

HPA Compendium of Chemical Hazards

Phosgene

Key Points

Fire

- Non-combustible gas under normal conditions
- Emits toxic vapours
- In the event of a fire involving phosgene, use fine water spray and wear liquid-tight protective clothing with breathing apparatus

Health

- Phosgene is extremely poisonous by inhalation, skin and eye exposure
- Acute inhalation at low concentrations may cause nose and throat irritation and coughing
- Acute inhalation at high concentrations may cause breathlessness and coughing and possible delayed serious lung damage
- Signs of toxicity may be delayed by several hours
- Skin and eye exposure may cause irritation, erythema and burns
- The effect of chronic exposure is thought to cause similar symptoms as acute exposure
- Phosgene is not thought to be carcinogenic or mutagenic

Environment

- Avoid release into environment
- Inform Environment Agency of any substantial release incidents

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Phosgene

General information

Key Points

Fire

- Non-combustible gas under normal conditions
- Emits toxic vapours
- In the event of a fire involving phosgene, use fine water spray and wear liquid-tight protective clothing with breathing apparatus

Health

- Phosgene is extremely poisonous by inhalation, skin and eye exposure
- Inhalation at low concentrations may cause irritation to the airways
- Inhalation at high concentrations may cause breathlessness and coughing and possible delayed serious lung damage
- Signs of poisoning may be delayed by several hours
- Skin and eye exposure may cause irritation and burns
- The effect of long-term exposure is thought to cause similar symptoms as short-term exposure
- Phosgene is not thought to be carcinogenic or mutagenic

Environment

- Avoid release into environment
- Inform Environment Agency of any substantial release incidents

Background

Phosgene is a colourless, reactive, non-flammable gas that is heavier than air. It is commonly stored under high pressure as a liquid.

Phosgene was first produced by John Davy (inventor of the 'Davy Lamp') at the start of the 19th century. The chemical was named by combining the Greek words 'phos' (meaning light) and genesis (birth), as Davy used sunlight to produce the chemical from carbon monoxide and chlorine.

Phosgene is an important industrial chemical, with several million tons produced globally each year. Phosgene gas is produced industrially by reacting carbon monoxide with chlorine over a catalyst at high temperature. The main commercial use of phosgene is in the manufacture of other chemicals such as plastics, pesticides, medicines, dyes and herbicides.



Phosgene is not used domestically and so exposure in the home is unlikely. However, phosgene can be produced accidentally if solvents containing chlorine are exposed to hot metal surfaces or flames.

As with all chemicals, the health effects of phosgene are related to the concentration to which you are exposed. Phosgene is

categorised as being very toxic and at low concentrations it may cause eye, nose and throat irritation. Exposure to higher concentrations may cause breathlessness and a cough which produces white or yellow sputum.



Delayed, serious lung damage may occur after exposure to high concentrations. Spills of liquefied phosgene on the skin may cause irritation and burns. Children may be more sensitive to the effects of phosgene due to their smaller size. Phosgene is particularly dangerous as exposure may go unnoticed and there may be a delay of several hours before signs of poisoning become apparent. Therefore, it is very important that anyone who has been potentially exposed to phosgene must be referred to hospital for observation.

People who have been exposed to phosgene generally make a complete recovery, although this may take some months for those exposed to high concentrations. Smokers and people with existing lung diseases may experience more severe and persistent lung injury.

Phosgene is unlikely to cause harm to the unborn child and is not considered to be a cancer-causing chemical (carcinogen).

Frequently Asked Questions

What is phosgene?

Phosgene is a colourless, non-flammable, toxic gas that is heavier than air.

What is phosgene used for?

The main use of phosgene is in the manufacture of other chemicals such as plastics, pesticides, dyes and herbicides.

How does phosgene get into the environment?

A rare cause of phosgene in the environment is accidental release from an industrial site or transport vehicle (so-called 'fugitive emissions'). Phosgene can also be present in smoke from fires which are fuelled by certain types of plastic or chlorine-containing solvents.

If there is phosgene in the environment will I have any adverse health effects?

