PHOSGENE

CAS number:	75-44-5
Synonyms:	Carbonyl chloride, chloroformyl chloride
Chemical formula:	CCl_2O
Structural formula:	—

Workplace exposure standard (amended)

TWA:	**0.1 ppm (0.41 mg/m^3)**
STEL:	**0.4 ppm (1.6 mg/m^3)**
Peak limitation:	**—**
Notations:	**—**
IDLH:	**2 ppm**

Sampling and analysis: The recommended value is quantifiable through available sampling and analysis techniques.

Recommendation and basis for workplace exposure standard

A TWA of 0.1 ppm (0.41 mg/m^3) is recommended to protect for irritant effects in exposed workers.

A STEL of 0.4 ppm (1.6 mg/m^3) is recommended to protect for irritant effects in acutely exposure workers.

Discussion and conclusions

Phosgene is used as an intermediate in the production of dyes, isocyanates, plastics and pharmaceuticals. It may be formed from chlorinated organic compounds at high temperatures or under UV radiation.

Critical effects of exposure are respiratory irritation and pulmonary oedema.

Quantitative human exposure data are limited. A NOAEC of 2 ppm for signs of respiratory irritation in dogs was estimated from a series of acute inhalational experiments and extrapolated to an equivalent eight-hour exposure of 0.14 ppm in workers (DFG, 2008; SCOEL, 2011). The available animal exposure data suggest additional effects from cumulative exposure are unlikely (SCOEL, 2011). A LOAEC of 0.2 ppm for pulmonary oedema is reported in a sub-acute inhalation study with animal models (ACGIH, 2018). Changes in biochemical markers for inflammatory responses in rats at 0.05 ppm are reported in an acute single inhalation exposure study and served as the basis for the previous MAK of 0.02 ppm. However, this endpoint is not considered relevant to humans (DFG, 2008).

The three primary sources (ACGIH, DFG and SCOEL), other than SWA, derived a TWA of 0.1 ppm based on a threshold for respiratory irritation estimated from a series of animal inhalation studies. This value is recommended to be adopted and is expected to be protective of pulmonary irritation.

The STEL of 0.4 ppm by SCOEL (2011) is recommended to protect for effects of short-term excursions and is based on the acute NOAEC of 2 ppm in dogs.

Recommendation for notations

Not classified as a carcinogen according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS).

Not classified as a skin sensitiser or respiratory sensitiser according to the GHS.

There are insufficient data to recommend a skin notation.

APPENDIX

Primary sources with reports

Source	Year set	Standard
SWA	***1995***	***TWA: 0.02 ppm (0.08 mg/m³); STEL: 0.06 ppm (0.25 mg/m³)***
ACGIH	***2001***	***TLV-TWA: 0.1 ppm (0.40 mg/m³)***

TLV-TWA intended to protect for respiratory tract irritation, pulmonary oedema, lung congestion and emphysema.

Summary of information:

Olfactory fatigue, induced by prolonged exposures at 0.5–1 ppm, may hinder early detection. Onset of pulmonary oedema reported at 0.2 ppm in animals; TLV-TWA of 0.1 ppm expected protective of these effects in exposed workers. TLV-TWA derivation not discussed.

Human data:

- LC_{50} ≈500 ppm (1 min); exposure at 3 ppm (170 min) equally lethal as 30 ppm (17 min)
- Data provided by US Chemical Warfare Service (pre-1921) indicated 1 ppm tolerable over prolonged exposure
- No quantitative chronic exposure data regarding irreversible lung damage in humans
- No indication individuals with chronic respiratory diseases have different susceptibility to adverse pulmonary effects.

Animal data:

- Acute exposure at lethal concentrations causes delayed deaths 6–24 h post-exposure (species not specified)
- Pathological changes (not specified) in lungs at 0.5 ppm (rats, 2 h)
- Pulmonary vasoconstriction at lethal concentrations (not specified) in rabbits; survivors developed pulmonary oedema, emphysema, and mucosal sloughing
- Emphysema and pulmonary congestion after 4–9 d at 72 ppm (dogs, 30 min)
- Pulmonary oedema in 41% of test animals at 0.2 ppm (mice, rats, guinea pigs, rabbits, cats, goats, 5 h/d, 5 d); depressed ciliary function and lung lesions at 1 ppm:
  - primary basis of TLV-TWA recommendation
- No cumulative lung damage at 1.5–3.8 ppm and 5–6 ppm over 40 d compared with 2 d (cats)
- Tolerance to oedema development following prolonged exposures at 1 ppm for 6 h/d (no further experimental details provided); irreversible pulmonary emphysema and fibrotic changes likely to cause tolerance without overt signs of acute intoxication
- No ADME, mutagenicity, or carcinogenicity data presented.

Insufficient data to recommend a TLV-STEL or notations for carcinogenicity, skin absorption, or sensitisation.

DFG	***2008***	***MAK: 0.1 ppm (0.41 mg/m³)***

Summary of additional information:

Critical effect is local irritation, primarily in lungs due to substance hydrophobicity. Available occupational data are insufficient to derive MAK.

