FOREWORD INTRODUCTION

PHOSPHORYL TRICHLORIDE

CAS N°: 10025-87-3

SIDS Initial Assessment Report

For

SIAM 19

Berlin, Germany, 19-22 October 2004)

1.	**Chemical Name:**	Phosphoryl trichloride
2.	**CAS Number:**	10025-87-3
3.	**Sponsor Country:**	Germany Contact Point: BMU (Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit) Contact person: Prof. Dr. Ulrich Schlottmann Postfach 12 06 29 D- 53048 Bonn
4.	**Shared Partnership with:**	
5.	**Roles/Responsibilities of the Partners:**	
~	Name of industry sponsor /consortium	Bayer AG, Germany Contact person: Dr. Burkhardt Stock D-51368 Leverkusen Gebäude 9115
~	Process used	The BUA Peer Review Process : see next page
6.	**Sponsorship History**	
~	How was the chemical or category brought into the OECD HPV Chemicals Programme ?	by ICCA-Initiative
7.	**Review Process Prior to the SIAM:**	last literature search (update): 14 March 2004 (Human Health): databases medline, toxline; search profile CAS-No. and special search terms 9 March 2004 (Ecotoxicology): databases CA, biosis; search profile CAS-No. and special search termsOECD/ICCA
8.	**Quality check process:**	As basis for the SIDS-Dossier the IUCLID was used. All data have been checked and validated by BUA. A final evaluation of the human health part has been performed by the Federal Institute for Risk Assessment (BfR) and of the ecotoxicological part by the Federal Environment Agency (UBA).

9. Date of Submission: Deadline for circulation: 23 July 2004

10. Date of last Update: Last literature search: IUCLID Chapters 1-4:
Chapter 5: 2003-05-01

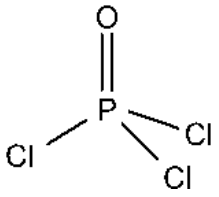
11. Comments: **OECD/ICCA - The BUA* Peer Review Process**

Qualified BUA personnel (toxicologists, ecotoxicologists) perform a quality control on the full SIDS dossier submitted by industry. This quality control process follows internal BUA guidelines/instructions for the OECD/ICCA peer review process and includes:

- a full (or update) literature search to verify completeness of data provided by industry in the IUCLID/HEDSET
- Review of data and assessment of the quality of data
- Review of data evaluation
- Check of adequacy of selection process for key studies for OECD endpoints, and, where relevant, for non-OECD endpoints by checking original reports/publications
- Review of key study description according to robust summary requirements; completeness and correctness is checked against original reports/publications (if original reports are missing: reliability (4), i.e. reliability not assignable)
- Review of validity of structure-activity relationships
- Review of full SIDS dossier (including SIAR, SIAP and proposal for conclusion and recommendation for further work)
- In case of data gaps, review of testing plan or rationale for not testing

* BUA (GDCh-Beratergremium für Altstoffe): Advisory Committee on Existing Chemicals of the Association of German Chemists (GDCh)

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	10025-87-3
Chemical Name	Phosphoryl trichloride
Structural Formula	

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Phosphoryl trichloride is hydrolyzed in seconds or minutes in water or moist air. Studies on metabolism and toxicokinetics of the parent compound are not feasible. Distribution in the body is limited due to hydrolysis. Phosphoryl trichloride is a toxicant acting at the portal-of-entry. It is unlikely to reach organs distant from the portal of entry. Therefore, systemic toxicity not related to the effects of irritation is not expected by any route. The products of hydrolysis, hydrochloric acid and phosphoric acid, also act at the portal of entry.

The acute toxicity of phosphoryl trichloride following inhalation is high. The 4-h-LC_{50} of phosphoryl trichloride is 48.4 ppm (308 mg/m³) to 11.1 ppm (71 mg/m³) for rats and 52.5 ppm (335 mg/m³) for guinea pigs. Clinical signs included severe respiratory tract irritation, nasal discharge and eye irritation. The oral LD_{50} was determined as 36 to 380 mg/kg bw for rats showing a very steep dose/mortality relation in individual studies. After dermal exposure the LD_{50} was > 250 mg/kg in rabbits. Signs of toxicity were decreased locomotor activity, necrosis and eschar.

Phosphoryl trichloride reacts with water, forming hydrochloric acid and phosphoric acid. Due to this hydrolytic reaction, phosphoryl trichloride is corrosive to the skin, eyes and respiratory tract. Studies with phosphoryl trichloride concerning sensitising properties are not available. The hydrolysis product hydrochloric acid gave no indication for a sensitising potential in humans and experimental animals. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected due to its structure.