The presence of phosgene in the environment does not always lead to exposure. Clearly, in order for it to cause any adverse health effects you must come into contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact. Following exposure to any chemical, the adverse health effects you may encounter depend on several factors, including the amount to which you are exposed (dose), the way you are exposed, the duration of exposure, the form of the chemical and if you were exposed to any other chemicals.

Exposure to phosgene may result in transient (brief) eye, throat and chest irritation. There may then be a symptom-free period of 30 minutes to one day, after which signs of lung damage (coughing, chest pain and breathlessness) may occur. Exposure to high concentrations of phosgene may eventually lead to a serious condition called pulmonary oedema (pronounced "ed-eem-a"), where fluid enters the lung and limits the body's ability to absorb oxygen from the air. As these serious effects are delayed and may occur in the absence of initial signs or symptoms, it is important that anyone who has been knowingly exposed to phosgene be taken to hospital for observation.

Like most other chemicals, the concentration of phosgene has to be above a certain level to cause health effects. A one-off exposure (sufficient to cause mild eye nose or throat irritation) is unlikely to result in long-term health effects. After exposure to high concentrations, recovery may take many months for some people.

Smokers and people with existing lung diseases may experience more severe and persistent respiratory symptoms.

How will I be exposed to phosgene?

Phosgene is a gas and the eyes and lungs are most likely to be exposed. Phosgene may also be transported in liquid form in which case contact may cause frost-bite and skin irritation.

Can phosgene cause cancer?

Exposure to phosgene has not been linked to the development of cancer. In other words, phosgene is not thought to be carcinogenic.

Does phosgene affect children or damage the unborn child?

There is little information on the effects of phosgene on children. However, they may be more susceptible to the effects of phosgene due to their smaller size. There is no evidence to suggest that phosgene, at concentrations that do not affect the mother, can affect the health of the unborn child. However, exposure to phosgene during pregnancy should be avoided.

Are people exposed to phosgene at work at risk of adverse health effects?

Work-places are subject to legal restrictions on the allowable concentration of phosgene in the air. These 'exposure limits' are set well below those which are thought to cause health effects following daily exposure to phosgene.

What should I do if I am exposed to phosgene?

It is very unlikely that the general population will be exposed to a level of phosgene high enough to cause adverse health effects.

Phosgene

Incident management

Key Points

Fire

- Non-combustible
- Toxic vapours emitted
- In the event of a fire involving phosgene, use fine water spray and liquid-tight protective clothing with breathing apparatus

Health


- Toxicity due to inhalation, skin and ocular exposure
- Very toxic and corrosive
- There may be a delay of several hours between inhalation exposure and onset of signs and symptoms
- Inhalation causes nose and throat irritation and coughing. At higher concentrations breathlessness, nausea and vomiting may occur
- Dermal exposure causes skin irritation and burns
- Ocular irritation causes irritation, lacrimation and corneal perforation

Environment

- Avoid release into the environment
- Inform Environment Agency of substantial release incidents

Hazard Identification

Standard (UK) Dangerous Goods Emergency Action Codes^(a)

UN		1076	Phosgene	
EAC		2XE	Use fine water spray. Wear liquid-tight chemical protective clothing in combination with breathing apparatus*. Spillages and decontamination run-off should be prevented from entering drains and watercourses. There may be a public safety hazard outside the immediate area of the incident**.	
APP		B	Gas-tight chemical protective suit with breathing apparatus***.	
Hazards	Class	2.3	Toxic gas	
	Sub risks	8	Corrosive substance	
HIN		268	Toxic gas, corrosive	

UN – United Nations number; EAC – Emergency Action Code; APP – Additional Personal Protection; HIN - Hazard Identification Number



* Liquid-tight chemical protective clothing (BS 8428) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).

** People should stay indoors with windows and doors closed, ignition sources should be eliminated and ventilation stopped. Non-essential personnel should move at least 250 m away from the incident.

