acute symptoms, and irritating effects of hydrazoic acid that form when sodium azide is handled, based on the SCOEL recommendations. It is also recommended to remove the WES-Ceiling of 0.11ppm (0.29 mg/m^3) due to weakness of the studies used to support a WES-Ceiling and that the proposed WES-TWA should also be protective against acute, irritating effects of hydrazoic acid that may form.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Sodium-azide#section=Chemical-and-Physical-Properties
CAS Number	26628-22-8
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/1F7B7BE2-6631-4F48-ADA1-69F2727B4283

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Sodium azide."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2000. *"Stickstoffwasserstoffsäure."* MAK Value Documentation in German language, 2000. The MAK-Collection for Occupational Health and Safety; p 1. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb778279d0030

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Scientific Committee on Occupational Exposure Limits (SCOEL), 2009. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for sodium azide."* SCOEL/SUM/51

TEREPHTHALIC ACID

CAS NO: 100-21-0

Summary

Workplace Exposure Standards for terephthalic acid (CAS: 100-21-0)

	CURRENT	PROPOSED
WES-TWA	10 **mg/m³**	5mg/m³
WES-STEL	–	10mg/m³
WES-Ceiling	–	–
Notations	–	–

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for terephthalic acid

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for terephthalic acid of 5mg/m³, and
2. adopt a WES-STEL for terephthalic acid of 10mg/m³.

To protect for respiratory tract irritation.

Discussion

Terephthalic acid (*p*-phthalic acid) is used for the production of polyterephthalic acid esters for plastic films and sheets; as a reagent for alkali in wool; and, as a poultry feed additive (**Safe Work Australia**, 2020; **ACGIH®**, 2001).

Terephthalic acid has a slight acidic odour (ACGIH®, 2001).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of terephthalic acids noted that the critical effects were local respiratory tract irritation (DFG MAK, 2012).

The DFG noted that the **MAK** value of 5mg/m³ for terephthalic acid, **peak limitation Category I** with an excursion factor of 2, were based a **NOAEC** of 10mg/m³ from a 28-day nose-only inhalation study in rats (10mg/m³ was the highest concentration tested, so no **LOAEC** was established), and comparison with a similarly strong acid, formic acid (formic acid, pKs = 3.75; terephthalic acid, pK_s = 3.52). The DFG noted that phthalic acids were not metabolised to a significant extent, and the local irritation was likely a result of the acid function indicating little inter-species differences (DFG MAK, 2012).

The DFG concluded that an **"H"** notation was not warranted for terephthalic acid, based on data indicating that dermal absorption would not contribute significantly to systemic toxicity (DFG MAK, 2012).

The DFG also noted that there was insufficient data to justify a **"Sa"** or **"Sh"** notations for terephthalic acid (DFG MAK, 2012).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of terephthalic acid noted that the critical effects were pulmonary and urinary tract effects reported in rodent (ACGIH®, 2001).

The ACGIH® review concluded that:

> "There are no published reports of either controlled human inhalation studies or industrial experience with terephthalic acid upon which to base the **TLV**. Terephthalic acid can be considered practically nontoxic in acute studies in animals with the only confirmed effect limited to the development of bladder stones and subsequent bladder cancers (considered secondary to the development of bladder calculi) in lifetime studies after the ingestion of very high doses for as little as 2 weeks. There were only scant data on the extent of systemic absorption of terephthalic acid in animals or in humans following either acute or chronic exposure by the oral or inhalation route. The existing data suggested that terephthalic acid was rapidly cleared and that it did not preferentially accumulate in any tissue or organ (Hoshi and Kuretani, 1967). Therefore, terephthalic acid is considered by ACGIH as a particulate not otherwise specified with a recommended **TLV-TWA** of 10mg/m³. Based on the equivocal tumorigenicity data available from two terephthalic acid dietary studies in rats (Heck and Tyl, 1985; US EPA, 1984), a carcinogenicity notation is not considered appropriate." (references cited in ACGIH®, 2001).

The ACGIH® noted that there was insufficient data available to recommend **Skin** or **SEN** notations, or a **TLV-STEL** for terephthalic acid (ACGIH®, 2001).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA of 10mg/m³ for terephthalic acid, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for terephthalic acid that a WES-TWA of 5mg/m³ and a WES-STEL of 10mg/m³ are adopted, to protect against respiratory tract irritation, based on the DFG recommendations.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Terephthalic-acid#section=Chemical-and-Physical-Properties
CAS Number	100-21-0
Conversion factors	1mg/m³ = 0.15ppm (25°C; 101.3**kPa**) 1ppm = 6.79mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Phthalic acid (CAS 88-99-3) www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/C67E4C10-9670-479F-B09A-A901F9DDB4FD Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Terephthalic acid."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 2012. *"o-Phthalic acid [88-99-3; phthalic acid], m-phthalic acid [121-91-5; isophthalic acid], p-phthalic acid [100-21-0; terephthalic acid]."* MAK Value Documentation, 2012; The MAK Collection for Occupational Health and Safety; pp 1-12. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb8899isme5215

Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

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TITANIUM DIOXIDE

CAS NO: 13463-67-7

Summary

Workplace Exposure Standards for titanium dioxide (CAS: 13463-67-7)

	CURRENT	PROPOSED
WES-TWA	10 **mg/m³**	2.5mg/m³ **(r)** 0.2mg/m³ (**ultrafine fraction**)
WES-STEL	-	-
WES-Ceiling	-	-
Notations	-	

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for titanium dioxide

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for titanium dioxide (respirable fraction) of 2.5mg/m³, and
2. adopt a WES-TWA for titanium dioxide (ultrafine fraction) of 0.2mg/m³.

To protect for lower respiratory tract irritation and pneumoconiosis.

Discussion

Titanium dioxide is predominantly used as a pigment in coatings, plastics and rubber, and paper, with other uses in catalysts, ceramics, coated fabrics and textiles, floor coverings, roofing granules and welding fluxes (IARC, 2010).

Cancer risks

The International Agency for Research on Cancer [**IARC**] evaluation of titanium dioxide concluded that:

> There is ***inadequate evidence in humans*** for the carcinogenicity of titanium dioxide.
>
> There is ***sufficient evidence in experimental animals*** for the carcinogenicity of titanium dioxide.

With an overall evaluation that:

> Titanium dioxide is *possibly carcinogenic to humans* (**Group 2B**) (IARC, 2010).

The IARC evaluation of titanium dioxide noted:

> "The single most informative study was a multicountry study of titanium dioxide production workers that found a slightly increased risk for lung cancer compared with the general population and a suggestive dose–response, but no overall excess risk for kidney cancer. The two other cohort studies reported no increased risks and evidence from the case–control study did not indicate an increased risk for either lung or kidney cancer."

"In two studies of rats that inhaled titanium dioxide, one observed an excess incidence of lung tumours in both sexes and another in females only. Studies of rats exposed intratracheally found increases in the incidence of lung tumours. No increases were observed among mice and hamsters exposed intratracheally."

"... the Working Group considered that the available mechanistic evidence for titanium dioxide was not strong enough to warrant a classification other than Group 2B." (IARC, 2010).

The US National Toxicology Program (**NTP**) Report on Carcinogens (**RoC**), Fourteenth Edition has no evaluation on the carcinogenic potential of titanium dioxide (NTP RoC, 2016).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of titanium dioxide (respiratory fraction) noted that the substance is a biopersistent granular dust and that the reported induction of lung tumours in rats after inhalation exposures to high concentrations of titanium dioxide were a consequence of an inflammatory mechanism of action with a threshold (DFG MAK, 2019).

The DFG based the **MAK** value of 0.3mg/m^3 multiplied by the material density for the respirable fraction (i.e. the MAK value of 0.3mg/m^3 applies to dusts with a density of 1**g/cm^3**), **peak limitation Category II** with an excursion factor of 8, on the general threshold limit established for the respirable fraction of all biopersistent granular dusts with a material density of 1g/cm^3 that was modelled from NOAEC values from long-term rat inhalation studies using pigment grade titanium dioxide (**MMAD**, 1.1**µm**; **GSD**, 1.6; material density, 4.3) (DFG MAK, 2012; DFG MAK, 2019). The premise being that the inherent toxicity of these granular dusts is negligible, and the limit concentration prevents the endogenous, adaptive inflammation threshold from being reached, preventing inflammation and proliferation, oxidative stress mediated by inflammatory cells, incomplete phagocytosis of particles and retardation or inhibition of particle clearance: a lung overload phenomenon centred on the alveoli (DFG MAK, 2012).