From a 4 months inhalation study with phosphoryl trichloride in rats, a NOAEC could not be derived, since weight loss, respiratory irritation and increased kidney weights were still observed at the lowest exposure level of 0.48 mg/m³ (=LOAEC). The evaluation of this study is limited as methodology and results were published in little detail. Most findings were confined to the site of first contact and can be explained by the irritating/corrosive properties of the compound and its degradation products. The LOAEC found in a 90-day study with hydrochloric acid was 15 mg/m³. The excess phosphate produced by hydrolysis of phosphoryl trichloride may play a role in the development of effects on kidney, bone and calcium levels in animals. Also by other routes (oral, dermal) phosphoryl trichloride is expected to produce effects at the site of first contact (irritation, corrosion). The long term effects observed in humans (chronic bronchitis, angina, sleeping disorders) are considered as sequelae of the irritation in the lungs which after prolonged periods may lead to an impairment of lung function.

Phosphoryl trichloride as well as the hydrolysis product hydrochloric acid did not show mutagenic activity in a bacterial mutagenicity assay. As phosphoryl trichloride decomposes to hydrochloric and phosphoric acid in aqueous media the resulting acidity of the hydrolysis products may cause unspecific effects of low pH in in-vitro tests. The change in pH may induce chromosomal aberrations and other DNA damage. Specific effects of phosphoryl trichloride are not expected, due to the rapid hydrolysis. In vivo, the hydrolysis products, phosphoric and hydrochloric acid, will be neutralized immediately in the physiologic medium at low concentrations. The reduced pH levels could lead to chromosomal changes and DNA damage at the portal-of-entry of phosphoryl

trichloride. However, it is unlikely that systemic changes in pH would occur after exposure to phosphoryl trichloride, that are sufficient in magnitude to induce this effect in distant tissues or organs. Due to the corrosive nature of phosphoryl trichloride the performance of studies in animals with doses inducing corrosive effects is not warranted.

No carcinogenicity studies with phosphoryl trichloride were identified. The hydrolysis product hydrochloric acid gave no indications for an increased tumor incidence after life-time exposure in laboratory animals. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected. At low concentrations the hydrolysis products, phosphoric and hydrochloric acid, will be neutralised immediately in the physiologic medium at the portal of entry. Nevertheless prolonged irritation could give rise to a constant stimulus to local cell proliferation.

Studies with phosphoryl trichloride concerning effects on fertility and development were not available and there were also no data on fertility effects for the hydrolysis products phosphoric acid and hydrochloric acid. Because phosphoryl trichloride as well as its hydrolysis products is a toxicant acting at the portal-of-entry, and because it is unlikely to reach the reproductive organs or the embryo/fetus, toxicity to reproduction or developmental toxicity in mammals are not likely to occur following exposure to phosphoryl trichloride by any route. Studies with PCl_3 did not show respective effects. The other product of hydrolysis and subsequent partial neutralisation of phophorus trichloride, mono sodium phosphite, gave also no indication of a carcinogenic potential after long term oral exposure.

Environment

Phosphoryl trichloride is a moisture/water sensitive fluid with a melting point of 1.3 °C, a boiling point of 105.1 °C, and a density of 1.675 g/cm³ at 20 °C. The vapour pressure of the substance is 53.3 hPa at 27.3 °C. The log K_{ow}, the water solubility and several other parameters cannot be determined due to hydrolysis. Phosphoryl trichloride hydrolyzes completely in water within less than 10 s at 20 °C (via the hydrolysation intermediate phosphorodichloric acid), forming phosphoric acid and hydrochloric acid. Any emission into water, air, or the terrestrial compartment would be affected by humidity and also results in the formation of the hydrolysis products. Hydrochloric acid dissociates readily in water causing a pH shift which determines the impact of phosphoryl trichloride on aquatic life. The tolerance of water organisms towards pH is diverse. Recommended pH values for test species listed in OECD guidelines are between 6 and 9.

Phosphoric acid is of medium acidity ($pK_a = 2.1$) and partly dissociates in water causing a pH shift. Phosphoric acid and phosphates may affect aquatic life due to their fertilizing effect. Several aquatic toxicity tests have been undertaken in non-buffered solution. The observed toxicity effects in these studies can be attributed to the acidity of the degradation products and are not used for the hazard assessment. Acute toxicity of phosphoryl trichloride to fish was evaluated by using fish tests with phosphorus trichloride and phosphorus pentachloride. Toxicity of phosphorus trichloride (buffered) on *Danio rerio* (tested according to the German guideline proposal "Lethal effects on *Brachydanio rerio*") yielded a 96 h-LC_0 (nominal concentration) ≥ 1000 mg/l.