*** Gas-tight chemical protective clothing (BS EN 943 part 2) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).




^a Dangerous Goods Emergency Action Code List, HM Fire Service Inspectorate, Publications Section, The Stationery Office, 2009.

Chemical Hazard Information and Packaging for Supply Classification^(a)

Classification	T+	Very toxic	
	C	Corrosive	
Risk phrases	R26	Very toxic by inhalation	
	R34	Causes burns	
Safety phrases	S1/2	Keep locked up and out of the reach of children	
	S9	Keep container in a well ventilated place	
	S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice	
	S36/37/39	Wear suitable protective clothing, gloves and eye/face protection	
	S45	In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)	

^a Annex VI to Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures- Table 3.2.
<http://esis.jrc.ec.europa.eu/index.php?PGM=cla> (accessed 11/2011)

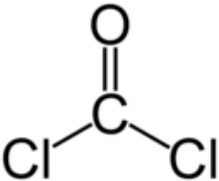
*Globally Harmonised System of Classification and Labelling of Chemicals (GHS)^(a)**

Hazard Class and Category	Press. Gas	Compressed gas	
	Acute Tox. 2	Acute toxicity (inhalation), category 2	
	Skin Corr. 1B	Skin corrosion, category 1B	
Hazard Statement	H330	Fatal if inhaled.	
	H314	Causes severe skin burns and eye damage	
Signal Words	DANGER		

* Implemented in the EU on 20 January 2009.

^a Annex VI to Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures- Table 3.1.
<http://esis.jrc.ec.europa.eu/index.php?PGM=cla> (accessed 11/2011)

Physicochemical Properties

CAS number	75-44-5
Molecular weight	99
Empirical formula	CCl ₂ O
Common synonyms	Carbonic dichloride; Carbonyl chloride; Chloroformyl chloride
State at room temperature	Gas
Volatility	Vapour pressure = 1,215 mm Hg at 20 °C
Specific gravity	1.4 at 0 °C (water = 1)
Vapour density	3.5 at 20 °C (air = 1)
Flammability	Non flammable
Lower explosive limit	Data not available
Upper explosive limit	Data not available
Water solubility	Slightly soluble
Reactivity	May react violently with water, ammonia and primary amines
Reaction or degradation products	Reacts with water to form hydrochloric acid and carbon dioxide. Carbon monoxide and chlorine also produced
Odour	Freshly mown or musty hay odour
Structure	

References^(a,b,c)

^a WHO / UN / ILO International Programme on Chemical Safety: International Chemical Safety Card (ICSC) 0007: Phosgene, 2002.

^b The Dictionary of Substances and their Effects. Ed. S Gangolli. Second Edition, Volume 6, 1999.

^c The Merck Index (14th Edition), Entry 7335: Phosgene, 2006

Threshold Toxicity Values

EXPOSURE VIA INHALATION		
ppm	mg m⁻³	SIGNS AND SYMPTOMS
3 – 5	12 – 20	Irritation of eyes, throat and upper respiratory system
62	251	Fatal (30 minute exposure)
500	2022	Fatal (1 minute)

Reference^(a)

^a Phosgene (MEDITEXT® Medical Management). In: Klasco RK (Ed): TOMES® System. Thomson Micromedex, Greenwood Village, Colorado (accessed 02/2010).

Published Emergency Response Guidelines

Emergency Response Planning Guideline (ERPG) Values^(a)

	Listed value (ppm)	Calculated value (mg m ⁻³)
ERPG-1*	-	-
ERPG-2**	0.5	2.02
ERPG-3***	1.5	6.07

* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odour.

** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.

*** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects.

Acute Exposure Guideline Levels (AEGLs)^(b)

	ppm				
	10 min	30 min	60 min	4 hr	8 hr
AEGL-1[†]	-	-	-	-	-
AEGL-2^{††}	0.60	0.60	0.30	0.08	0.04
AEGL-3^{†††}	3.6	1.5	0.75	0.20	0.09

[†] The level of the chemical in air at or above which the general population could experience notable discomfort.

^{††} The level of the chemical in air at or above which there may be irreversible or other serious long-lasting effects or impaired ability to escape.

