# Appendix 1 Dossier of substances included within our 2020 EAL Consultation

# Introduction

This document provides a short technical background to the decisions that underpin the derivation of the new Environmental Assessment Levels (EALs) in the Environment Agency's consultation.

The document briefly summarises the toxicity to human health, primarily via inhalation, of priority substances in air following short-term and long-term exposure. Substances have been prioritised for EAL review based on their appearance in the Pollution Inventory for 2016 (the last published dataset). Ten substances listed here have an existing EAL, which will be withdrawn following this consultation and replaced with the recommended guideline. In addition, EALs are introduced for two new substances.

Toxicity summaries are provided for each of the twelve substances presented in the consultation. Key individual references for each substance are provided at the end of each summary. A list of abbreviations and definitions is provided at the end of the document.

# Practical Compliance Constraints on a Short Term EAL

Depending on the toxicity of a substance, both a short- and long-term EAL may be appropriate, reflecting adverse effects to health over different exposure periods. Notwithstanding the possible differences in the toxicology (dose-response and endpoints) between potential short-term and long-term health effects, there is a practical limit on the value of a short-term EAL if the long-term EAL or statutory value is not to be exceeded. The limit depends on whether the long-term EAL is based on either a threshold or a non-threshold health effect.

#### **Threshold Effects**

The long-term EAL is usually based on a 24-hour time weighted mean concentration. The highest short-term air concentration that will not exceed the long-term EAL can be estimated by multiplying the long-term value by 24 for a short-term hourly upper limit. There is no short-term daily upper limit.

#### Non-thresholded Effects

The long-term EAL is usually based on the annual mean (either 90% of 1-hour values or all 24-hour values averaged over a year). The highest short-term air concentration that will not exceed the long-term EAL or statutory value can be estimated by multiplying the long-term value by either 365 or 8,760 (24 \* 365) for a short-term daily or hourly upper limit, respectively.

Any proposed short-term EAL should be less than the appropriate daily or hourly upper limit to be useful without any practical constraint imposed by the need to ensure compliance with the long-term EAL or statutory value. If a recommended short-term EAL is equal to or exceeds the upper limit then it is assumed that compliance with the longterm EAL will be protective of short-term exposures and health effects.

# 1. Arsenic and its compounds (CAS Number 7440-38-2 and others)

Arsenic is a naturally occurring metalloid, which is commonly present in air as mixtures of arsenite (As III) and arsenate (As V) compounds (EPAQS 2009). Because of the high vapour pressure of some compounds such as arsenic (III) trichloride, it can be present as vapour and particulate matter in the environment.

Arsenic is classified as a human carcinogen and the most important effect for inhaled inorganic arsenic appears to be the induction of lung cancer. There is insufficient evidence to conclude whether it is genotoxic via the inhalation route or whether the relationship between dose and risk is linear at low levels of exposure (EPAQS 2009).

## **Regulatory Guidelines**

#### **Recommended Environmental Assessment Level in Air**

Long-term EAL	Not recommended (use Target Value)
Short-term EAL	None (constrained by compliance with the regulatory guideline)

## Supporting Information

Since there is a statutory Target Value for inorganic arsenic under the Ambient Air Directive, no long-term EAL has been recommended. Short-term exposures to higher

concentrations of inorganic arsenic (mostly As III) have reported respiratory irritation and death. A short-term EAL of 1.1 mg/m<sup>3</sup> as an hourly mean can be calculated from the 1-hour Acute Exposure Guideline Level (AEGL-2) value after correction from arsenic (III) trioxide to arsenic (NAC/AEGL 2009).<sup>1</sup> Although this short-term EAL is in agreement with the indicative safe range suggested by EPAQS (2009) for non-carcinogenic effects, it is still greater than an hourly upper limit of 0.053 mg/m<sup>3</sup> (the practical compliance constraint calculated from the Target Value).

### References

EPAQS, 2009. Metals and Metalloids. Expert Panel on Air Quality Standards. ISBN 978-0-85521-185-1.

NAC/AEGL, 2009. Interim Acute Exposure Guideline Levels (AEGLs) for Arsenic Trioxide (CASRN 1327-53-3).