The DFG noted that, by definition, biopersistent granular dusts (larger than ultrafine or nanometric) were not systemically available, so any dermal absorption would be too small to exert significant systemic effects and an **"H"** designation was not warranted. While no sensitisation studies in animals were available, titanium dioxide was not known to cause sensitisation in humans, so **"Sa"** or **"Sh"** designations were also not warranted (DFG MAK, 2019; DFG MAK, 2012; DFG MAK, 2009).

The DFG also noted that the evaluation of titanium dioxide (respiratory fraction) did not change the MAK value for the inhalable fraction, the general threshold limit value for dust of 4mg/m^3, due to the lack of new data (DFG MAK, 2012).

The DFG indicated that the evaluations did not cover ultrafine titanium dioxide particles, which are expected to induce effects in the airways at exposure concentrations considerably lower than those for pigment-sized particles (DFG MAK, 2009).

ACGIH

The American Conference of Governmental Industrial Hygienists' (**ACGIH®**) review of titanium dioxide noted that the critical effects were lower respiratory tract irritation, and pneumoconiosis (ACGIH®, 2022).

The ACGIH® review assigned an **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans** to titanium dioxide. Sufficient data ere not available to recommend **TLV-STEL**, **DSEN**, or **RSEN** notations for titanium dioxide (ACGIH®, 2022).

> "Because the human data are insufficient for establishing a **TLV**, human-equivalent concentrations for titanium dioxide were derived from the steady-state particle lung burdens reported in (Bermudez *et al*. 2002; Bermudez *et al*. 2004) at the **NOAEL** concentrations using parameters (material density, lung surface areas) and approaches that are reported in the literature (Kreyling *et al*. 2019; Kuempel *et al*. 2006; Oberdorster 1989). Tracheobronchial and alveolar deposition fractions were determined assuming light intermittent exercise with oronasal breathing and were summed. The human-equivalent lung burdens were normalized to lung surface area, resulting in estimated human-equivalent aerosol concentrations of 2.3 to 2.8mg/m^3 for fine-scale particles and 0.1 to 0.2mg/m^3 for nanoscale particles. A **TLV-TWA** of 0.2mg/m^3 for respirable nanoscale particulate matter (physical size of individual particles <100**nm**) and of 2.5mg/m^3 for respirable fine-scale particulate matter (physical size of individual particles >100nm) are recommended for titanium dioxide. These values are intended to minimize the potential for respiratory tract irritation and potentially overwhelming of normal clearance mechanisms, possibly leading to fibroproliferative changes. Unless the user is deliberately generating or using nanoscale particles, the fine-scale TLV-TWA should be sufficiently protective" (ACGIH®, 2022).

NIOSH

The National Institute for Occupational Safety and Health (**NIOSH**) recommended exposure limits of 2.4mg/m^3 for fine titanium dioxide (TiO_2) and 0.3mg/m^3 for ultrafine (including nanoscale). NIOSH **REL**s are a daily 10-hr **TWA** based on a 40-hr working week. The RELs for titanium dioxide are based on reviews of human and animal health data up to 2011. NIOSH defines fine particles as those collected by respirable sampling and ultrafine (nanoscale) as the fraction of respirable particles with primary particle diameter <100nm (NIOSH, 2011).

"NIOSH has determined that ultrafine TiO_2 is a potential occupational carcinogen but that there are insufficient data at this time to classify fine TiO_2 as a potential occupational carcinogen. However, as a precautionary step, NIOSH used all of the animal tumor response data when conducting dose-response modeling and determining separate RELs for ultrafine and fine TiO_2. These recommendations represent levels that over a working lifetime are estimated to reduce risks of lung cancer to below one in 1,000" (NIOSH, 2011)."

"TiO_2 and other poorly soluble, low-toxicity (**PSLT**) particles of fine and ultrafine sizes show a consistent dose-response relationship for adverse pulmonary responses in rats, including persistent pulmonary inflammation and lung tumors, when dose is expressed as particle surface area. The higher mass-based potency of ultrafine TiO_2 compared to fine TiO_2, is associated with the greater surface area of ultrafine particles for a given mass. The NIOSH RELs for fine and ultrafine TiO_2 reflect this mass-based difference in potency."

"NIOSH has concluded that TiO_2 is not a direct-acting carcinogen, but acts through a secondary genotoxicity mechanism that is not specific to TiO_2 but primarily related to particle size and surface area. The most relevant data for assessing the health risk to workers are results from a chronic animal inhalation study with ultrafine (<100nm) TiO_2 in which a statistically significant increase in adenocarcinomas was observed (Heinrich *et al*. 1995). This is supported by a pattern of TiO_2 induced responses that include persistent pulmonary inflammation in rats and mice (Everitt *et al*. 2000; Bermudez *et al*. 2004) and cancer responses for PSLT particles related to surface area. Therefore, on the basis of the study by Heinrich *et al*. (1995) and the pattern of pulmonary inflammatory responses, NIOSH has determined that exposure to ultrafine TiO_2 should be considered a potential occupational carcinogen" (NIOSH, 2011).

Adverse effects may not be material specific and inhaling TiO_2 appears to be associated with generic effect of exposure to sufficiently high concentrations of poorly soluble low-toxicity particles. For fine size (pigment grade) TiO_2 (>100nm), NIOSH concluded that there was insufficient data to classify it as a potential occupational carcinogen and that surface area was the critical metric for assessing inhalation exposure in the workplace (NIOSH, 2011).

Conclusions

Based on the documentation cited and informed by the conclusions of the NIOSH, DFG and ACGIH® reviews, WorkSafe considers its current WES-TWA for titanium dioxide of 10mg/m³ for the inhalable fraction, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for titanium dioxide that a WES-TWA of 2.5mg/m³ for the respirable fraction and a WES-TWA of 0.2mg/m³ for the ultrafine fraction be adopted to protect for lower respiratory tract irritation and pneumoconiosis, based on ACGIH® recommendations.

Available data indicated that ***skin*** and ***sen*** notations were not warranted for titanium dioxide.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/26042#section=Chemical-and-Physical-Properties
CAS Number	13463-67-7
Exposure standards from around the world	http://limitvalue.ifa.dguv.de

References: PubChem 2020; **IFA**, 2020

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®). (2022). *Titanium dioxide*. Cincinnati, Ohio: ACGIH®. Retrieved January 10, 2024, from https://www.acgih.org/titanium-dioxide Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1991. *"Titanium dioxide."* MAK Value Documentation, 1991; pp 1-6. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1346367e0002

Deutsche Forschungsgemeinschaft (DFG), 2009. *"Titanium dioxide (respirable fraction)."* The MAK Collection Part 1, MAK Value Documentations 2014; pp 1-66. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1346367e4714

Deutsche Forschungsgemeinschaft (DFG), 2012. *"General threshold limit value for dust (R fraction) – (Biopersistent granular dusts)."* The MAK Collection Part 1, MAK Value Documentations 2014; pp 1-78. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb0230stwe5314

Deutsche Forschungsgemeinschaft (DFG), 2019. *"Titanium dioxide, respirable fraction."* The MAK Collection for Occupational Health and Safety 2019, Vol 4, No 2; pp 857-869. (in German). https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb1346367d0067

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International Agency for Research on Cancer (IARC), 2010. *"IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 93: Carbon Black, Titanium Dioxide, and Talc."* Lyon, France. https://publications.iarc.fr/111

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TRIETHYLAMINE

CAS NO: 121-44-8

Summary

Workplace Exposure Standards for triethylamine (CAS: 121-44-8)

	CURRENT	PROPOSED
WES-TWA	3**ppm** (12**mg/m³**)	0.5ppm (2.1mg/m³)
WES-STEL	5ppm (20mg/m³)	1ppm (4.2mg/m³)
WES-Ceiling	-	-
Notations	***skin***	*skin*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for triethylamine

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt a WES-TWA for triethylamine of 0.5ppm (2.1mg/m³)
2. adopt a WES-STEL for triethylamine of 1ppm (4.2mg/m³), and
3. maintain the *skin* notation for triethylamine.

To protect for visual impairment and upper respiratory tract irritation.

Discussion

Triethylamine is used as in the preparation of quaternary ammonium compounds; in the production of pharmaceuticals, pesticides, resins and polyurethane foam; and, as a catalyst for organic sand binders (**Safe Work Australia**, 2020; **ACGIH®**, 2015).

