

Phosgene

Robust Summaries

CAS Number 75-44-5

Submission to the US EPA HPV Challenge Program

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1. KLIMISCH *ET AL.* RELIABILITY CATEGORIES

The following scoring developed by Klimisch *et al.*, (1997) was used to determine the reliability of the studies referenced in this document.

Code	Category
1	Valid without restriction
2	Valid with restriction
3	Not reliable
4	Not Assignable

Subcategories

Code	Category
1	Valid without restriction
1a	GLP guideline study
1b	Comparable to Guideline study
1c	Meets National standards method (AFNOR/DIN)
1d	Meets generally accepted scientific method and is described in sufficient detail

2	Valid with restriction
2a	Guideline study without detailed description
2b	Guideline study with acceptable restrictions
2c	Comparable to Guideline study with acceptable restrictions
2d	Meets National standards method with acceptable restrictions
2e	Meets generally accepted scientific standards, well documented and acceptable for assessment
2f	Accepted calculation method
2g	Data from Handbook or collection of data

3	Invalid
3a	Documentation insufficient for assessment
3b	Significant methodological deficiencies
3c	Unsuitable test system

4	Not Assignable
4a	Abstract
4b	Secondary literature
4c	Original reference not yet available
4d	Original reference in foreign language
4e	Documentation insufficient for assessment

2. MELTING POINT

PHOSGENE (CAS# 75-44-5)

METHOD

Handbook data from International Programme on Chemical Safety (IPCS)
GLP procedures not likely followed
Reported in 1995

RESULTS

Melting Point = -127.8°C

Data from selected secondary literature state melting point to be -118°C (The Merck Index, 1987; Dupont Chemical Solutions Enterprise, 1984); -127.8°C (Schneider & Diller, 1991; Hardy, 1982); -180°C (EPA, 1985); and -104°C (Perry & Green, 1997). The secondary sources range from -104°C to -180°C , and they do not describe methodology or experimental procedures.

CONCLUSION

The melting point value reported by the IPCS (1995) is within the range of other values reported in the secondary literature.

DATA QUALITY

Reliability code = 2 (2G). The melting point value is derived from a well-documented, reliable publication.

REFERENCE

IPCS, 1995

3. BOILING POINT

PHOSGENE (CAS# 75-44-5)

METHOD

Handbook data from International Programme on Chemical Safety (IPCS)
GLP procedures not likely followed
Reported in 1995

RESULTS

Boiling Point = 7.56°C

Data from selected secondary literature state boiling point to be 7 °C (Daubert & Danner, 1985, 1989); and 8.2°C (EPA, 1985; Perry & Green, 1985). The secondary sources do not describe methodology or experimental procedures.

CONCLUSIONS

The boiling point value is similar to other values reported in the secondary literature.

DATA QUALITY

Reliability code 2 (2G). The boiling point value is derived from a well-documented, reliable publication.

REFERENCE

IPCS, 1995.

4. VAPOR PRESSURE

PHOSGENE (CAS# 75-44-5)

METHOD

Handbook data from International Programme on Chemical Safety (IPCS)
GLP procedures not likely followed
Reported in 1995

RESULTS

Vapor Pressure value is 1616 hPa (161.6 kPa) at 20°C.

Additional data from secondary literature state vapor pressure is 1215 mm Hg at 20°C (The Merck Index, 1987), and 157.3 kPa at 20°C (Phosgene Summary Document # 15091). Other secondary sources are in the same range.

CONCLUSIONS

The vapor pressure value is similar to ranges found in other secondary literature references.

DATA QUALITY

Reliability code = 2 (2G). The vapor pressure value is derived from a reliable, well-documented publication.

REFERENCE

IPCS, 1995.

5. WATER SOLUBILITY

PHOSGENE (CAS# 75-44-5)

METHOD

Handbook data from International Programme on Chemical Safety (IPCS)
GLP procedures not likely followed
Reported in 1995

RESULTS

Phosgene decomposes rapidly in water, and therefore no accurate estimates of water solubility can be experimentally derived.

CONCLUSION

Phosgene readily reacts with water and hydrolyzes very rapidly. Data from numerous handbooks report that phosgene hydrolyzes rapidly in aqueous solutions to carbon dioxide and hydrochloric acid. The half-life in water has been estimated at 0.026 seconds (Manogue and Pigford, 1960), which precludes accurate estimates of water solubility.

DATA QUALITY

Reliability code = 2 (2G).

REFERENCE

IPCS, 1995.