Tests with invertebrates were done with phosphoryl trichloride and phosphorus trichloride, for proving the validity of the evaluation approach. With *Daphnia magna* an EC_{50} (48 h) of > 100 mg/l in buffered solution was determined for both substances (92/69/EEC, method C.2). Algal toxicity was determined with phosphoryl trichloride and phosphorus trichloride. In a growth inhibition test with *Desmodesmus subspicatus* (92/69/EEC, method C.3) in buffered solution no effect was observed at 100 mg/l (nominal).

There is no result available on chronic toxicity. With activated sludge a 3 h-EC_{50} of 9450 mg/l (nominal) and an EC_0 of 3520 mg/l (nominal) were measured according to the ISO 8192 (pH not reported) for phosphorus trichloride.
There are test results available for acute testing from three trophic levels (all in buffered media). Using the lowest acute test result (> 100 mg/l) and an assessment factor of 1000 (EU Technical Guidance Document), a $PNEC_{aqua}$ > 0.1 mg/l is obtained.

Exposure

The global production capacity of phosphoryl trichloride was estimated to be 0.2 million tonnes for about 15 producers in 2002. Approximately 0.15 million tonnes/year of the manufacturing capacity are in the OECD countries and 0.05 million tonnes/year in non-member countries.
Phosphoryl trichloride is a basic chemical which is used industrially as an intermediate. Because of its reactivity

phosphoryl trichloride has a large number of applications as an intermediate in chemical processes (percentages reported for the USA 2001):

- Plastics and elastomers additives (55 %)
- Functional fluids, e.g. phosphate ester hydraulic fluids (22 %)
- Pesticides (7 %)
- Lubricant oil additives (4 %)
- Surfactants and sequesterants (2 %)
- Miscellaneous (10 %)

At one company in the Sponsor country phosphoryl trichloride is manufactured and processed in closed systems. The exhausts from manufacturing and processing (including filling) of phosphoryl trichloride are connected to air washing units. Thus, at this company, during production and processing virtually no phosphoryl trichloride is emitted into the atmosphere. Due to water-free production, processing, and rapid hydrolysis phosphoryl trichloride is not detectable in the wastewater. In this company, the exposure of workers is well below the maximum admissible concentration of phosphoryl trichloride in the workplace air (MAK) of 1.3 mg/m^3 (0.2 ppm). The exposure of workers to the hydrolysis product hydrochloric acid is also well below the MAK value of 8 mg/m^3 (5 ppm) for hydrogen chloride. Immunoglobulines against phosphoryl trichloride have not been detected.

No direct use is known. Phosphoryl trichloride is not listed in the Norwegian and Swiss product registers. In the Finnish, and Swedish product registers, in total, there are about a dozen industrial preparations, all with a non-dispersive use in closed systems. Entries in the Danish Product Register are confidential. An exposure of consumers to phosphoryl trichloride is unlikely to occur.

The use of phosphoryl trichloride as a solvent in cryoscopy respectively as an anhydrous solvent in general is limited to some scientific laboratories. Phosphoryl trichloride can be converted by multistage -chemical synthesis to nerve gases. Therefore the production and export of phosphoryl trichloride is stringently controlled under the International Chemical Weapons Convention.

RECOMMENDATION AND RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

Human Health: The chemical possesses properties indicating a hazard for human health (acute toxicity, corrosiveness). Based on data presented by the Sponsor country (relating to production by one producer which accounts for 5 – 25 % of global production and relating to the use pattern of several OECD countries), exposure is limited to the technically feasible extent in occupational settings in the sponsor country. There is no exposure of consumers. No recommendation for further testing within the context of the SIDS program is therefore warranted. Although there are no valid data regarding reproductive effects, due to the fast hydrolysis it is unlikely that POCl3 could reach organs and tissues distant from the site of first contact, therefore, and due to the corrosive properties, studies in animals are not warranted. The chemical is currently of low priority for further work.