Triethylamine has a fish- or ammonia-like odour, with reported odour thresholds of 0.1 and 0.48ppm (PubChem, 2021; ACGIH®, 2015).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of triethylamine noted that the critical effects were visual impairment and upper respiratory tract irritation (ACGIH®, 2015).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 0.5ppm (2.07mg/m³) is recommended to minimize the potential for acute effects in humans. A **TLV-STEL** of 1ppm (4.14mg/m³) is recommended to minimize transient visual disturbances that are produced at higher exposure concentrations of triethylamine (**TEA**). The first apparent sign of adverse response to TEA in humans has been corneal change, producing visual disturbances such as hazing, blurring, and halo vision. In the workplace, these symptoms were reported to occur at 3 to 4ppm but not at 1 to 1.25ppm (Akesson *et al*., 1985, 1986). In a controlled setting using four human volunteers, 4-hour exposures to 0.72ppm did not produce changes in visual acuity or contrast sensitivity. Exposure to 1.56ppm produced measurable changes in contrast sensitivity. Following a 4-hour exposure to 9.74ppm, both visual acuity and contrast sensitivity were impaired (Jarvinen, 1998). In addition to acute exposure to TEA producing severe irritation to the eyes and skin of laboratory animals and humans, symptoms of respiratory

irritation have been seen in workers exposed to TEA (Benya and Harbison, 1994; Kustov *et al*., 1960; Smyth *et al*., 1951; Potts *et al*., 1986; Amor, 1950; Akesson *et al*., 1985, 1986; Warren and Selchan, 1988).

"There were no human data for skin absorption. However, the **LD_{50}** dose to rabbits following dermal exposure was 420mg/kg; therefore, a **Skin** notation is recommended. Based on a 2-year drinking water study (Davison *et al*., 1965), an**A4**, **Not Classifiable as a Human Carcinogen**, notation is assigned." (references cited in ACGIH®, 2015).

The ACGIH® found there was insufficient data available to recommend **DSEN** or **RSEN** notations for triethylamine (ACGIH®, 2015).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of triethylamine noted that the critical effects were visual disturbances (DFG MAK, 1999; DFG MAK, 2002).

The DFG noted that the **MAK** value of 1ppm for triethylamine, **peak limitation Category I** with an excursion factor of 2, were based on studies with volunteers that reported no subjective visual disturbances at 2.4ppm, and in workers exposed to average concentrations of 1.44 and 2.7ppm for 8 hours (DFG MAK, 1999).

The DFG concluded that an **"H"** notation was not warranted for triethylamine, based on studies in rabbits with undiluted triethylamine that, while giving LD50 values of 415 and 578 mg/kg body weight, were caustic preventing any conclusions on dermal absorption (DFG MAK, 1999).

The DFG reported that available data on triethylamine indicated a **"S"** notation was not warranted (DFG MAK, 1999).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) noted that the critical effects were visual disturbances (SCOEL, 1999).

SCOEL considered a **NOAEL** of 0.7ppm (3mg/m^3) and **LOAEL** of 1.5ppm (6.5 mg/m^3) for slight visual disturbances in human volunteers, to be the best available basis for setting exposure limits. Consequently SCOEL recommended an 8hour TWA for triethylamine of 1ppm (4.2mg/m^3). A 15-minute STEL of 3ppm (12.6mg/m^3) was recommended based on observations that occupational exposures to a TWA of 2.6ppm (11mg/m^3) with a peak concentration of 5.7ppm (24mg/m^3) resulted in visual disturbances to 3 out of 4 workers (SCOEL, 1999).

As dermal absorption could significantly contribute to the total body burden, a 'skin' notation was also recommended. (SCOEL, 1999).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH® and DFG reviews, WorkSafe considers its current WES-TWA of 3ppm (12mg/m^3) and WES-STEL of 5ppm (20mg/m^3) for triethylamine, to be inadequate to manage health risks from possible workplace exposure.

It is recommended for triethylamine that a WES-TWA of 0.5ppm (2.1mg/m^3) and a WES-STEL of 1ppm (4.2mg/m^3) are adopted, to protect against visual impairment and upper respiratory tract irritation, based on the ACGIH® recommendations. The *skin* notation should be retained.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/triethylamine#section=Chemical-and-Physical-Properties
CAS Number	121-44-8
Conversion factors	1mg/m³ = 0.24ppm (25°C; 101.3**kPa**) 1ppm = 4.13mg/m³ (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Ethanamine, N,N-diethyl www.epa.govt.nz/database-search/approved-hazardous-substances-with-controls/view/997D38F8-A52C-4958-84D4-2B474B59B18D Hazardous substances classification codes www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

References: PubChem 2021; **IFA**, 2021; **EPA**, 2021

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Triethylamine."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

Deutsche Forschungsgemeinschaft (DFG), 1999. *"Triethylamine."* MAK Value Documentation, 1999; The MAK Collection for Occupational Health and Safety; pp 267-280. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb12144e0013

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Environmental Protection Authority (EPA), 2021. Hazardous substances classification codes. www.epa.govt.nz/industry-areas/hazardous-substances/rules-for-hazardous-substances/hazardous-substances-classification-codes

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Scientific Committee on Occupational Exposure Limits (SCOEL), 1999. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for triethylamine."* SCOEL/SUM/55

VANADIUM PENTOXIDE, as V

CAS NO: 1314-62-1

Summary

Workplace Exposure Standards for vanadium pentoxide, as V (dust and fume) (CAS: 1314-62-1)

	CURRENT	PROPOSED
WES-TWA	0.05**mg/m³**	0.05mg/m³
WES-STEL	–	–
WES-Ceiling	–	–
Notations	–	Does not apply to other vanadium compounds

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for vanadium pentoxide, as V (dust and fume)

Recommendation and basis for WES

It is proposed that WorkSafe:

1. revise the WES-TWA for vanadium to apply only to vanadium pentoxide, as V (dust and fume) of 0.05mg/m³.

To protect for upper respiratory tract irritation.

Discussion

Vanadium, usually as vanadium pentoxide, is most often encountered in the workplace due to its presence in oil, coal and certain metal ores during or after combustion (soot) or processing. Vanadium pentoxide is used in some catalytic processes, and possible exposure can occur during catalyst recovery (**Safe Work Australia**, 2020; **ACGIH®**, 2009; SCOEL, 2004).

Vanadium pentoxide is odourless (PubChem, 2022).

Cancer risks

The International Agency for Research on Cancer (**IARC**) evaluation of vanadium pentoxide concluded that:

> There is ***inadequate evidence in humans*** for the carcinogenicity of vanadium pentoxide.
>
> There is ***sufficient evidence in experimental animals*** for the carcinogenicity of vanadium pentoxide.

With an overall evaluation that:

> Vanadium pentoxide is possibly carcinogenic to humans (**Group 2B**). (IARC, 2006).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of vanadium pentoxide noted that the critical effects were upper and lower respiratory tract irritation (ACGIH®, 2009).

The ACGIH® review concluded that:

"Vanadium pentoxide exposure produces upper respiratory symptoms in both man and animals (Kiviluoto, 1980; Knecht *et al*., 1985; Sjoberg, 1951; Zenz and Berg, 1967; Williams, 1952; Woodin *et al*., 2000; Lees, 1980; Lewis, 1959; Vintinner *et al*., 1955; Kiviluoto *et al*., 1979a). In the Lewis (1959) study, there was a statistically significant difference in eye, nose, and throat irritation, productive cough, and wheezing when vanadium pentoxide concentrations were, with one exception, between 0.1 and 0.3mg/m^3. Objective confirmation of irritant effects at the 0.2 to 0.5mg/m^3 level on chronic exposure is suggested by an increase in the number of neutrophils and lymphocytes in nasal swab and an infiltration of mononuclear cells and structural changes of the mucous membrane surfaces (Kiviluoto *et al*., 1979a). Eosinophils were not increased in nasal swab samples after exposure to vanadium pentoxide (Zenz and Berg, 1967; Kiviluoto *et al*., 1979a; Kiviluoto, 1980).

"No studies suggesting an immune-mediated hypersensitivity to vanadium compounds were found. In subchronic inhalation studies of cynomolgus monkeys, Knecht *et al*. (1992) found that cytological, immunological and skin test results indicated the absence of allergic sensitization. However, plasma cells in nasal swabs were increased in a vanadium pentoxide exposed group compared to referents (Kiviluoto *et al*., 1979a). There is scant evidence to suggest that vanadium pentoxide exposure causes asthma. The evidence consists of *in vitro* data showing that sodium metavanadate applied to human bronchus *in vitro* resulted in smooth-muscle contraction (Cortijo *et al*., 1997). Case reports of asthma among exposed workers (Musk and Tees, 1982) and small-scale case-control and cross-sectional studies suggest that vanadium pentoxide exposure is associated with increased bronchial responsiveness (Pistelli *et al*., 1991; Irsigler *et al*., 1999).