6. PHOTODEGRADATION

PHOSGENE (CAS# 75-44-5)

METHOD

Direct Photolysis:

- Accepted estimation procedures
- Study on phosgene sources and sinks in the atmosphere
- GLP procedures not used
- Study reported in 1992

Indirect Photolysis:

- Laboratory experimental procedures
- Study on phosgene gas reaction with hydroxyl radicals
- GLP procedures not used
- Study reported in 1988

RESULTS

Direct Photolysis:

Helas and Wilson (1992) estimate a half-life for direct photolysis of phosgene ranging from 13 to 36 years, based on an assumed quantum yield of 1 and noon actinic fluxes at equinox for 45° N latitude.

Indirect Photolysis

The rate constant for reaction of phosgene with photochemically generated hydroxyl radical was determined by Witte and Zetsch (1988) to be $3.8 \times 10^{-16} \text{ cm}^3\text{-molecule}^{-1}\text{-sec}^{-1}$. Using the EPA-accepted average hydroxyl radical concentration of $1.5 \times 10^6 \text{ molecule-cm}^{-3}$ (EPIWIN, 2000), the half-life for indirect photolysis is estimated to be in excess of 77 years.

CONCLUSION

Phosgene does not react appreciably with photochemically produced hydroxyl radicals (IPCS, 1995). Direct and indirect photolysis in air is negligible under irradiation conditions approximating those of sunlight (Grosjean, 1991). The dominant process for removal of phosgene in the troposphere is hydrolytic reaction with water droplets in fog and clouds. The tropospheric hydrolysis of phosgene has been estimated over a range of latitudes (Helas and Wilson, 1992). The estimated tropospheric lifetime ranges around 10 hours, and is not believed to exceed 1 day. Dry deposition of phosgene vapor to surface water, soil, and vegetation also contributes to shortened lifetimes of the chemical in the troposphere. Lifetimes of approximately 7 days are attributed to this deposition process (Helas and Wilson, 1992).

DATA QUALITY

Reliability code = 2 (2E, 4D)

REFERENCES

- Helas, G. and S. R. Wilson. 1992. On sources and sinks of phosgene in the troposphere. *Atmospheric Environment* 26A(16):2975-2982.
- Witte, F. and C. Zetsch. 1988. Messung der Reaktion von asugewählten umweltrelevanten Altstoffen. *Schlubber*. UBA, November 1988.

7. STABILITY IN WATER

PHOSGENE (CAS# 75-44-5)

METHOD

Laboratory experimental procedures
Study on phosgene gas dissolved in aqueous solutions
GLP procedures not used
Study reported in 1960

RESULTS

Phosgene dissolved in shore laminar jets of aqueous solutions decomposed rapidly. Rate constants for hydrolysis were estimated in a series of experiments in water and in sodium nitrate and sodium hydroxide solutions at 25°C.

Estimated half-life of phosgene in water was approximately 0.026 seconds.

Phosgene hydrolyzed to carbon dioxide and hydrochloric acid in aqueous solutions. The lack of stability of phosgene in water due to rapid hydrolysis is substantiated by other laboratory studies on the gas phase hydrolysis of phosgene (Butler and Snelson, 1979).

CONCLUSIONS

Phosgene undergoes rapid hydrolysis in aqueous solutions. It is sparingly soluble in water and reacts with water very rapidly. These characteristics make it difficult to accurately define water solubility estimates and octanol-water partition coefficients. Modeled data (EPIWIN) for water solubility and partition coefficients provide inaccurate estimates for these parameters because the models do not take into account the rapid hydrolysis of phosgene in aqueous solutions.

REFERENCE

Manogue and Pigford, 1960.

8. TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

PHOSGENE (CAS# 75-44-5)

METHOD

Laboratory experimental procedures
Study on phosgene gas dissolved in aqueous solutions
GLP procedures not used
Study reported in 1960

RESULTS

Aqueous-phase diffusion coefficient estimated as $1.27 \times 10^{-5} \text{ cm}^2\text{-sec}^{-1}$

CONCLUSION

Equilibrium distribution coefficients, such as the octanol-water partition coefficient (K_{ow}), air-water partition coefficient (K_{aw}), and octanol-air partition coefficient (K_{oa}) are commonly used to predict the distribution and transport of a chemical among air, water, soil, and sediment compartments of the environment. The Level I and Level III fugacity models, developed by Mackay, provide a convenient means of applying these equilibrium distribution coefficients in determining the environmental distribution and transport of a chemical under equilibrium (level I) and non-equilibrium steady-state (level III) conditions. However, due to the virtually instantaneous reaction of phosgene in water, the transport of the material between environmental compartments cannot be predicted using equilibrium distribution coefficients involving the water phase. Environmental media such as clouds, surface water, surface soils, and vegetation will act as sinks for removal of atmospheric phosgene emissions. The rates of these reactions are governed by the kinetics of diffusion from the gas phase into these media, rather than by chemical equilibrium between the gas and condensed water phases. Therefore, the liquid-phase diffusion coefficient, as reported by Manogue and Pigford (1960) is a key parameter for determining transport of phosgene from the atmosphere to condensed aqueous phases.