# 2. Benzene (CAS Number 71-43-2)

Benzene is a petroleum hydrocarbon used in many workplace applications (EPAQS 1994). It is ubiquitous in ambient air through volatilisation and combustion processes and is naturally broken down by chemical reactions in the atmosphere.

Benzene is a well-known genotoxic carcinogen with chronic exposure associated with the development of certain leukaemias (ATSDR 2007, EPAQS 1994, WHO 2000 and 2010). Short-term exposures to higher levels of benzene have been associated with a range of health effects including immunotoxicity; haematotoxicity; respiratory, cardiovascular, neurological and renal toxicity; skin and eye irritation; and in some cases death (ATSDR 2007).

### **Regulatory Guidelines**

Ambient Air Directive Limit Value0.005 mg/m³ as an annual mean

## Recommended Environmental Assessment Level in Air

Long-term EAL

Not recommended (use Limit Value)

<sup>&</sup>lt;sup>1</sup> A correction of 0.379 was applied to account for the relative mass difference between arsenic (74.92 g/mol) and arsenic (III) trioxide (197.84 g/mol).

Short-term EAL	30 µg/m³ as a 24-hour mean

# **Supporting Information**

Since there is a statutory Limit Value for benzene under the Ambient Air Directive, no longterm EAL has been recommended. A short-term EAL of 0.03 mg/m<sup>3</sup> as a 24-hour mean concentration is recommended to protect the general public, which is based on the acute Minimal Risk Level (MRL) proposed by ATSDR (2007) for immunological effects.

### References

ATSDR, 2007. Toxicological Profile for Benzene, TP3.

EPAQS, 1994. Expert Panel on Air Quality Standards for benzene. ISBN 0-11-752859-5.

WHO, 2000. Air Quality Guidelines for Europe, Second Edition.

WHO, 2010. Guidelines for Indoor Air Quality: Selected Pollutants.

# 3. Chloroform (CAS Number 67-66-3)

Chloroform, also known as trichloromethane, is a clear, colourless and volatile liquid at room temperature with a pleasant etheric odour (IPCS 2004). Its main uses are in the production of halocarbons and pesticides, as a solvent and degreasing agent, in fire extinguishers, and in the rubber industry. Chloroform is also unintentionally formed during chlorination processes such as paper bleaching and water treatment.

Adverse effects from exposure to chloroform have been reviewed by several authoritative bodies (ATSDR 1997, IPCS 2004, NAC/AEGL 2012). Acute exposures to high concentrations of chloroform can cause central nervous system (CNS) depression, subnarcotic effects, ocular and respiratory irritation, nausea, vomiting and dizziness. The main targets of systemic short-term and chronic toxicity are the CNS, liver and the kidneys. Available epidemiological data is equivocal on its potential carcinogenicity in humans, although it is a carcinogen of the liver and kidney in animals. Tumours seen in animal studies are induced only at doses causing chronic cytotoxicity and most authoritative bodies consider chloroform is not genotoxic.

## **Regulatory Guidelines**

# **Recommended Environmental Assessment Level in Air**

Long-term EAL	100 μg/m³ as a 24-hour mean
Short-term EAL	None (constrained by compliance with the long- term EAL)

# **Supporting Information**

Long-term chronic Health-Based Guidance Values (HBGVs) have been proposed by ATSDR (1997), IPCS (2004), and the industry REACH Dossier, based on either liver or kidney toxicity. Although they are derived from different pivotal studies, there is close agreement between them (from  $0.099 - 0.18 \text{ mg/m}^3$ ). A long-term EAL of  $0.1 \text{ mg/m}^3$  as a 24-hour mean is recommended to protect the general public, which is based on the chronic MRL proposed by ATSDR (1997), who concluded that liver toxicity was the most sensitive effect.

Short-term exposures to higher concentrations of chloroform results in a range of reported effects including liver toxicity, foetotoxicity, and death over exposure durations from hours to days (ATSDR 1997, NAC/AEGL 2012). A proposed short-term EAL of 0.5 mg/m<sup>3</sup> as a 24-hour mean, which is based on the acute MRL proposed by ATSDR (1997), would exceed the long-term EAL.