"No radiographic evidence of pneumoconiosis has been associated with vanadium pentoxide exposure (Vintinner *et al*., 1955; Sjoberg, 1950, Kiviluoto, 1980)."

The critical effect upon which the **TLV-TWA** recommendation is made is chronic upper airway irritation. There are several epidemiologic studies linking upper respiratory symptoms to vanadium pentoxide exposure (Sjoberg, 1951; Woodin *et al*., 2000; Kiviluoto, 1980; Kiviluoto *et al*., 1979a; Vintinner *et al*., 1955; Lewis, 1959), and on controlled exposure (Zenz and Berg, 1967). The lowest mean exposure linked to respiratory symptoms was 0.0089mg V/m^3 with some samples exceeding 0.05mg **V**/m^3 (Woodin *et al*., 2000). However, in this study, in addition to V_2O_5 dust, exposures consisted of unspecified PM10 dust and ozone. Exposure concentrations were estimated using work-diaries and assumed respirator protection factors. For these reasons, the precision of exposure-response estimates should be questioned.

"In the human study that provided the best lowest-observed-adverse-effect level (**LOAEL**) exposure-response information, subjects exposed at 0.2 to 0.5mg V/m^3 measured as total dust for 11 years in the vanadium industry did not have an increased prevalence of upper respiratory symptoms. These subjects did, however, have increased leukocytes on nasal biopsy and increased self-reported "wheezing" compared to a referent group (Kiviluoto, 1980; Kiviluoto *et al*., 1979a). Although the Kiviluoto *et al*. 1979a) description contains some ambiguities, it appears that the differences in nasal biopsy results between the exposed and referents resolved after exposure was reduced to the 0.01 to 0.04mg V/m^3 range measured as total dust (Kiviluoto *et al*., 1979a). The human data of Kiviluoto *et al*. (1979a) support a TLV-TWA of 0.01 to 0.04mg/m^3 measured by a "total dust" air sampler. In view of the

upper airway location of the critical effect, upon which this TLV-TWA is recommended, an inhalable particulate matter designation is appropriate. Insufficient data on particle size distribution were available to determine a precise conversion factor. However, based on the fact that 80% of the particulate was >5µm and upon the work of Werner *et al*. (1996), a conversion factor of two may reflect the levels that would have been measured had an inhalable particulate matter sampler been used and would have been higher than those using a total dust sampler. The adjusted range of inhalable-equivalent concentrations not associated with nasal changes is 0.02-0.08mg V/m3. For these reasons, a TLV-TWA eight-hour inhalable particulate matter value of 0.05mg V/m^3, the adjusted mean of the no effect range is recommended and is expected to protect workers exposed to vanadium pentoxide from airway inflammatory changes. The human exposure studies of Zenz and Berg (1967) showing positive effects at 0.1mg/m^3 vanadium dust in which 98% of the particles were less than 5µ [*sic*] in diameter indicate that this TLV-TWA is not excessively conservative. It should be noted that although the TLV-TWA 0.05mg/m^3 value for vanadium pentoxide is measured as elemental vanadium, this recommendation does not extend to other vanadium-containing compounds. With regard to carcinogenicity, our literature search found no human epidemiologic evidence of carcinogenic activity. However, epidemiological studies capable of discerning a carcinogenic effect have not been done. There is clear evidence of the carcinogenic activity of inhaled vanadium pentoxide in mice of both genders at exposures as low as 1mg/m^3 with a no-observed-adverse-effect level (**NOAEL**) (**NTP**, 2002). However, the squamous carcinomas, lacking metastases or local invasivity, were felt to be uncharacteristic of malignant neoplasia. There is also some, or equivocal, evidence of carcinogenic activity in rats (NTP, 2002); the neoplastic response in male rats exposed to 1mg/m^3 was just within the NTP-2000 diet or NIH07 diet (inhalation) historical control ranges, while there was equivocal evidence in female rats. Thus, the NTP study supports an **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, notation." (references cited in ACGIH®, 2009).

The ACGIH® noted that there was insufficient data to recommend a **TLV-STEL**, or skin or sensitiser notations for vanadium pentoxide (ACGIH®, 2009).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of vanadium and its inorganic compounds noted that the critical effects were carcinogenic (in animals) and genotoxic effects (DFG MAK, 2009).

The DFG noted that a **MAK** value could not be set for bioavailable vanadium compounds as no NOAEL could be determined from human or animal studies (DFG MAK, 2009; 1992). Vanadium and its other inorganic compounds, including vanadium pentoxide, were classified in Carcinogen category 2; and, in Germ cell mutation category 2 due evidence of **DNA** damage in testes and two positive dominant lethal assays in rats and mice (DFG MAK, 2009).

The DFG noted that there was no data available for vanadium compounds to assign **"H"** notations (DFG MAK, 2009).

"Sh" and **"Sa"** notations were not assigned for vanadium compounds due to the lack of evidence of positive effects (DFG MAK, 2009).

SCOEL

The Scientific Committee on Occupational Exposure Limits (**SCOEL**) evaluation of vanadium pentoxide noted that the critical effects were genotoxicity and respiratory tract irritation (SCOEL, 2004).

The SCOEL noted that a health-based **OEL** could not be derived for vanadium pentoxide because *in vivo* and *in vitro* studies suggested that vanadium pentoxide is genotoxic and reprotoxic. The SCOEL did note that exposures to vanadium pentoxide at concentrations of less than 0.1mg/m3 did not appear to cause respiratory tract irritation (SCOEL, 2004).

Conclusions

Based on the documentation cited, and informed by the conclusions of the ACGIH®, DFG and SCOEL reviews, WorkSafe considers its current WES-TWA of 0.05mg/m^3 for vanadium pentoxide to be adequate to manage health risks from possible workplace exposure but the limit does not apply to other vanadium compounds.

It is recommended for vanadium pentoxide, as V, (dust and fume) that the WES-TWA of 0.05mg/m^3 to protect against upper respiratory tract irritation, based on the ACGIH® recommendations. It should be noted that due the potential of vanadium and its inorganic compounds for genotoxicity, exposure at the recommended WES-TWA may not eliminate all risk, as no thresholds have been established, and exposures should be kept as low as possible.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/14814#section=Chemical-and-Physical-Properties
CAS Number	1314-62-1
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Vanadium pentoxide www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/34803B21-FD16-49EE-B50C-4F4950E53391

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Vanadium pentoxide."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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Deutsche Forschungsgemeinschaft (DFG), 2009. *"Vanadium and its inorganic compounds (inhalable fraction)."* MAK Value Documentation in German language, 2009. The MAK-Collection for Occupational Health and Safety; pp 249-285. https://onlinelibrary.wiley.com/doi/epdf/10.1002/3527600418.mb744062e0025

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Scientific Committee on Occupational Exposure Limits (SCOEL), 2004. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for vanadium pentoxide."* SCOEL/SUM/62

VINYL ACETATE

CAS NO: 108-05-4

Summary

Workplace Exposure Standards for vinyl acetate (CAS: 108-05-4)

	CURRENT	PROPOSED
WES-TWA	5**ppm** (18**mg/m³**)	5ppm (18mg/m³)
WES-STEL	10ppm (35mg/m³)	10ppm (35mg/m³)
WES-Ceiling	-	-
Notations	***carcinogen category 2***	*carcinogen category 2*

TABLE 1: Current and proposed Workplace Exposure Standards (**WES**) for vinyl acetate

Recommendation and basis for WES

It is proposed that WorkSafe:

1. adopt the interim WES-TWA for vinyl acetate of 5ppm (18mg/m³)
2. adopt the interim WES-STEL for vinyl acetate of 10ppm (35mg/m³), and
3. maintain the *carcinogen category 2* notation.

To protect for upper respiratory tract and eye irritation.

Discussion

Vinyl acetate is used to produce polyvinyl acetate emulsions (adhesives, paints, printing inks, textiles, and paper products), acrylic fibres, and polyvinyl alcohol (**Safe Work Australia**, 2020; **ACGIH®**, 2018; **SCOEL**, 2005).