DATA QUALITY

Reliability code = 2 (2e)

REFERENCE

Manogue and Pigford, 1960.

SUPPLEMENTAL REFERENCES

64-Helas, G. & S.R. Wilson.-On sources and sinks of phosgene in the troposphere.-1992-Atmos Environ 26A: 2975-82.

135-WHO-Environmental Health Criteria 193. Phosgene-1997-WHO. Environmental Health Criteria; 193; Phosgene. XVII+70. WHO: Geneva, Switzerland. ISBN 92-4-157193-4.; 193 (0). 1997.XVII+ 70p.

145--Environmental Health Criteria for Phosgene. Second Draft.-1995-International Programme on Chemical Safety PCS/EHC.94.47, Oct. 1995.

80-Kindler, T.P. et al.-The fate of atmospheric phosgene and the stratospheric chlorine loadings of its parent compounds: CCL₄, C₂CL₄, C₂HCL₃, CH₃CCL₃, and CHCL₃.-1995-J Geophys Res 100: 1235-51.

9. BIODEGRADATION

PHOSGENE (CAS# 75-44-5)

METHOD

Laboratory experimental procedures
Study on phosgene gas dissolved in aqueous solutions
GLP procedures not used
Study reported in 1960

RESULTS

CONCLUSIONS

Biodegradation occurs only in environmental compartments that contain liquid water (e.g. surface waters, sediments, wet soils). Hydrolysis of phosgene occurs instantaneously in these media, with a measured half-life on the order of 0.026 seconds (Manogue and Pigford, 1960). Biodegradation is therefore not a relevant fate process for phosgene.

DATA QUALITY

Reliability code = 2 (2e)

REFERENCE

Manogue and Pigford, 1960

10. ACUTE TOXICITY

PHOSGENE (CAS# 75-44-5)

Source and chemical characterization of phosgene not reported.

METHODS

Method/guideline:	OECD guideline #403
Type:	Acute lethality
GLP (Y/N):	Yes
Year study performed:	1989/90
Species/strain:	SPF-bred Wistar rats; Swiss mice
Sex:	Males and females for both rats and mice
Number of animals: concentration	5 males and 5 females for each species at each exposure time and concentration
Route of administration:	Inhalation
Age:	Rats – 5-6 weeks (150-170 grams/males, 130-140 grams/females) Mice – 7-8 weeks (28-34 grams/males, 23-27 grams/females)
Doses per time period:	8 doses/5 min, 7 doses/10 min, 5 doses/30 min, 4 doses/60 min
Concentrations:	Ranged from 26 to 856 mg/m ³ (6.5 to 214 ppm)
Exposure durations:	5, 10, 30 or 60 minutes
Post dose observation period:	1,2,4,7 and 14 days
Study design:	All rats were autopsied for gross pathological lesions

RESULTS

Mortality rates for rats and mice are reported for each sex at each time and concentration

Calculated LC₅₀ values (95% confidence intervals) are given for 10, 30, and 60 minute exposures as follows:

10 min exposures		
Rat (male/female combined)	334	(306-363) mg/m ³
Mouse (male)	322	(269-394) mg/m ³
Mouse (female)	244	(201-304) mg/m ³
30 min exposures		
Rat (male/female combined)	84	(77-92) mg/m ³
Mouse (male)	76	(61-93) mg/m ³
Mouse (female)	47	(30-61) mg/m ³
60 min exposures		
Rat (male/female combined)	49	(45-54) mg/m ³
Mouse (male)	39	(29-51) mg/m ³
Mouse (female)	21	(12-30) mg/m ³

Description, severity, time of onset and duration of clinical signs at each dose level: Not described

Necropsy findings: Not described

CONCLUSIONS

The LC₅₀ values for rats (males/females combined) and male mice are comparable at each exposure time, but the values for male mice appear greater than those for female mice at each exposure time. The acute toxicity of phosgene has been studied extensively, as is apparent from the lengthy list of referenced studies, and the LC₅₀ values are generally consistent.

DATA QUALITY

Reliability code = 1 (1a) – (Guideline study without restrictions)

REFERENCES

Zwart *et al.*, 1990. [mice and rat data]

Arts *et al.*, 1989. [rat data only]

Note: Same rat data and conclusions are reported in both referenced studies.

11. GENETIC TOXICITY IN VITRO (GENE MUTATIONS)

TEST SUBSTANCE

Phosgene (CAS# 75-44-5)

Source of phosgene and other test materials are provided, but no analysis of purity is given

METHODS

Method/guideline followed: OECD guideline for Ames assay bacterial mutagenicity study, using the liquid incubation procedure.