## References

ATSDR, 1997. Toxicological Profile for Chloroform, TP 6.

IPCS, 2004. Chloroform, Concise International Chemical Assessment Document (CICAD) 58. Geneva: International Programme on Chemical Safety.

NAC/AEGL, 2012. Acute Exposure Guideline Levels for Selected Airborne Chemicals. Volume 12. ISBN 978-0-309-25501-1.

# 4. Chromium VI and its compounds (CAS Number 7440-47-3)

Chromium is a metallic element, which is hard, dense and resistant to chemical attack (EPAQS 2009). Hexavalent chromium (Cr VI) is used for chrome plating, manufacture of dyes and pigments, leather tanning, wood preservation, drilling muds, rust corrosion inhibitors, textiles and toners.

Cr VI is a potent carcinogen with evidence from occupational studies on associations between exposure and increased risk of lung cancer (ATSDR 2012, EPAQS 2009, WHO 2000). Inhalation of Cr VI causes local nasal and lung irritation and altered pulmonary

function, and systemic haematological effects (microcytic, hypochromic anaemia) and also reproductive toxicity (effects on male reproductive organs). Chromium sensitization, the major immunological effect of Cr VI, typically presents as allergic contact dermatitis resulting from dermal exposures in sensitized individuals, although respiratory effects of sensitization (asthma) may also occur. Accidental or intentional ingestion of extremely high doses of Cr VI compounds by humans has resulted in severe respiratory, cardiovascular, gastrointestinal, haematological, hepatic, renal, and neurological effects as part of the sequela leading to death.

### **Regulatory Guidelines**

### **Recommended Environmental Assessment Level in Air**

Long-term EAL	0.00025 μg/m³ as Cr VI (annual mean in PM <sub>10</sub> fraction)
Short-term EAL	None (constrained by compliance with the long-term EAL)

# **Supporting Information**

Long-term HBGVs have been proposed based on increased incidence of lung cancer in occupational studies. Air concentrations associated with an excess lifetime cancer risk (ELCR) at 1 in 100,000 have range from 0.00025  $\mu$ g/m<sup>3</sup> to 0.0008  $\mu$ g/m<sup>3</sup>. The recommended long-term EAL is 0.00025  $\mu$ g/m<sup>3</sup> as Cr VI (the annual mean from the PM<sub>10</sub> fraction), which is based on the unit risk calculated by WHO (2000).

Short-term exposure to higher concentrations of Cr VI results in potential sensitisation with respiratory irritation reported in workers exposed to 2  $\mu$ g/m<sup>3</sup> (ATSDR 2012). This is comparable with an hourly upper limit of 2.2  $\mu$ g/m<sup>3</sup> and much higher than a daily upper limit of 0.09  $\mu$ g/m<sup>3</sup> (the practical compliance constraints calculated from the long-term EAL). Therefore a short-term EAL is not recommended.

### References

ATSDR, 2012. Toxicological Profile for Chromium. TP 7.

EPAQS, 2009. Metals and Metalloids. Expert Panel on Air Quality Standards.

US EPA, 1998. Chemical Assessment Summary for Chromium VI, CASRN 18540-29-9.

WHO, 2000. Air Quality Guidelines for Europe, Second Edition.

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# 5. Ethylene dichloride (CAS Number 107-06-2)

Ethylene dichloride or 1,2-dichloroethane is a high volume industrial chemical, which is primarily used in the manufacture of vinyl chloride, mostly for polyvinyl chloride (PVC) production, and in the production of other organic solvents (SCOEL 2016).

Exposure to ethylene dichloride causes CNS depression and also respiratory and ocular irritation at high concentrations (ATSDR 2001, SCOEL 2016, and WHO 2000). It is also known to cause systemic toxicity to the liver and the kidneys. Exposures at relatively low concentrations in animal studies have resulted in pulmonary oedemas. It is genotoxic *in vitro*, but results are less conclusive *in vivo*. Increased incidence of tumours in rodents has been observed in the liver, lung and mammary glands following long-term inhalation exposure (Nagano et al. 2006).