Vinyl acetate has a sweet, ether-like odour at low concentrations that becomes sharp and sour with time or at higher concentrations, and with odour thresholds reported from 0.36-0.5ppm (PubChem, 2022; ACGIH®, 2018; SCOEL, 2005).

Cancer risks

The International Agency for Research on Cancer (**IARC**) evaluation of vinyl acetate concluded that:

> There is ***inadequate evidence in humans*** for the carcinogenicity of vinyl acetate.
>
> There is ***limited evidence in experimental animals*** for the carcinogenicity of vinyl acetate.

With an overall evaluation that:

> Vinyl acetate is *possibly carcinogenic to humans* (**Group 2B**). (IARC, 1995).

IARC noted that: vinyl acetate is rapidly transformed to acetaldehyde in human blood and animal tissues; there is ***sufficient evidence in experimental animals*** for the carcinogenicity of acetaldehyde; both vinyl acetate and acetaldehyde induce nasal cancer in rats after inhalation; and, vinyl acetate and acetaldehyde are genotoxic in human cells *in vitro* and in animals *in vivo* (IARC, 1995).

DFG

The Deutsche Forschungsgemeinschaft (**DFG**, German Research Foundation) re-evaluation of vinyl acetate noted that the critical effects were nasal irritation and the induction of nasal tumours in rats (DFG MAK, 2020).

The DFG noted that the **MAK** value of 10ppm for vinyl acetate, **peak limitation Category I** with an excursion factor of 2, were based on a **NOAEC** of 19ppm for acidification in the nasal epithelia of humans from a **PBPK** model, and reports of slight sensory irritation from volunteers exposed to 20ppm. The DFG stated that non-linear dose-response curves from carcinogenicity studies and genotoxicity studies *in vitro* indicated that the genotoxicity of vinyl acetate was not primarily responsible for nasal tumour induction, which mechanistic studies had shown only occurred after acidification, cytotoxicity and cell proliferation (DFG MAK, 2020).

The DFG noted that an *in vitro* dermal absorption study indicated that toxicologically significant amounts of vinyl acetate could potentially be absorbed, so an **"H"** notation was assigned (DFG MAK, 2020).

"Sh" and **"Sa"** notations were not assigned for vinyl acetate due to the lack of data (DFG MAK, 2020; 2005).

ACGIH®

The American Conference of Governmental Industrial Hygienists' (ACGIH®) review of vinyl acetate noted that the critical effects were upper respiratory tract and eye irritation (ACGIH®, 2018).

The ACGIH® review concluded that:

> "A **TLV-TWA** of 10ppm (35mg/m^3) is recommended to minimize the potential risk of respiratory tract irritation reported in animals exposed to vinyl acetate (**VA**) vapor above 50ppm, the no-observed-adverse-effect level (**NOAEL**) for microscopic evidence of respiratory tract irritation in Sprague-Dawley rats and Swiss-derived CD-1 mice (Bogdanffy *et al*., 1994a). A **TLV-STEL** of 15ppm (53mg/m^3) is recommended to minimize the potential for eye and upper respiratory tract irritation reported in short-term exposures to humans a 22ppm and 72ppm (Deese and Joyner, 1969; Smyth and Carpenter, 1973 as cited in U.S. ATSDR, 1992).
>
> "A carcinogenicity notation of **A3**, **Confirmed Animal Carcinogen with Unknown Relevance to Humans**, is assigned, based on the multiple site tumorigenic responses in male rats exposed to VA above 600ppm (Bogdanffy *et al*., 1994a). In a drinking water study, F344 rats exposed to 2,500mg/L VA displayed excess risks of cancer (Lijinsky and Reuber, 1983). There is evidence of genotoxicity in human and animal cells *in vitro* (Bartsch *et al*., 1987; Jung *et al*., 1992; JETOC, 2004; Brams e al., 1987; Norppa *et al*., 1985; Jantunen *et al*, 1986; Mustonen *et al*., 1986; Mäki-Paakanen and Norppa, 1987; Kirby, 1983 as cited in European Commission, 2008), and in animal cells *in vivo* (Mäki-Paakanen and Norppa, 1987; Takeshita *et al*., 1986; Simon *et al*., 1985; Lahdetie, 1988; European Commission, 2008).
>
> "No reliable epidemiological evidence was identified." (references cited in ACGIH®, 2018).

The ACGIH® noted that there was insufficient data to recommend **Skin** or **RSEN** notations for vinyl acetate, while limited evidence did not support the recommendation of a **DSEN** notation (ACGIH®, 2018).

SCOEL

The Scientific Committee on Occupational Exposure Limits (SCOEL) evaluation of vinyl acetate noted that the critical effects were nasal and upper respiratory tract irritation (SCOEL, 2005).

The SCOEL noted that the health-based **OEL** of 5ppm and STEL of 10ppm were based on NOAELs of 10ppm for irritation in humans, and 50ppm for histological changes in respiratory tissues in rodents. The SCOEL stated the premise being that a threshold appeared to exist where physiological buffering systems prevented intracellular acidification that could induce cytotoxicity and cellular proliferation in the presence of **DNA**-reactive and genotoxic acetaldehyde (SCOEL, 2005).

A "skin" notation was not recommended due to the volatility of vinyl acetate limited potential dermal exposure; and, available evidence suggested that vinyl acetate was not a skin sensitiser, while there was no data on possible respiratory sensitisation (SCOEL, 2005).

Conclusions

Based on the documentation cited, and informed by the conclusions of the DFG, ACGIH® and SCOEL reviews, WorkSafe considers its current interim WES-TWA of 5ppm (18mg/m^3) and WES-STEL of 10ppm (35mg/m^3) for vinyl acetate to be adequate to manage health risks from possible workplace exposure.

It is recommended for vinyl acetate that the interim WES-TWA of 5ppm (18mg/m^3) and the interim WES-STEL of 10ppm (35mg/m^3) are adopted, to protect against upper respiratory tract and eye irritation, based on the SCOEL recommendations. Prevention of local irritation should be protective against potential carcinogenicity, but due the potential of vinyl acetate for genotoxicity, exposure at the recommended WES-TWA may not eliminate all risk, as no thresholds have been established, and exposures should be kept as low as possible.

Appendices

Appendix 1: Additional information

Glossary	Definition of terms used in this document
Physicochemical properties	https://pubchem.ncbi.nlm.nih.gov/compound/Vinyl-acetate#section=Chemical-and-Physical-Properties
CAS Number	108-05-4
Conversion factors	1mg/m^3 = 0.28ppm (25°C; 101.3**kPa**) 1ppm = 3.52mg/m^3 (25°C; 101.3kPa)
Exposure standards from around the world	http://limitvalue.ifa.dguv.de
HSNO Classification	HSNO Classification: Acetic acid ethenyl ester www.epa.govt.nz/database-search/chemical-classification-and-information-database-ccid/view/40011187-4E9D-4B03-B3B0-6AA738DBBCD8

References: PubChem 2022; **IFA**, 2022; **EPA**, 2022

Appendix 2: References

American Conference of Governmental Industrial Hygienists (ACGIH®), 2003. *"Vinyl acetate."* Chemical Substances 8th Edition Documentation. Cincinnati, Ohio: ACGIH®. From ACGIH®, *Documentation of the Threshold Limit Values and Biological Exposure Indices*, 8th Edition. Copyright 2020. Reprinted with permission (see the Statement of Position Regarding the TLVs® and BEIs® and Policy Statement on the Uses of TLVs® and BEIs®)

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National Center for Biotechnology Information. PubChem Database. Accessed April 2022. *Vinyl acetate*, CID: 7904. https://pubchem.ncbi.nlm.nih.gov/compound/Vinyl-acetate

Safe Work Australia (2020). Safe Work Australia Draft Evaluation Report and Recommendations – *Vinyl acetate*. https://engage.swa.gov.au/65429/widgets/323765/documents/192036

Scientific Committee on Occupational Exposure Limits (SCOEL), 2005. *"Recommendation from the Scientific Committee on Occupational Exposure Limits for Vinyl Acetate."* SCOEL/SUM/122