Type:	Reverse mutation assay
System of testing:	Bacterial
GLP:	GLP claims not specified, but documentation and test conditions appear to meet at least the spirit of GLP.
Year study performed:	1983
Species/Strain:	<i>Salmonella typhimurium</i> strains TA 98 and TA 100
Metabolic activation:	Liver S9 was prepared from Aroclor 1254 (500 mg/kg)-treated rats as described by Ames <i>et al.</i> (1975). Mutagenicity was assessed with and without the S9 rat liver activation system.
Concentration tested:	Not specified, but unchanged phosgene was detected in the incubation medium by GC analysis only above a gaseous concentration of 10,000 ppm.
Statistical methods:	Not specified, although data points in graphs have brackets to indicate variability
Specific test conditions:	Phosgene vapors were prepared at various concentrations in nitrogen and bubbled through the liquid suspension medium. However, the report is predominantly a presentation of methods and results for dichloroacetylene, which rapidly decomposes to several products including phosgene.

RESULTS

No specific mutagenicity results are reported for phosgene. However, the authors state: "Phosgene is non-mutagenic under the conditions of the *S. typhimurium* test system, because it reacts rapidly in the test medium. We detected unchanged phosgene in the solution only above a gaseous concentration of 10,000 ppm."

CONCLUSIONS

Phosgene would not be mutagenic under the conditions of liquid suspension in the Ames assay, because this volatile gas reacts rapidly and completely with the components of the incubation system. This does not allow measurable exposure concentrations of phosgene to be attained in the test system. Thus, the extreme reactivity and toxicity of phosgene obviates the feasibility of further genetic toxicity testing.

DATA QUALITY

Reliability code = 2 (2C) – (Comparable to guideline study with acceptable restrictions). Report appears adequate for hazard assessment, based on the above conclusions. The quality of the report for methods and results of dichloroacetylene and the other materials tested strongly supports the credibility of the authors' conclusion.

REFERENCE

Reichert *et al.*, 1983.

12. REPEATED DOSE TOXICITY

TEST SUBSTANCE

Phosgene (CAS# 75-44-5)

Source and chemical characterization of phosgene not reported.

METHOD

Method/guideline followed: Experimental study to investigate lung effects, not an OECD guideline study

Test type:	12-week inhalation toxicity study.
GLP:	Study appears to be in compliance with GLP, since conducted by USEPA laboratory
Year study performed:	1997
Species:	Rat
Strain:	Fischer 344
Route of administration:	Inhalation
Duration of test:	4 or 12 weeks for all dose levels
Doses/concentration level:	0.1, 0.2, 0.5, 1.0 ppm
Exposure period:	6 hrs/day
Frequency of treatment:	0.1 ppm for 5 days/week; 0.2 ppm for 5 days/week; 0.5 ppm for 2 days/week; 1.0 ppm for 1 day/week
Sex:	males only
Control group and treatment:	clean air only 5 days/week for 4 or 12 weeks
Post-exposure observation period:	One group of rats exposed for 12 weeks were allowed to recover for 4 weeks. Other two groups exposed for 4 or 12 weeks were evaluated after the last exposure to phosgene
Statistical methods:	multivariate analysis of variance [MANOVA]
Study design:	Only effects on the lung were investigated. These included lung weight and displacement volume, lung

histopathology, and biochemical assays (hydroxyproline and desmosine analysis).

RESULTS

NOAEL: None

LOAEL: 0.1 ppm (based on lung weight and displacement volume)

Toxic response/effects by dose level: No lethality was reported in any of the exposed groups. Lung weight and displacement volume were significantly changed at 4 weeks, even at the 0.1 ppm exposure concentration. There was no further change at 12 weeks.

Pulmonary histological changes [thickening and inflammation] were associated with phosgene exposure, at the terminal bronchiolar regions at 0.1 and 0.2 ppm concentrations, and in the more peripheral areas at 1.0 ppm [the 0.5 ppm samples were inadvertently lost]. The severity of changes seemed to depend on phosgene concentrations, and not concentration X time of exposure.

Histopathology following 4 weeks of clean air recovery after 12 weeks of phosgene exposure indicated almost complete recovery at 0.1 ppm; the 0.2 ppm group appeared to have resolved considerably; collagen staining remained at the same level of intensity in the 12 weeks group at 0.2 and 1.0 ppm.

CONCLUSIONS

The authors conclude that daily exposure to 0.1 ppm phosgene for 6 hrs/day, 5 days/week, for 4 and 12 weeks can cause subtle histological changes in the lungs of rats. Higher concentrations cause more pronounced effects, which appear to depend more on phosgene concentration than time of exposure. No lethality was reported.

DATA QUALITY

Reliability = 2 (2C) – (Comparable to guideline study with acceptable restrictions). EPA study was well conducted and reported, but restrictions are that only male rats were used.

REFERENCE

Kodavanti *et al.*, 1997.

13. REFERENCES

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