### **Regulatory Guidelines**

None	

### **Recommended Environmental Assessment Level in Air**

Long-term EAL	3 μg/m³ as an annual mean
Short-term EAL	None (insufficient evidence)

# **Supporting Information**

The recommended long-term EAL of  $0.003 \text{ mg/m}^3$  as an annual mean is derived from the Benchmark Concentration (BMC<sub>10</sub>) of 30.8 mg/m<sup>3</sup> (analysis of data from Nagano et al. 2006) provided by the industry REACH dossier divided by an appropriate margin of safety of 10,000. While SCOEL (2016) and the industry REACH dossier both addressed the prior lack of evidence on a dose-response relationship between inhalation and increased tumour incidence, only the latter also corrected for continuous exposure.

There was insufficient evidence on which to derive a short-term EAL. The current 8-hour workplace exposure limit (WEL) of 21 mg/m<sup>3</sup> (HSE 2020) is close to the hourly upper limit of 27 mg/m<sup>3</sup> and greatly exceeds a daily upper limit of 1.1 mg/m<sup>3</sup> (the practical compliance constraint calculated from the long-term EAL).

### References

ATSDR, 2001. Toxicological Profile for 1,2-Dichloroethane. TP 38.

HSE, 2020. Workplace exposure limits. EH40/2005 (Fourth Edition). London: TSO.

NAGANO K., UMEDA Y., SENOH H., GOTOH K., ARITO H., YAMAMOTO S., MATSUSHIMA T., 2006. Carcinogenicity and chronic toxicity in rats and mice exposed by inhalation to 1,2-dichloroethane for two years. J. OCCUP. HEALTH, 48, 424 – 436.

SCOEL, 2016. Dichloroethane (Ethylene dichloride). Recommendation from the Scientific Committee on Occupational Exposure Limits. SCOEL/REC/302.

WHO, 2000. Air Quality Guidelines for Europe, Second Edition.

# 6. Methyl Chloroform (CAS Number 71-55-6)

Methyl chloroform or 1,1,1-trichloroethane is a colourless volatile liquid at room temperature with an ethereal chloroform-like odour (ATSDR 2006). Mainly used in production of hydrochlorofluorocarbons, it was also widely used in vapour degreasing and cold cleaning of metal parts, adhesives, coatings and inks, textiles, and in electronics. However, it has been rapidly phased out under the Montreal Protocol because of its ozone-depletion properties and is registered under REACH for only intermediate uses.

Adverse effects from exposure to methyl chloroform have been reviewed by several authoritative bodies (ATSDR 2006, IPCS 1992, and US EPA 2007). The most sensitive target for acute and short-term toxicity is the CNS. Evidence for chronic exposures is limited.

#### **Regulatory Guidelines**

None

### Recommended Environmental Assessment Level in Air

Long-term EAL	5,000 μg/m³ as a 24-hour mean
Short-term EAL	None (constrained by compliance with the long-term EAL)

## Supporting Information

There is a lack of evidence on the long-term effects from chronic exposure to methyl chloroform. The long-term EAL of 5 mg/m<sup>3</sup> as a 24-hour mean is based on the Reference Concentration (RfC) proposed by US EPA (2007), who considered acute (neurotoxicity), as well as sub-chronic and chronic effects (liver toxicity) in deciding on the most health protective HBGV.

Short-term exposure to higher concentrations of methyl chloroform results in symptoms of CNS depression and subtle neurological effects (ATSDR 2006). A proposed short-term

EAL of 10.8 mg/m<sup>3</sup> as a 24-hour mean, which is based on the acute MRL proposed by ATSDR (2006), would exceed the long-term EAL.

### References

ATSDR, 2006. Toxicological Profile for 1,1,1-Trichloroethane, TP 70.

IPCS, 1992. 1,1,1-Trichloroethane, Environmental Health Criteria Monograph 136. International Programme on Chemical Safety: World Health Organization.

US EPA, 2007. Chemical Assessment Summary for 1,1,1-Trichloroethane CASRN 71-55-6.