Environment: The chemical is currently of low priority for further work due to its low hazard profile

SIDS Initial Assessment Report

1. Identity

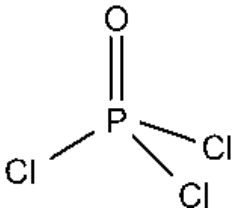
1.1 Identification of the Substance

CAS Number: 10025-87-3

Chemical Name: Phosphoryl trichloride

Molecular Formula: $POCl_3$

Structural Formula:



Molecular Weight: 153.33

Synonyms: Phosphoric chloride
Phosphorus oxychloride
Phosphoryl chloride

1.2 Purity/Impurities/Additives

Technical phosphoryl trichloride has a purity of > 99.5 % w/w (Riess, 2002) or > 99.7 % w/w (Bayer AG, 2002). The following impurities have been reported (Bayer AG, 2002):

- Phosphorus trichloride ≤ 0.3 % w/w
- Iron ≤ 0.0005 % w/w
- Arsenic ≤ 0.000002 % w/w
- Distillation residue ≤ 0.3 % w/w

1.3 Physico-Chemical properties

Table 1 Summary of physico-chemical properties

Property	Value	Reference	IUCLID
Substance type	Inorganic compound		1.1.1
Physical state	Colourless liquid, pungent odour	Riess (2002)	1.1.1
Melting point	1.3 °C	Merck (2001)	2.1
Boiling point at 1013 hPa	105.1 °C	Riess (2002)	2.2
Density at 20 °C	1.675 g/cm³	Riess (2002)	2.3
Vapour pressure at 27.3 °C	53.3 hPa	Sax (1979)	2.4
Octanol/water partition coefficient (log Kow)	Not applicable*		2.5
Water solubility	Not stable in water due to hydrolysis*		2.6.1
Conversion factors at 25 °C (calculated)	1 ppm = 6.36 mg/m^3 1 mg/m^3 = 0.157 ppm	MAK (1984)	2.14
pH value at 25 °C	Approximately 1 (at 5 g/l)*	Bayer AG (2003a)	2.14
Vapour density in relation to air	5.3	Sax (1979)	2.14

*Rapid hydrolysis, *cf.* Chapter 2.2.3

2 GENERAL INFORMATION ON EXPOSURE

2.1 Production Volumes and Use Pattern

Phosphoryl trichloride is manufactured by a radical reaction of phosphorus trichloride with oxygen while cooling at 50 - 60 °C (Buechel, Moretto and Woditsch, 2000):

$2\ PCl_3 + O_2 \rightarrow 2\ POCl_3$

The reaction is performed either continuously or batchwise. Air can be used instead of oxygen (Riess 2002). Traces of sulfur, sulfur compounds, and heavy metals (e.g. iron, copper, cobalt) decrease the reaction rate (Buechel, Moretto and Woditsch, 2000; Riess, 2002).

It is not known, whether phosphoryl trichloride is still industrially produced from phosphorous(V) oxide, phosphorus trichloride, and chlorine according to the following equation:

$P_4O_{10} + 6\ PCl_3 + 6\ Cl_2 \rightarrow 10\ POCl_3$

Raw phosphoryl trichloride is purified by fractional distillation. (Buechel, Moretto and Woditsch, 2000).

In the chemical industry phosphoryl trichloride is also formed as a by product at the industrial synthesis of organic acid chlorides by reaction of free acid with phosphorus pentachloride (Oltramare et al., 1975).

In 1995 the phosphoryl trichloride manufacturing capacities were about 39 900 tonnes in the USA, 100 000 tonnes in Western Europe, and 30 000 tonnes in Japan. The phosphoryl trichloride consumption of the USA increased from 24 300 tonnes in 1983 to about 30 700 tonnes in 1994 (Buechel, Moretto and Woditsch, 2000).

The global production capacity of phosphoryl trichloride was estimated to be 200 000 tonnes for about 15 producers in 2002. Approximately 150 000 tonnes/year of the manufacturing capacity are in the OECD countries and 50 000 tonnes/year in non-member countries. In Western Europe there are 4 producers of phosphoryl trichloride. Three of them have production plants in Germany. In 2003, Bayer manufactured about 10 000 - 50 000 tonnes of phosphoryl trichloride in the Bayer Leverkusen industrial park (Bayer Chemicals, 2004a).

Phosphoryl trichloride is a basic chemical which is used industrially as an intermediate. Because of its properties phosphoryl trichloride has a large number of chemical applications (Greenwood and Earnshaw, 1988), e.g.