^{†††} The level of the chemical in air at or above which the general population could experience life-threatening health effects or death.

^a American Industrial Hygiene Association (AIHA). 2010 Emergency Response Planning Guideline Values and Workplace Environmental Exposure Level Guides Handbook, Fairfax, VA (accessed 01/2011).

^b U.S. Environmental Protection Agency. Acute Exposure Guideline Levels, <http://www.epa.gov/oppt/aegl/pubs/chemlist.htm> (accessed 01/2011)

Exposure Standards, Guidelines or Regulations

Occupational standards

WEL^(a)	LTEL(8 hour reference period): 0.02 ppm (0.08 mg m ⁻³)
	STEL(15 min reference period): 0.06 ppm (0.25 mg m ⁻³)

Public health guidelines

DRINKING WATER QUALITY GUIDELINE^(b)	No guideline value specified
AIR QUALITY GUIDELINE	No guideline value specified
SOIL GUIDELINE VALUE AND HEALTH CRITERIA VALUES	No guideline value specified

WEL – Workplace exposure limit; LTEL - Long-term exposure limit; STEL – Short-term Exposure Standards, Guidelines or Regulations

^a List of approved workplace exposure limits (as consolidated with amendments October 2007). <http://www.hse.gov.uk/cosHH/table1.pdf> (An update to EH40/2005: Workplace Exposure Limits 2005. The Stationery Office, London) (accessed 01/2011).

^b The Water Supply (Water Quality) Regulations 2000 (England) and the Water Supply (Water Quality) Regulations 2001 (Wales) (accessed 01/2011)..

Health Effects

Major route of exposure^(a)

- Due to its gaseous nature, inhalation and ocular exposure are most likely.
- Dermal features usually only occur from splashes of liquefied material.
- Ingestion is unlikely.

Immediate signs or symptoms of acute exposure^(a,b)

- Inhalation of 3 ppm causes nose, throat irritation and 4.8 ppm causes coughing. Higher concentrations (>30 ppm) cause pain in the chest and breathlessness; nausea and vomiting may occur. Continued exposure to phosgene concentrations above 100 ppm may be rapidly fatal. Following initial symptoms there may be an asymptomatic period before the onset of non-cardiogenic pulmonary oedema with severe breathlessness and a productive cough.
- The presence or absence of initial symptoms does not reflect the severity of poisoning as non-cardiogenic pulmonary oedema may still develop up to 24 hours (rarely 72 hours) later in individuals who show minimal or no immediate effects. However, non-cardiogenic pulmonary oedema is more likely to develop the greater the exposure (>150 ppm) to phosgene. Rarely, in very severe cases, circulatory collapse may follow the development of non-cardiogenic pulmonary oedema.
- Dermal exposure to 3 ppm causes skin irritation and splashes from liquefied material may cause burns.
- Ocular exposure causes irritation at 3 ppm and may also cause lacrimation. Splashes from liquefied material may cause corneal opacification, conjunctival adhesions and perforation.

TOXBASE - <http://www.toxbase.org> (accessed 01/2011)

^a TOXBASE: Phosgene, 08/2001.

^b TOXBASE: Phosgene – medical briefing.

Decontamination and First Aid

Important Notes

- Ambulance staff, paramedics and emergency department staff treating chemically-contaminated casualties should be equipped with Department of Health approved, gas-tight (Respirex) decontamination suits based on EN466:1995, EN12941:1998 and prEN943-1:2001, where appropriate.
- Decontamination should be performed using local protocols in designated areas such as a decontamination cubicle with adequate ventilation.
- Phosgene is a volatile substance and secondary contamination is unlikely to occur.

Dermal exposure^(a,b)

- Remove patient from exposure.
- The patient should remove all clothing and personal effects.
- Double-bag soiled clothing and place in a sealed container clearly labelled as a biohazard.
- Brush away any adherent solid particles and gently blot away any adherent liquid from the patient.
- Wash hair and all contaminated skin with copious amounts of water (preferably warm) and soap for at least 10-15 minutes. Decontaminate open wounds first and avoid contamination of unexposed skin.
- Pay special attention to skin folds, axillae, ears, fingernails, genital areas and feet.