# 7. Monoethanolamine (CAS Number 141-43-5)

Monoethanolamine (MEA), 2-aminoethanol, or ethanolamine is a colourless, viscous liquid with an ammoniacal odour (HSE 2016), whose vapour is denser than air. It is widely used in industry in the production of detergents and soaps, dyestuffs, rubber vulcanisation, and as a scrubber for acidic gases in enclosed atmospheres such as submarines. MEA is used in a range of consumer products including cosmetics and personal care products, washing and cleaning products, coating products, biocides, inks and toners, and adhesives and sealants.

### **Regulatory Guidelines**

None

### **Recommended Environmental Assessment Level in Air**

Long-term EAL	100 μg/m³ as a 24-hour mean
Short-term EAL	400 μg/m³ as a 1-hour mean

There are few authoritative reviews on the adverse effects from exposure to MEA (CNESST 2019, HSE 2016, SCOEL 1996). It is a strong respiratory, ocular and skin irritant. CNESST (2019) concluded that MEA is a skin and respiratory sensitiser, but this opinion has been disputed (HSE 2001 and 2016).

# **Supporting Information**

Short-term inhalation exposure to MEA vapour results in localised respiratory irritation. The pivotal study for derivation of a short-term EAL is the sub-acute duration rodent study submitted as evidence in support of an application under REACH (HSE 2016) with a No Observed Adverse Effect Concentration (NOAEC) of 10 mg/m<sup>3</sup>. No correction for continuous exposure is applied because irritation is considered a concentration-dependent effect. The short-term EAL of 0.4 mg/m<sup>3</sup> as a 1-hour mean is obtained by dividing the NOAEC by an uncertainty factor (UF) of 25.

The critical health effects from long-term inhalation exposure are considered to be respiratory irritation and neurobehavioral toxicity. The pivotal study for derivation of a long-term EAL is the same sub-acute rodent study used for the short-term EAL (HSE 2016). The long-term EAL of 0.1 mg/m<sup>3</sup> as a 24-hour mean is obtained by dividing the NOAEC of 10 mg/m<sup>3</sup> by a UF of 100. Although no UF for sub-acute to chronic duration is required because irritation is considered a concentration-based effect, an additional UF was included to take account of uncertainty over long-term effects.

## References

<u>CNESST, 2019. Agents causing occupational asthma with key references.</u> <u>COMMISSION DES NORMES, DE L'ÉQUITÉ, DE LA SANTÉ ET DE LA SÉCURITÉ DU</u> <u>TRAVAIL, QUÉBEC, CANADA.</u>

HSE, 2016. Substance Evaluation Report for 2-aminoethanol, Version 2. Health and Safety Executive.

SCOEL, 1996. Recommendation from the Scientific Committee on Occupational Exposure Limits for Ethanolamine. SCOEL/SUM/24.

# 8. Naphthalene (CAS Number 91-20-3)

Naphthalene is the smallest and most volatile polycyclic aromatic hydrocarbon (WHO 2010). It is a combustion product from fossil fuels, which are released from industrial and domestic heat and power sources and from vehicle exhausts. It is an important component of creosote, a commonly used wood preservative, and was used historically in mothballs.

Adverse effects from exposure to naphthalene have been reviewed by a few authoritative bodies (ATSDR 2005, US EPA 1998, and WHO 2010). Most evidence for the toxicity of naphthalene comes from animal experiments. The principal health concerns are respiratory tract lesions, including respiratory tract carcinogenicity demonstrated in animal studies, and haemolytic anaemia in humans (WHO 2010).

## **Regulatory Guidelines**

None

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### **Recommended Environmental Assessment Level in Air**

Long-term EAL	3 μg/m³ as a 24-hour mean
Short-term EAL	None (insufficient evidence)

# Supporting Information

Long-term chronic HBGVs have been proposed by ATSDR (2005), US EPA (1998), and WHO (2010). They were all based on a lowest observable adverse effect level (LOAEL) for respiratory toxicity in rodents from 2-year inhalation studies. Variation in the final guidelines were in part the result of differences in use of toxicokinetic models and adjustments as well as the chosen UF. A long-term EAL of 0.003 mg/m<sup>3</sup> as a 24-hour mean is recommended to protect the general public, which is based on the chronic MRL proposed by ATSDR (2005). Its derivation is also consistent with the recently proposed indoor air quality guideline (IAQ) for the UK (Shrubsole et al. 2019).