- Synthesis of alkyl- and arylphosphates by reaction with alcohols, phenols, or epoxides
- Production of carbonic acid halogenides
- Use as non aqueous solvent

Due to these properties phosphoryl trichloride is used as an intermediate for the manufacturing of wide range of chemicals (percentages reported for the USA 2001; TIG, 2004):

- Plastics and elastomers additives (55 %)
- Functional fluids, e.g. phosphate ester hydraulic fluids (22 %)
- Pesticides (7 %)
- Lubricant oil additives (4 %)
- Surfactants and sequesterants (2 %)
- Miscellaneous (10 %)

No direct use is known (Bayer Chemicals, 2004a). Phosphoryl trichloride is not listed in the Norwegian (SPIN, 2004) and Swiss product registers (Swiss Product Register, 2003). In the Finnish and Swedish product registers, in total, there are about a dozen industrial preparations containing phosphoryl trichloride. Entries in the Danish Product Register are confidential. In the Finnish product register, there are 6 different preparations for industrial use, 5 with the specification of manufacture of chemicals and chemical products and one for the manufacture of radio, television and communication equipment, all in the category with a non-dispersive use in closed systems (SPIN, 2004).

The use of phosphoryl trichloride as a solvent in cryoscopy (Merck, 2001) respectively as an anhydrous solvent in general (Roempp, 2003) is limited to some scientific laboratories.

Phosphoryl trichloride can be converted by multistage chemical synthesis to nerve gases. Therefore the production and export of phosphoryl trichloride is stringently controlled under the International Chemical Weapons Convention (1993). The Chemical Weapons Convention lists phosphoryl trichloride as precursor to chemical weapons.

2.2 Environmental Exposure and Fate

2.2.1 Sources of Environmental Exposure

Information on exposure from manufacturing and processing of the chemical is available for the Bayer production plant at Leverkusen, Germany.

Phosphoryl trichloride is manufactured, processed, and filled in closed, waterfree systems (e.g. transport via pipeline, sampling without dead volume, gas-shuttle pipe for filling processes). There is no direct wastewater in connection with the phosphoryl trichloride production process itself. Cleaning of the reactors takes place only in the case of maintenance (Bayer Chemicals, 2004a).

The exhaust from manufacturing and processing of phosphoryl trichloride is connected to a central gas washing unit. Water from the air washing unit is led to the industrial biological waster water treatment plant. There is no detectable emission of phosphoryl trichloride into the atmosphere. For this reason, phosphoryl trichloride is not listed in the official Emission Declaration of 2000 (Bayer Chemicals, 2004a).

Waste from the manufacturing and processing of phosphoryl trichloride is incinerated in a incinerator for hazardous wastes equipped with an exhaust air cleaning device (Bayer Chemicals, 2004a).

The wastewater from the Bayer production plant is lead to the Leverkusen industrial and municipal wastewater treatment plant. During the wastewater treatment (hydraulic retention time about 3 d) a rapid hydrolysis of phosphoryl trichloride (half-life < 10 seconds, *cf.* Chapter 2.2.3) occurs. Therefore, phosphoryl trichloride is not monitored at the industrial wastewater treatment plant outlet. However, the pH value of the outlet is monitored continuously and the phosphate content is determined daily (Bayer Chemicals, 2004a).

The concentrated sewage sludge of the wastewater treatment plant is incinerated in a hazardous waste incinerator especially constructed for this sludge (Bayer Chemicals, 2004a).

There is no information available on environmental exposure from production and use as synthesis intermediate at other manufacturing and processing sites. Because of the hydrolytic properties a relevant entry of phosphoryl trichloride into the environment seems to be unrealistic.

2.2.2 Photodegradation

Estimation of the photodegradation of phosphoryl trichloride is not applicable by current assessment models due to the inorganic character of the substance. Direct photolysis of gaseous phosphoryl trichloride is not expected due to the lack of adsorption of light with a wavelength above 225 nm (Jan-Khan and Samuel, 1936).

In aerosol droplets phosphoryl trichloride will be affected by humidity rather than light (*cf.* Chapter 2.2.3).

2.2.3 Stability in Water

In water, phosphoryl trichloride hydrolyzes to phosphoric acid and hydrochloric acid with $t_{1/2}$ < 10 seconds (Riess, 2002):

$POCl_3 + 3\ H_2O \rightarrow H_3PO_4 + 3\ HCl$.

Since HCl, which is formed in a ratio of 3 : 1 with regard to H_3PO_4, is a much stronger acid than H_3PO_4 ($pK_a < 0$ (Roempp, 2003) versus pK_{a1} 2.1 (Windholz, 1976)) all effects on pH are mainly caused by HCl.