Ocular exposure^(c)

- Remove patient from exposure.
- Remove contact lenses if necessary and immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10-15 minutes.
- Patients with corneal damage or those whose symptoms do not resolve rapidly should be referred for urgent ophthalmological assessment.

Inhalation^(a)

- Remove patient from exposure.
- Ensure a clear airway and adequate ventilation.
- Give oxygen to symptomatic patients.
- Exposed individuals should be assessed at hospital irrespective of the presence or severity of symptoms.
- Apply other measures according to the patient's clinical condition.

Ingestion

- Not applicable.

This document will be reviewed not later than 3 years or sooner if substantive evidence becomes available.

TOXBASE - <http://www.toxbase.org> (accessed 01/2011)

^a TOXBASE: Phosgene, 08/2001.

^b TOXBASE: Skin decontamination – corrosives, 2002.

^c TOXBASE: Chemicals splashed or sprayed into the eyes, 2007.

Phosgene

Toxicological overview

Key Points

Kinetics and metabolism

- Main route of entry is inhalation
- Very rapidly hydrolysed within respiratory tract to carbon dioxide and hydrochloric acid
- Little or no systemic absorption

Health effects of acute exposure

- Extremely poisonous by inhalation
- Signs of poisoning may be delayed by up to 24 hours post exposure
- Inhalation may lead to eyes, nose and throat irritation, dyspnoea and coughing.
- Pulmonary oedema, cyanosis, shock and respiratory arrest may also occur
- Skin exposure causes irritation and erythema
- Ocular exposure results in lacrimation and inflammation

Health effects of chronic exposure

- Limited data, but effect of acute exposure expected to be similar to acute exposure
- Phosgene is not thought to be carcinogenic or mutagenic

Toxicological Overview

Summary of Health Effects

The clinical manifestations of phosgene exposure are often immediate in presentation and include irritation of the eye, nose and throat. However, exposure to low concentrations of phosgene may result in no initial symptoms, allowing inhalation of the vapour for longer periods.

Adverse effects resulting from inhalation exposure to phosgene have been categorised into three distinct phases: Initial irritation followed by a latent phase (up to 24 hours) subsequent to the onset of chest pain, discomfort, thirst, headache, nausea, increased cough (with haemoptysis), production of large quantities of frothy white or yellow sputum, cyanosis, feeling of suffocation and non-cardiogenic pulmonary oedema (occurring up to 48 hours post exposure).

All individuals known to have been exposed to phosgene should be assessed at hospital irrespective of the presence or severity of early signs and symptoms as these are not reliable prognostic indicators.

Kinetics and metabolism

The primary route of exposure is by inhalation. Phosgene is highly reactive; its short half-life in aqueous solution ($t_{1/2} \sim 0.026$ s) tends to preclude systemic absorption and distribution. Hydrolysis of phosgene within the moist environment of the pulmonary system may cause the liberation of hydrochloric acid and carbon dioxide which are distributed and eliminated according to normal physiological processes [1]. The generation of hydrochloric acid does not play a key role in the toxicity of phosgene [2].

Sources and route of exposure

There are four potential sources of phosgene in the environment: combustion of chlorinated hydrocarbons, photo-degradation of organochlorine compounds, fugitive release and deliberate release. Combustion of chlorinated hydrocarbons such as methylene chloride (paint stripper), trichloroethylene and tetrachloroethane may liberate smoke and fumes containing phosgene. Contact of chlorinated solvents with hot metal surfaces may also liberate significant quantities of phosgene, for example, during the welding of metal that has been prepared by cleaning with chlorinated solvents [3]. Organochlorine pollutants such as chloroform and tetrachloroethylene and polymers such as polyvinyl chloride (PVC) may decompose in the atmosphere (on exposure to solar radiation) to form significant quantities (several hundred thousand tonnes) of phosgene each year [1].