There was insufficient evidence on which to derive a short-term EAL.

### References

ATSDR, 2005. Toxicological profile for naphthalene, 1-methylnaphthalene, and 2methylnaphthalene. TP 67.

SHRUBSOLE C., DMITROULOPOULOU S., FOXALL K., GADEBERG B., DOUTSI A., 2019. IAQ guidelines for selected volatile organic compounds (VOCs) in the UK. BUILDING AND ENVIRONMENT, 165, 106382.

US EPA, 1998. Chemical Assessment Summary for Naphthalene CASRN 91-20-3.

WHO, 2010. Guidelines for Indoor Air Quality: Selected Pollutants. ISBN 978 92 890 0213 4.

# 9. N-nitrosodimethylamine (CAS Number 62-75-9)

N-nitrosamines are hydrocarbons with the generic chemical formula of  $(R_1R_2)$ -N-N=O, where  $R_1$  and  $R_2$  are alky groups, which are formed primarily by reaction of amines with oxidising agents including chlorine disinfectants, nitrites, and atmospheric nitrogen oxides. They have been detected in flue gases from carbon capture systems, which use amine-based solvents as reagents (SEPA 2014). N-nitrosodimethylamine (NDMA) is one of the most widely studied and has been detected in cosmetics, food, medicines, and drinking water (IPCS 2002).

N-nitrosamines are potent carcinogens (NIPH 2011, IPCS 2002) with epidemiological and animal studies reporting associations between exposure and cancers of the stomach, bowel, liver, kidneys, nasal cavity, and lungs. However, most available data for NDMA concerns its oral toxicity and evidence on other adverse effects is limited.

Regulatory Guidelines		
None		

# **Recommended Environmental Assessment Level in Air**

Long-term EAL	0.0002 μg/m³ as an annual mean
Short-term EAL	None (insufficient evidence)

# **Supporting Information**

Carcinogenicity is the critical health effect from long-term chronic exposure to NDMA, although limited inhalation data is available. While other organisations have based their HBGVs on oral exposure, there is concern that NDMA is more potent via the inhalation route. The recommended long-term EAL of 0.2 ng/m<sup>3</sup> as an annual mean is derived from a Benchmark Dose Level (BMDL<sub>10</sub>) of 0.023 mg/m<sup>3</sup> (a new analysis of data on the incidence of tumours in the naval cavity in rodents from an inhalation study by Klein et al. 1991), adjusted for continuous exposure, divided by an appropriate margin of safety of 10,000.

There was insufficient evidence on which to derive a short-term EAL.

## References

IPCS, 2002. N-Nitrosodimethylamine, Concise International Chemical Assessment Document 38. Geneva: International Programme on Chemical Safety, World Health Organization.

KLEIN R.G., JANOWSKY I., POOL-ZOBEL B.L., SCHEMZER P., HERMANN R., AMELUNG F., SPIEGELHALDER B., ZELLER W.J., 1991. Effects of long-term inhalation of N-nitrosodimethylamine in rats. IARC SCIENTIFIC PUBLICATIONS, 105, 322 – 328.

NIPH, 2011. Health Effects of Amines and Derivatives Associated with CO2 Capture: Nitrosamines and Nitramines. Norwegian Institute of Public Health: Oslo.

<u>SEPA, 2014. Review of amine emissions from carbon capture systems. Version 2.01.</u> <u>Scottish Environment Protection Agency: Stirling.</u>

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# 10. Tetrachloroethylene (CAS Number 127-18-4)

Tetrachloroethylene, tetrachloroethene, perchloroethylene, or PERC is a readily volatile, colourless liquid at room temperature and pressure with an ether-like odour (WHO 2010). It is a widely used industrial chemical as a raw material from hydrofluorocarbons, a degreaser and an industrial solvent. It is used in the manufacture of metal parts, textiles, paint removers, printing inks, adhesives, fragrances and in specialised cleaning fluids and dry-cleaning agents.

Adverse effects from exposure to tetrachloroethylene have been reviewed by several authoritative bodies (ATSDR 2019, US EPA 2012, and WHO 2010). The main health effects reported in human and animal studies from inhalation exposure are cancer and non-carcinogenic effects including irritation (ocular, respiratory tract, and skin), and toxicity to CNS, liver and kidneys (WHO 2010). Recent reviews focus on its neurotoxicity.