Glossary

TERM	MEANING
#	
1-NP	1-Nitropropane.
1,1,2-TCE	1,1,2-Trichloroethane.
2-DAE	2-Diethylaminoethanol.
2-HMSI	2-Hydroxy-*N*-methylsuccinimide.
2,4-D	2,4-Dichlorophenoxyacetic acid.
5-HNMP	5-Hydroxy-*N*-methyl-2-pyrrolidone.
A	
A3 Confirmed Animal Carcinogen with Unknown Relevance to Humans	The agent is carcinogenic in experimental animals at relatively high dose, by route(s) of administration, at site(s), of histological type(s), or by mechanism(s) that may not be relevant to worker exposure. Available epidemiologic studies do not confirm an increased risk of cancer in exposed humans. Available evidence does not suggest that the agent is likely to cause cancer in humans except under uncommon or unlikely routes or levels of exposure. An ACGIH® term.
A4 Not Classifiable as a Human Carcinogen	Agents which cause concern that they could be carcinogenic for humans but which cannot be assessed conclusively because of lack of data. *In vitro* or animal studies do not provide indications of carcinogenicity which are sufficient to classify the agent into one of the other categories. An ACGIH® term.
A5 Not Suspected as a Human Carcinogen	The agent is not suspected to be a human carcinogen on the basis of properly conducted epidemiological studies in humans. These studies have sufficiently long follow-up, reliable exposure histories, sufficiently high dose, and adequate statistical power to conclude that exposure to the agent does not convey a significant cancer risk to humans, OR, the evidence suggesting a lack of carcinogenicity in experimental animals is supported by mechanistic data. An ACGIH® term.
ACGIH®	The American Conference of Governmental Industrial Hygienists (ACGIH®) is a member-based organisation, established in 1938, that advances occupational and environmental health. Examples of this include their annual edition of the TLVs® and BEIs® book and work practice guides. Store at https://portal.acgih.org
AHR	Airway hyper-reactivity.
AIHA	American Industrial Hygiene Association.
Al	Aluminium.
ANSES	Agence Nationale de Sécurité Sanitaire de l'Alimentation, de l'Environnement et du Travail.
B	
BALF	Bronchoalveolar lavage fluid.
BAT	Biologische Arbeitsstoff-Toleranzwerte [Biological Tolerance Value], a DFG term.
BE	2-Butoxyethanol.
BEI®	Biological Exposure Index – an ACGIH® term.
BHR	Bronchial hyperreactivity.
bio	Exposure can also be estimated by biological monitoring. A WorkSafe term.
$BMDL_{05}$	Bench-mark dose, 95% lower confidence limit.
b.w. or bw	Body weight.

TERM	MEANING
C	
CaO	Calcium oxide.
$Ca(OH)_2$	Calcium hydroxide.
Carcinogen category 1	DFG MAK designation: Substances that cause cancer in man and can be assumed to contribute to cancer risk. Epidemiological studies provide adequate evidence of a positive correlation between the exposure of humans and the occurrence of cancer. Limited epidemiological data can be substantiated by evidence that the substance causes cancer by a mode of action that is relevant to man. [Note: category definitions are periodically revised.]
Carcinogen category 2	DFG MAK designation: Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can contribute to cancer risk. Limited data from animal studies can be supported by evidence that the substance causes cancer by a mode of action that is relevant to man and by results of *in vitro* tests and short-term animal studies. [Note: category definitions are periodically revised.]
Carcinogen category 3	DFG MAK designation: Substances that cause concern that they could be carcinogenic for man but cannot be assessed conclusively because of lack of data. *In vitro* tests or animal studies have yielded evidence of carcinogenicity that is not sufficient for classification of the sub-stance in one of the other categories. The classification in Category 3 is provisional. Further studies are required before a final decision can be made. A MAK value can be established provided no genotoxic effects have been detected. [Note: category definitions are periodically revised.]
Carcinogen category 3A	DFG MAK designation: Substances that cause cancer in humans or animals or that are considered to be carcinogenic for humans for which the criteria for classification in Category 4 or 5 are in principle fulfilled. However, the database for these substances is insufficient for the establishment of a MAK or BAT value. [Note: category definitions are periodically revised.]
Carcinogen category 3B	DFG MAK designation: Substances for which *in vitro* or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories. Further studies are required before a final decision can be made. A MAK or BAT value can be established provided no genotoxic effects have been detected. [Note: category definitions are periodically revised.]
Carcinogen category 4	DFG MAK designation: Substances that cause cancer in humans or animals or that are considered to be carcinogenic for humans and for which a MAK value can be derived. A nongenotoxic mode of action is of prime importance and genotoxic effects play no or at most a minor part provided the MAK and BAT values are observed. Under these conditions no contribution to human cancer risk is expected. The classification is supported especially by evidence that, for example, increases in cellular proliferation, inhibition of apoptosis or disturbances in cellular differentiation are important in the mode of action. The classification and the MAK and BAT values take into consideration the manifold mechanisms contributing to carcinogenesis and their characteristic dose-time-response relationships. [Note: category definitions are periodically revised.]
Carcinogen category 5	DFG MAK designation: Substances that cause cancer in humans or animals or that are considered to be carcinogenic for humans and for which a MAK value can be derived. A genotoxic mode of action is of prime importance but is considered to contribute only very slightly to human cancer risk, provided the MAK and BAT values are observed. The classification and the MAK and BAT values are supported by information on the mode of action, dose-dependence and toxicokinetic data. [Note: category definitions are periodically revised.]
CAS	Chemical Abstracts Service.
CASN or CAS No.	Chemical Abstracts Service Number.
Ceiling or Ceiling Limit Value	Ceiling Limit Value – absolute exposure limit that should not be exceeded at any time.
CFC-11	Fluorotrichloromethane (Trichlorofluoromethane; **CASN**: 75-69-4).

TERM	MEANING
CFC-112a	1,1,1,2-Tetrachloro-2,2-difluoroethane.
CFC-113	1,1,2-Trichloro-1,2,2-trifluoroethane.
Cl_2	Chlorine.
CLP	EU Classification, Labelling and Packaging of substances and mixtures.
CN-	Cyanide ion.
CNS	Central nervous system.
CO	Carbon monoxide.
COPD	Chronic obstructive pulmonary disease.
Cr(VI)	Chromium 6 or hexavalent chromium.
CYP2E1	Cytochrome P450 family 2; subfamily E; member 1.
CYP2F	Cytochrome P450 family 2; subfamily F.
D	
DBTC	Di-*n*-butyltin dichloride.
DCPD	Dicyclopentadiene.
DEAE	2-Diethylaminoethanol.
DECOS	Dutch Expert Committee on Occupational Standards a Committee [DECOS] of the *Health Council of the Netherlands*. The latter was established in 1902 as an independent scientific advisory body with a remit: "to advise the government and Parliament on the current level of knowledge with respect to public health issues and health (services) research..." (Section 22, Health Act).
DEHP	Di(2-ethylhexyl)phthalate.
DGUV-IFA	Deutschen Gesetzlichen Unfallversicherung ([German Social Accident Insurance] - Institut für Arbeitsschutz [Institute for Occupational Safety and Health].
DFG	Deutsche Forschungsgemeinschaft (German Research Foundation), the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Federal Republic of Germany. The science-based MAK values are recommended to the German Minister of Labour and Social Affairs for possible adoption under the German Hazardous Substances Ordinance.
DMAC	Dimethylacetamide.
DMDI	Methylene bis(4-cyclohexylisocyanate).
DMTC	Dimethyltin dichloride.
DNA	Deoxyribonucleic acid.
DNEL	Derived No Effect Level.
DPGME	Dipropylene glycol methyl ether.
DSEN	A notation indicating the substance is a dermal sensitiser. DSEN is used in place of SEN when specific evidence of sensitisation by the dermal route is confirmed by human or animal data. An ACGIH® term.
dsen	Dermal sensitiser. See also **sen**. A WorkSafe term.

TERM	MEANING
E	
ECB	The European Chemicals Bureau.
ECHA	The European Chemicals Agency (an agency of the European Union).
EPA	The New Zealand Environmental Protection Authority.
Evidence suggesting lack of carcinogenicity **(animals)**	Adequate studies in at least two species show that the agent is not carcinogenic; Conclusion is limited to the species, tumour sites, age at exposure, and conditions and level of exposure studied. An IARC term.
Evidence suggesting lack of carcinogenicity **(humans)**	Several adequate studies covering the full range of exposure levels are mutually consistent in not showing a positive association at any observed level of exposure; Conclusion is limited to cancer sites and conditions studied. An IARC term.
F	
F	Chemical symbol for fluoride.
F0	Parents to first filial generation, F1.
F_2	Chemical symbol for fluorine.
FC-22	Chlorodifluoromethane.
FCAT	Freund's complete adjuvant test.
FEV_1	Forced expiratory volume in 1 second.
Fume	Fumes are very small airborne solid particulates with diameters generally less than 1μm. They may be formed by both thermal mechanisms (for example, condensation of volatilised solids, or incomplete combustion) and chemical processes (for example, vapour phase reactions). Agglomeration of fume particles may occur, resulting in the formation of much larger particles.
FVC	Forced vital capacity: the volume of air that can be forcibly blown out after full inspiration (litres).
G	
GESTIS	Gefahrstoffinformationssystem.
GHS	Globally Harmonized System of Classification and Labelling of Chemicals.
Group 1	IARC designation: The agent is carcinogenic to humans.
Group 2A	IARC designation: The agent is probably carcinogenic to humans.
Group 2B	IARC designation: The agent is possibly carcinogenic to humans.
Group 3	IARC designation: The agent is not classifiable as to its carcinogenicity to humans.
Group 4	IARC designation: The agent is probably not carcinogenic to humans.
GSD	Geometric Standard Deviation describes how spread out are a set of numbers whose preferred average is the geometric mean. In this context, the spread of particle sizes.
GSTT1-1	Glutathione S-transferase (GST) theta 1.