Health Effects of Acute / Single Exposure

Human Data

General toxicity

The adverse health effects of phosgene exposure are primarily related to the pathological responses of the pulmonary system, the critical effect being pulmonary oedema [4]. The threshold toxicity levels for phosgene are summarised in Table 1.

Table 1: Estimated threshold toxicity values for human (inhalation) exposure to phosgene. LCt values refer to the dose that would result in 1, 50 or 100% fatalities in an exposed population. Dose expressed as Ct; the product of concentration and time of exposure. Data from EHC 193 [1].

Concentration		Effect(s)
ppm	mg m ⁻³	
0.4	1.6	Perception of odour
1.5	6	Recognition of odour
3	12	Irritation of eyes, nose and throat
Dose		
ppm min	mg min m ⁻³	
>30	>120	Onset of lung damage
>150	>600	Pulmonary oedema
~300	~1200	LCt ₁
~500	~2000	LCt ₅₀
~1300	~5200	LCt ₁₀₀

Phosgene generally conforms to Haber's rule in that certain physiological effects of exposure (e.g. lung damage or death) are proportional to the product of concentration and duration of exposure (Ct), although deviation from Haber's rule occurs following chronic exposures [2]; (see animal section on chronic health effects, below).

Inhalation

There are three, distinct phases associated with the inhalation of phosgene at levels ranging from 30 – 300 ppm min (120 – 1200 mg min m⁻³), viz., an initial reflex syndrome, clinical latent period and clinical oedema phase [1]. During the initial phase, an individual may experience eye, nose and throat irritation and pain, dyspnoea and coughing. The duration of the latent phase is generally proportional to the level of exposure, generally lasting from 30 minutes to 24 hours [4]. However, the latent phase may be absent following exposure to a supra-lethal concentration of phosgene. The final phase involves the clinical manifestation of pulmonary oedema, associated with shortness of breath, productive cough (white or yellow frothy fluid, sometimes with haemoptysis), cyanosis, shock and respiratory arrest.

Ingestion

Not relevant.

Dermal / ocular exposure

At concentrations above 3 ppm, exposure of (moist) skin to phosgene may cause skin irritation and erythema. Ocular effects may also occur, such as lacrimation and inflammation (conjunctival hyperaemia). Splashes of liquefied phosgene may cause frost-bite and complete corneal opacification [1].

Delayed effects following an acute exposure

A single, acute exposure to phosgene is not generally associated with long-term sequelae. However, sensitive individuals (particularly smokers and those with a pre-existing pulmonary dysfunction such as emphysema) and those exposed to high concentrations may exhibit persistent, chronic signs such as shortness of breath and reduced physical capacity (exertional dyspnoea). It has been suggested that anoxia (resulting from pulmonary oedema) may be responsible for other chronic effects that have been tentatively (not conclusively) associated with phosgene intoxication. These include neurasthenia, epilepsy, peripheral Raynaud-like syndrome and dysfunction of the peroneal nerve (resulting in lower-leg paralysis) [1].

Animal Data

The acute effects of phosgene observed in animal models are consistent with those described for human. The lung is the primary target organ in all species with the characteristic pathological feature being the delayed clinical manifestation of pulmonary oedema. In most laboratory species, the lethal dose (LC₅₀) phosgene is 1000 – 2000 mg min m⁻³ [1].

The pulmonary effects of sub-lethal phosgene exposure in animals include oedema, petechial haemorrhage, bronchial epithelial necrosis, increase in lung weight, changes in blood gas chemistry (consistent with hypoxia) and increased protein, collagen and leukocytes in bronchoalveolar lavage (BAL) [5, 6].

Health Effects of Chronic / Repeated Exposure

Human Data

General toxicity

There is a paucity of data concerning the effects of chronic phosgene exposure in humans. In one study of workers at a phosgene factory, no long-term illness or deaths were attributable to phosgene exposure [7]. The average concentration of phosgene measured in the factory was 0.01 mg m^{-3} , equating to a Ct of $4.8 \text{ mg min m}^{-3}$ [1.2 ppm min] for an 8 hour working day.