#### **Regulatory Guidelines**

None

#### **Recommended Environmental Assessment Level in Air**

Long-term EAL	40 μg/m³ as a 24-hour mean
Short-term EAL	None (constrained by compliance with the long- term EAL)

### **Supporting Information**

Long-term chronic HBGVs have been based on various endpoints including kidney toxicity, carcinogenicity, and neurotoxicity. Recent reviews by ATSDR (2019) and US EPA (2012) have concluded that neurotoxicity is the most sensitive effect. A long-term EAL of 0.04 mg/m<sup>3</sup> as a 24-hour mean is recommended to protect the general public, which is based on the chronic MRL proposed by ATSDR (2019). It is also consistent with the recently proposed IAQ for the UK (Shrubsole et al. 2019).

Short-term exposures to higher concentrations have resulted in neurotoxicity at blood concentrations similar to those seen following chronic exposure (ATSDR 2019). Therefore a short-term EAL is not recommended.

#### References

ATSDR, 2019. Toxicological Profile for Tetrachloroethylene. TP 18.

SHRUBSOLE C., DMITROULOPOULOU S., FOXALL K., GADEBERG B., DOUTSI A., 2019. IAQ guidelines for selected volatile organic compounds (VOCs) in the UK. BUILDING AND ENVIRONMENT, 165, 106382.

US EPA, 2012. Chemical Assessment Summary for Tetrachloroethylene (Perchloroethylene): CASRN 127-18-4.

WHO, 2010. Guidelines for Indoor Air Quality: Selected Pollutants. ISBN 978 92 890 0213 4.

# 11. Trichloroethylene (CAS Number 79-01-6)

Trichloroethylene or trichloroethene is a volatile, colourless liquid with a sweet ethereal odour (WHO 2010). It is mainly used for vapour degreasing and cold cleaning of manufactured metal parts and for industrial dry cleaning, paper and textile printing, the production of printing inks, extraction processes, and paint production.

Adverse effects from exposure to trichloroethylene have been reviewed by several authoritative bodies (ATSDR 2019, US EPA 2011, WHO 2010). The main targets of its toxicity in humans and laboratory animals are the CNS, the liver and kidneys, the immune system, the male reproductive system and the developing foetus. Available human data supports an association between exposure and cancers of the kidneys, liver, and the lymphatic system.

## **Regulatory Guidelines**

None

## **Recommended Environmental Assessment Level in Air**

Long-term EAL	2 μg/m³ as an annual mean
Short-term EAL	None (constrained by compliance with the long-term EAL)

# **Supporting Information**

Long-term chronic HGBVs have been proposed by ATSDR (2019), US EPA (2011), and WHO (2010), which are based on various endpoints including developmental toxicity and carcinogenicity. A long-term EAL of 0.002 mg/m<sup>3</sup> as an annual mean is recommended to protect the general public, which is based on the unit risk calculated by US EPA (2011) for cancers of the kidneys, liver, bile duct, and Non-Hodgkin lymphomas at an ELCR of 1 in

100,000. The approach is consistent with the derivation of the recently proposed IAQ for the UK (Shrubsole et al. 2019).

Short-term exposure to higher concentrations results in neurotoxicity (ATSDR 2019). However, the available evidence is limited and existing guidelines exceed any daily or hourly limits derived from practical compliance constraints imposed by the long-term EAL. Therefore a short-term EAL is not recommended.

### References

ATSDR, 2019. Toxicological Profile for Trichloroethylene. TP 19.

SHRUBSOLE C., DMITROULOPOULOU S., FOXALL K., GADEBERG B., DOUTSI A., 2019. IAQ guidelines for selected volatile organic compounds (VOCs) in the UK. BUILDING AND ENVIRONMENT, 165, 106382.

US EPA, 2011. Chemical Assessment Summary for Trichloroethylene CASRN 79-01-6.

WHO, 2010. Guidelines for Indoor Air Quality: Selected Pollutants. ISBN 978 92 890 0213 4.