TERM	MEANING
H	
"H"	DFG MAK designation: *danger of percutaneous absorption*. Equivalent to the *skin notation* in the WorkSafe WES special guide.
HBROEL or HBR-OEL	Health-based recommended exposure limit. European Union term; a DECOS term.
HCN	Chemical symbol for hydrogen cyanide.
HMDI	Hexamethylene diisocyanate.
HSNO	Hazardous Substances and New Organisms Act 1996, New Zealand.
I	
IARC	International Agency for Research on Cancer – an agency of the World Health Organisation.
IDLH	Immediately Dangerous to Life or Health Concentration. IDLH values are established by NIOSH to (1) to ensure that the worker can escape from a given contaminated environment in the event of failure of the respiratory protection equipment, and (2) to indicate a maximum level above which only a highly reliable breathing apparatus, providing maximum worker protection, is permitted.
ID$^{(SK)}$	A critical review has determined that the quantity and quality of the available data are insufficient to accurately assess the hazards of skin exposure to assign any of the skin notations. A NIOSH notation.
IFA	Institut für Arbeitsschutz der Deutschen Gestzlichen Unfallversicherung [Institute for Occupational Safety and Health of the German Social Accident Insurance].
IgE	Immunoglobulin E.
IgG	Immunoglobulin G.
***Inadequate evidence* (animal)**	Studies permit no conclusion about carcinogenic effect. An IARC term.
***Inadequate evidence* (human)**	Studies permit no conclusion about causal association. An IARC term.
Inhalable fraction	Inhalable particulate fraction is that fraction of dust that can be breathed into the nose or mouth. Particulate size: mostly <100µm, 50% cut point. For sampling purposes the inhalable dust is to be collected according to the method set out in AS 3640-2009: Workplace Atmospheres – Method for Sampling and Gravimetric Determination of Inhalable Dust (Standards Australia, 2009). (*cf*. Respirable fraction) (Also referred to as: inhalable aerosol; inhalable particulate matter).
Inhalable Fraction and Vapour (ifv)	The Inhalable Fraction and Vapour (ifv) notation is used when a material exerts sufficient vapour pressure such that it may be present in both particle and vapour phases, with each contributing to a significant portion of exposure.
IPDI	Isophorone diisocyanate.
IPE	2-Isopropoxyethanol.
K	
Known to be a human carcinogen	There is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer. A US NTP term.

TERM	MEANING
L	
LD_{50}	Lethal Dose for 50% of the test population.
LH	Luteinising (luteinizing) hormone.
Ligand	A molecule (or ion) that binds with a central (metal) atom to form a coordination complex.
***Limited evidence* (animal)**	Data suggest a carcinogenic effect but: (for example) single study, benign tumours only, promoting activity only. An IARC term.
***Limited evidence* (human)**	Causal interpretation is credible; chance, bias, or confounding could not be ruled out. An IARC term.
LLNA	Local lymph node assay.
LOAEC	Lowest Observed Adverse Effect Concentration.
LOAEL	Lowest Observed Adverse Effect Level.
LOEL	Lowest Observed Effect Level.
M	
MAK	Maximale Arbeitsplatz-Konzentration, (maximum workplace concentration) is defined as the maximum concentration of a chemical substance (as gas, vapour or particulate matter) in the workplace air which generally does not have known adverse effects on the health of the employee nor cause unreasonable annoyance (for example, by a nauseous odour) even when the person is repeatedly exposed during long periods, usually for 8 hours daily but assuming on average a 40-hour working week. Values set by the DFG.
MDI	Methylene diphenyl diisocyanate.
MetHb	Methaemoglobin.
MIBC	Methyl isobutyl carbinol.
MIBK	Methyl isobutyl ketone (Hexone).
MIC	Methyl isocyanate.
MMA	Methyl methacrylate.
MMAD	Mass Median Aerodynamic Diameter (MMAD) is the diameter at which 50% of the particles by mass are larger and 50% smaller.
MMTC	Methyltrichlorotin.
Momentary value	A workplace air concentration which should not be exceeded at any time (equivalent to a WES-Ceiling). A DFG term.
N	
NAEC	No adverse effect concentration.
NAEL	No adverse effect level.
NaOH	Sodium hydroxide.
-NCO; NCO	Isocyanate group (-N=C=O).
NDI	1,5-Naphthylene diisocyanate.
NIOSH	The National Institute for Occupational Safety and Health is the United States federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness.

TERM	MEANING
NMA	*n*-Methyl aniline; *n*-Methylaniline.
NO_2	Nitric dioxide.
NOAEC	No Observed Adverse Effect Concentration.
NOAEL	No Observed Adverse Effect Level.
NOEL	No Observed Effect Level.
NTP	National Toxicology Program, US Department of Health and Human Services.
O	
OA	Occupational asthma.
OEL	Occupational Exposure Limit (equivalent to a WES).
Ototoxin	Substances that can cause hearing loss either in conjunction with noise exposure, or without concurrent noise exposure.
P	
P-450	Cytochrome P-450.
PB-PK or PBPK	Physiologically based pharmacokinetic model(s).
PBZ	Personal breathing zone.
Peak limitation Category 1 or I	Substances for which local irritant effects determine the MAK value, also respiratory allergens; Excursion factor = 1 [default]; Duration 15 minutes, average value; Number per shift = 4; Interval = 1 hour. A DFG term.
Peak limitation Category 2 or II	Substances with systemic effects; Excursion factor = 2 [default]; Duration 15 minutes, average value; Number per shift = 4; Interval = 1 hour. A DFG term.
ppb	Parts of vapour or gas per billion parts of air.
ppm	Parts of vapour or gas per million parts of air.
Pregnancy Risk Group B	According to currently available information damage to the embryo or foetus cannot be excluded after exposure to concentrations at the level of the MAK and BAT values. A DFG term.
Pregnancy Risk Group C	Damage to the embryo or foetus is unlikely when the MAK value or the BAT value is observed. A DFG term.
Pregnancy Risk Group D	Either there are no data for an assessment of damage to the embryo or foetus or the currently available data are not sufficient for classification in one of the groups A – C. A DFG term.
PSLT	Poorly soluble low-toxicity.
Q	
QSAR or (Q)SAR	Quantitative structure-activity relationship.
R	
R 112a	1,1,1,2-Tetrachloro-2,2-difluoroethane.
RAC	Committee for Risk Assessment (ECHA).
RADS	Reactive Airways Dysfunction Syndrome.