Source	Year set	Standard
Previous MAK of 0.02 ppm was withdrawn in view of re-evaluation of available animal studies. It was based on a LOAEC of 0.05 ppm for decreased ATP content in lungs in rats which is not relevant due to differences in pulmonary anatomy between rats and humans. The product of exposure concentration and duration (C×t product) for the development of pulmonary oedema is constant across several acute and sub-chronic animal inhalation studies and therefore, obeys Haber's rule. Based on this relationship, current MAK derived from NOAEC of 2 ppm (9 mg/m^3) for changes in protein concentration of bronchioalveolar lavage (BAL) fluid in acute inhalation study with dogs. Extrapolated to an 8-h exposure, this NAOEC is equivalent to 0.14 ppm, which is rounded down to the MAK of 0.1 ppm; further safety factors are considered unnecessary based on comparable respiratory minute volume between dogs and humans. Rapid hydrolysis prevents substance accumulation; systemic toxicity therefore not expected. Based on this reactivity, potential skin absorption, sensitisation, reproductive toxicity, and mutagenicity are not considered likely. Human data: • Available epidemiological studies not used to derive MAK due to inadequate documentation or study design: o no pulmonary abnormalities reported in 2 workplace studies (n=89 and 90) at average air concentrations of 0.125 ppm (inadequate study design) o no increased mortality or frequency of chronic lung diseases in production workers (n=326) exposed at >0.02 ppm (average: 0.003 ppm) compared with 6,288 controls (no duration specified). Animal data: • Increased Streptococcus survival in lungs and decreased ciliary action at 0.2 ppm (0.8 mg/m^3) in acute inhalation study (rats, 6 h); no difference to controls at 18 h post-exposure, minimal histological changes in bronchioles and no change in BAL fluid protein content: o reversible infectiousness demonstrated in separate sub-chronic inhalation study (rats, 6 h/d, 5 d/wk, 4–12 wk) • No specific effects at 2 ppm for 0.5 h (dogs, C×t product: 270 mg/m^3 permin); LOAEC of 3.7 ppm (C×t product: 495 mg/m^3 permin) for marginal changes in BAL fluid composition: o cited article calculated threshold concentration for increased BAL protein content from these data as 375 mg/m^3 per min • Non-mutagenic *in vitro* in bacteria with or without metabolic activation; assumed to be non-mutagenic based on chemical structure. Insufficient data to assign carcinogenicity notation.		
SCOEL	***2011***	***TWA: 0.1 ppm (0.4 mg/m^3); STEL: 0.5 ppm (2.0 mg/m^3)***
Summary of additional information: TWA derived from NOAEC of 2 ppm for changes in BAL protein content in acute inhalation study with dogs (analogous to DFG, 2008). 15-min STEL derived from same study; factor of 4 applied to account for 4 peak exposure events per shift. No evidence to warrant a skin or sensitiser notation. Human data: • Accidental overexposure caused cough, eye and respiratory tract irritation, increased sputum production, headache, vomiting, stomach pain, vertigo, and drowsiness • Lung oedema may occur 4–24 h post-exposure (no further information provided). Animal data: • LC_{50}: 2.1 ppm (rats, 4 h); 62.5 ppm (rats, 10 min); mortality within 24 h due to lung oedema		

Source	Year set	Standard
		• Transient changes in arachidonic acid metabolism at 0.1 ppm (rats, 4 h); endpoint considered less reliable than BAL protein content and therefore not used in OEL derivation • Increased infectiousness at 0.02 ppm in mice and rats (studies also cited in DFG, 2008) not considered in evaluation due to higher respiratory minute volume and thus greater susceptibility to airway irritants in rodent • Constant C×t product for markers of pulmonary irritation/oedema across acute and sub-chronic inhalation studies indicates threshold level for respiratory irritation depends on recurrent acute irritation and suggests substance does not cause cumulative irritational effects. Insufficient data to recommend carcinogenicity notation.
OARS/AIHA	***NA***	***NA***
No report.		
HCOTN	***NA***	***NA***
No report.		

Secondary source reports relied upon

Source		Year	Additional information
US NIOSH	✓	1994	• IDLH based on acute inhalation toxicity data in humans.

Carcinogenicity — non-threshold based genotoxic carcinogens

Is the chemical mutagenic? No

The chemical is not a non-threshold based genotoxic carcinogen.

Notations

Source	Notations
SWA	—
HCIS	—
NICNAS	—
EU Annex	—
ECHA	—
ACGIH	—
DFG	—
SCOEL	—
HCOTN	NA
IARC	NA

Source	Notations
US NIOSH	NA

NA = not applicable (a recommendation has not been made by this Agency); — = the Agency has assessed available data for this chemical but has not recommended any notations

Skin notation assessment

Calculation
Insufficient data to assign a skin notation.

IDLH

Is there a suitable IDLH value available?	Yes

Additional information

Molecular weight:	98.92
Conversion factors at 25°C and 101.3 kPa:	1 ppm = 4.05 mg/m^3; 1 mg/m^3 = 0.25 ppm
This chemical is used as a pesticide:	☐
This chemical is a biological product:	☐
This chemical is a by-product of a process:	☐
A biological exposure index has been recommended by these agencies:	☐ ACGIH ☐ DFG ☐ SCOEL

Workplace exposure standard history

Year	Standard
Click here to enter year	

References

American Conference of Industrial Hygienists (ACGIH®) (2018) TLVs® and BEIs® with 7th Edition Documentation, CD-ROM, Single User Version. Copyright 2018. Reprinted with permission. See the *TLVs® and BEIs® Guidelines section* on the ACGIH website.

Deutsche Forschungsgemeinschaft (DFG) (2008) Phosgene – MAK value documentation.

EU Scientific Committee on Occupational Exposure Limits (SCOEL) (2011) Recommendation from the Scientific Committee on Occupational Exposure Limits for phosgene. SCOEL/SUM/004.

US National Institute for Occupational Safety and Health (NIOSH) (1994) Immediately dangerous to life or health concentrations – phosgene.