# 12. Vinyl Chloride (CAS Number 75-01-4)

Vinyl chloride, chloroethene, or chloroethylene is a colourless and flammable gas with a slightly sweet odour (NAC/AEGL 2012). It is heavier than air and accumulates close to the ground. It is a high volume industrial chemical used as a monomer in the production of PVC plastics.

Adverse effects from exposure to vinyl chloride have been reviewed by several authoritative bodies (ATSDR 2006, US EPA 2000, WHO 2000). The CNS and the liver are the primary targets for acute and chronic exposure, respectively. It is a human carcinogen associated with cancers of the blood vessel linings at sites including liver and lungs.

### **Regulatory Guidelines**

None

### Recommended Environmental Assessment Level in Air

Long-term EAL	10 μg/m³ as an annual mean
Short-term EAL	1,300 μg/m³ as a 24-hour mean

# **Supporting Information**

Long-term chronic HBGVs have been proposed by ATSDR (2006), US EPA (2000), WHO (2000), and the industry REACH Dossier. They were based either on liver toxicity (non-cancer endpoint) or carcinogenicity, with the latter being the most sensitive effect. At an ELCR of 1 in 100,000, the HBGVs are in the range 0.002 to 0.02 mg/m<sup>3</sup>. A long-term EAL of 0.01 mg/m<sup>3</sup> is recommended to protect the general public, which is based on the unit risk calculated by WHO (2000).

Short-term exposures to higher concentrations of vinyl chloride results in symptoms of CNS depression and other neurological effects (ATSDR 2006, NAC/AEGL 2012). A short-term EAL of 1.3 mg/m<sup>3</sup> as a 24-hour mean is recommended to protect the general public, which is based on the acute MRL proposed by ATSDR (2006) for delayed ossification in mice offspring.

### References

ATSDR, 2006. Toxicological Profile for Vinyl Chloride. TP 6.

NAC/AEGL, 2012. Acute Exposure Guideline Levels for Selected Airborne Chemicals. Volume 11. ISBN 0-309-25481-7.

US EPA, 2000. Chemical Assessment Summary for Vinyl Chloride, CASRN 75-01-4.

WHO, 2000. Air Quality Guidelines for Europe, Second Edition.

# Abbreviations and Definitions

AEGL	Acute Exposure Guideline Levels for Hazardous Substances. They are threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10- minutes to 8-hours.
AEGL-2	An air concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects, or an impaired ability to escape.
AQS	Air Quality Standard
ATSDR	Agency for Toxic Substances and Disease Registry
ВМС	Benchmark Concentration
BMD	Benchmark Dose
BMDL	Lower 95 Percentile Confidence Level of the Benchmark Dose
CNS	Central Nervous System
ELCR	Excess lifetime cancer risk. It is defined as the estimated probability of an individual developing cancer over a lifetime as a result of exposure to a chemical. It is an "excess" cancer risk because there is already a background risk (about one in four) of an individual getting cancer. A minimal excess lifetime cancer risk is typically defined in the range of 1 in 10,000 to 1 in 1,000,000. In developing EALs, the default is 1 in 100,000.
EPAQS	Department of the Environment Expert Panel on Air Quality Standards (disbanded)
HBGV	Health-Based Guidance Value
HSE	Health and Safety Executive
IARC	International Agency for Research on Cancer

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IAQ	Indoor Air Quality Guideline
IPCS	International Programme on Chemical Safety (World Health Organization)
LOAEL	Lowest Observable Adverse Effect Level
MRL	Minimal Risk Level is defined as an estimate of the amount of a chemical a person can eat, drink, or breathe each day without a detectable risk to health. MRL values are developed for health effects other than cancer.
NAC/AEGL	National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances
NOAEC	No Observed Adverse Effect Concentration
RfC	Reference Concentration is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for a chronic duration (up to a lifetime) to the population (including sensitive sub-groups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It is generally use in the US EPA assessments of non-cancer effects.
UF	Uncertainty Factor
WEL	Workplace Exposure Limit is defined as a concentration in air that protects workers from toxic substances either over a short-term – a short term exposure limit (STEL, 15 minutes) or long-term – a time weighted average (TWA, 8 hours).
WHO	World Health Organization