TERM	MEANING
RBC	Red blood cells.
RD_0	Dose producing a 0% response.
RD_{50}	Dose producing a 50% response.
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals. An EU program and regulation.
Reasonably anticipated to be a human carcinogen	There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded, OR there is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset, OR there is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a hu-man carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans. A US **NTP** term.
REL	Recommended exposure limit (REL) is the name used by NIOSH for the occupational exposure limits (OELs) it recommends to protect workers from hazardous substances and conditions in the workplace.
Respirable fraction (r)	Respirable particulate fraction is that fraction of inhaled airborne particles that can penetrate beyond the terminal bronchioles into the gas-exchange region of the lungs (alveoli). Particulate size: mostly <4µm, 50% cut point. For sampling purposes the respirable dust samples are to be collected according to the method set out in the Standards Australia publication AS 2985-2009: Workplace Atmospheres – Method for Sampling and Gravimetric Determination of Respirable Dust (Standards Australia, 2009). (*cf*. Inhalable fraction) (Also referred to as: respirable aerosol; respirable particulate matter)
RoC or ROC	Report on Carcinogens, produced by the US National Toxicology Program.
rsen	A substance that can 'sensitise' the respiratory system, inducing a state of hypersensitivity to it, so that on subsequent exposures, an allergic reaction can occur (which would not develop in non-sensitised individuals). It is uncommon to become sensitised to a compound after just a single reaction to it. A WorkSafe term.
RSEN	A notation indicating the substance is a respiratory sensitiser. RSEN is used in place of SEN when specific evidence of sensitisation by the inhalation route is confirmed by human or animal data. An ACGIH® term.
S	
"S"	Sensitising. A DFG MAK notation.
"Sa"	Sensitising to airways. A DFG MAK notation.
Safe Work Australia	Safe Work Australia, an Australian government statutory body established in 2008 to develop national policy relating to work health and safety (WHS) and workers' compensation. www.Safe Workaustralia.gov.au
SCOEL	The Scientific Committee on Occupational Exposure Limits is a committee of the European Commission, established in 1995 to advise on occupational health limits for chemicals in the workplace within the framework of Directive 98/24/EC, the chemical agents directive, and Directive 90/394/EEC, the carcinogens at work directive.
SEG	The Scientific Expert Group on Occupational Exposure Limits [SEG] was a committee of the European Commission, established in 1995 to advise on occupational health limits for chemicals in the workplace within the framework of Directive 98/24/EC, the chemical agents directive, and Directive 90/394/EEC, the carcinogens at work directive. The Scientific Committee on Occupational Exposure Limits [SCOEL] has replaced SEG.

TERM	MEANING
sen	A substance that can 'sensitise' the skin or respiratory system, inducing a state of hypersensitivity to it, so that on subsequent exposures, an allergic reaction can occur (which would not develop in non-sensitised individuals). It is uncommon to become sensitised to a compound after just a single reaction to it. A WorkSafe term.
SEN	A notation indicating the substance is a sensitiser. DSEN and RSEN are used in place of SEN when specific evidence of sensitisation by the dermal or respiratory route, respectively, is confirmed by human or animal data. An ACGIH® term.
"Sh"	DFG MAK designation: *danger of sensitisation of the skin*.
skin	Skin absorption – applicable to a substance that is capable of being significantly absorbed into the body through contact with the skin. A WorkSafe term.
Skin	A notation indicating the potential for significant contribution to the overall exposure, by the cutaneous route, including mucous membranes and the eyes, by contact with vapours, liquids and solids. An ACGIH® term.
SK: SYS	Skin notation indicating the potential for systemic toxicity following exposure of the skin. A NIOSH term.
SK: SYS-DIR(COR)	Skin notation indicating the potential for acute toxicity and direct corrosive effects following exposure of the skin. A NIOSH term.
SK: SYS-DIR(COR)-SEN	Skin notation indicating the potential for acute toxicity, direct corrosive effects and immune-mediated reactions following exposure of the skin. A NIOSH term.
SK:SYS-DIR (IRR)	Skin notation indicating the potential for acute toxicity, and direct irritative effects following exposure of the skin. A NIOSH term.
Sn	Chemical symbol for tin.
STEL	Short-Term Exposure Limit. The STEL is a limit value above which exposure should not occur and usually relates to a 15-minute reference period.
STEL (WES-STEL)	The 15-minute time weighted average exposure standard. Applies to any 15-minute period in the working day and is designed to protect the worker against adverse effects of irritation, chronic or irreversible tissue change, or narcosis that may increase the likelihood of accidents. The WES-STEL is not an alternative to the WES-TWA; both the short-term and time-weighted average exposures apply. Exposures at concentrations between the WES-TWA and the WES-STEL should be less than 15 minutes, should occur no more than four times per day, and there should be at least 60 minutes between successive exposures in this range. A WorkSafe term.
Sufficient evidence **(animals)**	Causal relationship has been established through either: - Multiple positive results (2 species, studies, sexes of GLP); - Single unusual result (incidence, site/type, age, multi-site). An IARC term.
Sufficient evidence **(humans)**	Causal relationship has been established; Chance, bias, and confounding could be ruled out with reasonable confidence. An IARC term.
T	
TDI	Toluene diisocyanate.
TEA	Triethylamine.
TLV®	Threshold Limit Value [*see TLV-C, TLV-STEL and TLV-TWA below*]. An ACGIH® term.
TLV-Ceiling or TLV-C	Threshold Limit Value – Ceiling: the concentration that should not be exceeded during any part of the working exposure. If instantaneous measurements are not available, sampling should be conducted for the minimum period of time sufficient to detect exposures at or above the ceiling value. An ACGIH® term.
TLV-STEL	Threshold Limit Value – Short-Term Exposure Limit: a 15-minute TWA exposure that should not be exceeded at any time during a workday, even if the 8-hour TWA is within the TLV-TWA. An ACGIH® term.

TERM	MEANING
TLV-TWA	Threshold Limit Value – Time-Weighted Average: the TWA concentration for a conventional 8-hour workday and a 40-hour workweek, to which it is believed that nearly all workers may be repeatedly exposed to, day after day, for a working lifetime without adverse effect. An ACGIH® term.
TWA	Time-weighted average exposure.
TWA_{8hr}	8-Hour time-weighted average exposure.
U	
Ultrafine fraction	Particles with an individual size less than 100nm (aka nanoparticles).
US EPA	The US Environmental Protection Agency.
V	
V	Vanadium.
V_2O_5	Vanadium pentoxide.
VA	Vinyl acetate.
VDC	Vinylidene chloride (1,1-dichloroethylene).
W	
WEEL	Workplace Environmental Exposure Level – an American Industrial Hygiene Association OEL.
WES	Workplace Exposure Standard – WESs are values that refer to the airborne concentration of substances, at which it is believed that nearly all workers can be repeatedly exposed to, day after day, without coming to harm. The values are normally calculated on work schedules of five shifts of eight hours duration over a 40-hour week. A WorkSafe term.
WES-Ceiling	A concentration that should not be exceeded at any time during any part of the working day. A WorkSafe term.
WES-STEL	The 15-minute time-weighted average exposure standard. Applies to any 15-minute period in the working day and is designed to protect the worker against adverse effects of irritation, chronic or irreversible tissue change, or narcosis that may increase the likelihood of accidents. The WES-STEL is not an alternative to the WES-TWA; both the short-term and time-weighted average exposures apply. Exposures at concentrations between the WES-TWA and the WES-STEL should be less than 15 minutes, should occur no more than four times per day, and there should be at least 60 minutes between successive exposures in this range. A WorkSafe term.
WES-TWA	The average airborne concentration of a substance calculated over an eight-hour working day. A WorkSafe term.

TERM	MEANING
UNITS	
Units	
d/w	Days per week
h/d	Hours per day
Centi-	
cm/hr	Centimetre per hour
Deci-	
dL	Decilitre, or one-tenth of a litre
Gram-	
g	Gram
g/cm³	Gram substance per cubic centimetre of matrix
g/kg bw or g/kg b.w.	Grams of substance per kilogram body weight
Kilo	
kPa	Kilopascal
M	
Mole	The mole is the unit of measurement for amount of substance in the International System of Units. It is defined as exactly 6.02214076×10^{23} particles
Micro-	
µg	Microgram or one millionth of a gram
µg/L or µg/l	Microgram or one millionth of a gram per litre
µg/m³ or µg.m^{-3}	Micrograms of substance per cubic metre of air
µm	Micrometre or one millionth of a metre
Milli-	
mg	Milligram or one thousandth of a gram
mg/kg b.w. or mg/kg bw	Milligram of substance per kilogram body weight
mg/kg bw/day or mg/kg b.w./day or mg/kg/day or mg/kg bw/d	Milligram of substance per kilogram body weight per day (exposure rate)
mg/L or mg/l	Milligram of substance per litre
mg/m³ or mg.m^{-3}	Milligrams of substance per cubic metre (of air)
mL or ml	Millilitre or one thousandth of a litre
mL/kg or ml/kg	Millilitres of substance per kilogram body weight
mL/m³ or ml/m³	Millilitres of substance per cubic metre (of air)
Nano-	
ng	Nanogram [10^{-9} gram]
nm	Nanometres [10^{-9} metres]
Pico-	
pg	Picogram (10^{-12} gram)

Notes

Disclaimer

WorkSafe New Zealand has made every effort to ensure the information contained in this publication is reliable, but makes no guarantee of its completeness.

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Published: March 2024

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WSNZ_4689_MAR 24

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