No excess deaths or deaths from respiratory disease were demonstrable in workers in a uranium processing plant routinely exposed to “low” or occasionally “high levels” of phosgene [8, 9].

Genotoxicity, carcinogenicity, reproductive and developmental toxicity

There is no evidence to suggest that phosgene is carcinogenic or mutagenic. It is unlikely that biologically relevant quantities of phosgene will be systemically absorbed following inhalation exposure due to the very rapid hydrolysis of phosgene to hydrochloric acid and carbon dioxide [1]. Similarly, there have been no reports associating phosgene exposure with adverse reproductive or developmental effects [1].

Animal and In-Vitro Data

Inhalation

There are no reports on the long-term exposure of animals to phosgene, although the effects of repeated exposure have been subject to limited investigations. In one study, dogs were exposed 1 – 3 times per week to $96 - 160 \text{ mg min}^{-3}$ for up to 12 weeks. The main effects were chronic bronchiolitis and emphysema [1]. In a more recent study, “adaptation” to chronic phosgene exposure (up to 1 ppm, 6 hours per day, up to 5 days per week) was observed if the dose was not overwhelming and repeated daily [10]. Thus, whilst phosgene obeys Haber’s rule for short to medium term exposures, this is not the case for chronic exposures [2].

Immunotoxicity

Given that the pulmonary system is the target organ for phosgene, studies have investigated the effect of exposure on susceptibility to respired pathogens. Overall, there was a decrease in host resistance in response to various pathogens (Table 3).

Table 3: Effect of phosgene exposure on pulmonary immuno-competence in animals. N.s. = not specified. Data from [1].

Species	Dose		Effect
	C (mg m ⁻³)	T (hours)	
Rat	0.4 – 4	4	Decrease in pulmonary natural killer cells (≥ 2 mg m ⁻³).
Rat	4	4	Blood titre of rat-adapted influenza virus significantly higher than control up to 4 days post infection.
Rat	0.4 – 0.8	6	Significant decrease in pulmonary clearance of bacteria (<i>Streptococcus zooepidemicus</i>).
Mice	0.04 – 0.4	4	Significant elevation in mortality following infection with a <i>S. zooepidemicus</i> and melanoma tumour cell mixture (≥ 0.1 mg m ⁻³).
Rat	0.2 - 4	n.s.	Decrease in concentrations of prostaglandin E2 and leukotrienes (≥ 0.4 mg m ⁻³).
Rat	0.4 – 0.8	6h/day, 5days/week, 4 or 12 week duration	Decreased clearance of bacteria. Resolved 4 weeks after cessation of exposure.

It is not possible to interpret these animal studies in terms of potential health effects in humans due to the lack of adequate human data. However, it would seem prudent to assume that exposure to phosgene may affect susceptibility to respiratory infections in humans.

Genotoxicity

No available data.

Carcinogenicity

One study reported no increase in neoplasms in guinea pigs (n=20) and rats (n=20) following exposure to phosgene over 18 and 24 months, respectively. However, this study is inadequate to draw any conclusions regarding the carcinogenicity of phosgene [1]. There are no other studies reported.

Reproductive and developmental toxicity

There are no reports available on the reproductive effects of phosgene in any animal model.

References

- [1] International Programme on Chemical Safety (IPCS) (1997) Phosgene. Environmental Health Criteria 193.WHO, Geneva
- [2] Maynard, R. L. (2007) Chapter 24: Phosgene.T.C. Marrs, R.L. Maynard and D.R. Sidell, Chemical warfare agents: toxicology and treatment., John Wiley and Sons Ltd, Chichester
- [3] Leikauf, G. D. and Prows, D. R. (1991) Inorganic compounds of carbon, nitrogen and oxygen.Bingham E, Cohrssen B and Powell C.H., Patty's Toxicology, John Wiley and Sons, Ltd., Chichester
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This document will be reviewed not later than 3 years or sooner if substantive evidence becomes available.