The reaction of phosphoryl trichloride and water was studied by adding small amounts of neat phosphoryl trichloride into an excess of well stirred water, and following the generation of the acidic reaction products using a pH electrode. This experimental set up could not distinguish the apparent reaction rate from, e.g. the mixing delay or the inertia of the measuring system. The completeness of the chloride release was checked by titration with $AgNO_3$. The half-life of phosphoryl trichloride in water was estimated to be less than 10 seconds at 23 °C (Bayer Chemicals, 2004b).

This result is in line with other studies. The kinetics of phosphoryl trichloride hydrolysis was measured in dioxane solution containing 33 % water (Hudson and Moss, 1962). Initial hydrolysis of phosphoryl trichloride proceeds with a half-life of ca. 0.01 seconds to phosphorodichloric acid and hydrochloric acid. The hydrolysis of pure phosphorodichloric acid in water (separate experiment) was determined to be less rapid ($t_{1/2}$ = ca. 250 s), but loses its chlorine atoms simultaneously in both acidic solution as well as basic solution, resulting in the formation of phosphoric acid and hydrochloric acid (Hudson and Moss, 1962). In an insufficiently documented study, Rodriguez and Castro (1942) found half-lives of phosphoryl trichloride of 39 s at 20 °C and 19 s at 35 °C.

When $POCl_3$ hydrolyzes at a temperature of 0 °C (insufficiently documented study) (Grunze, 1959) the hydrolysis intermediate $POCl_2OH$ (phosphorodichloric acid) has a half-life of about 30 minutes.

In insufficiently described experiments which were designed to prepare $HOP(O)Cl_2$, vapors of phosphoryl trichloride and water did not react in a 1 : 1 molar ratio in the gas phase at “common” (below 65 °C) temperatures (Goubeau and Schulz, 1958). In aerosol droplets phosphoryl trichloride will be affected by humidity, which leads to its hydrolysis to hydrochloric acid and phosphoric acid.

Thus, an environmental impact of phosphoryl trichloride itself is not likely to occur. For assessment of its environmental effects the hazards of the hydrolysis products, phosphoric acid and hydrochloric acid, have to be assessed.

Phosphoric acid (CAS-No. 7664-38-2)

Phosphoric acid is a triprotic mineral acid, having three ionizable hydrogen atoms. It is miscible with water. Dilute phosphoric acid is partly dissociated. It will not adsorb on particulate matters or surfaces and in general, will not accumulate in living tissues, although it occurs in every living organism. Phosphoric acid and phosphates, respectively, are nutrients and are known to be essential for life. Excess phosphoric acid and phosphates may cause eutrophication of environmental waters (Roempp, 2003).

Hydrochloric acid (CAS-No. 7647-01-0)

Hydrochloric acid is a strong mineral acid, that dissociates readily in water to chloride ions and hydrated protons, and it is miscible with water. Dilute hydrochloric acid is nearly totally dissociated. This total ionisation also implies that hydrochloric acid will not adsorb on particulate matters or surfaces and will not accumulate in living tissues. For assessment of the environmental impact of hydrochloric acid it is referred to the validated results of the hazard assessments within the OECD SIDS-Program [OECD SIDS Hydrochloric Acid, 2002].

2.2.4 Transport between Environmental Compartments

Since phosphoryl trichloride hydrolyzes rapidly in water (*cf.* Chapter 2.2.3), no transfer coefficients can be measured.

2.2.5 Biodegradation

Since phosphoryl trichloride hydrolyzes rapidly in water (*cf.* Chapter 2.2.3), no biodegradation can be measured. The hydrolysis products chloride, phosphate and hydrogen ions, are inorganic end products of biodegradation.

2.2.6 Bioaccumulation

Since phosphoryl trichloride hydrolyzes rapidly in water (*cf.* Chapter 2.2.3), no BCF can be measured for phosphoryl trichloride. Since the hydrolysis products chloride, phosphate and hydrogen ions, are generally present in the natural environment, and can be excreted by physiological mechanisms, any bioaccumulation is not expected.

2.2.7 Environmental Monitoring

No monitoring data available.

2.3 Human Exposure

2.3.1 Occupational Exposure

Workplaces

During manufacturing and processing of phosphoryl trichloride workers may be exposed, with the dermal and inhalational routes being the primary routes of exposure. In accordance with the principles of Responsible Care and Sustainable Development, at Bayer Chemicals the exposure of workers is reduced to the lowest technically practicable level (Bayer Chemicals, 2004a).

At the Bayer manufacturing site, workplaces where phosphoryl trichloride is manufactured or processed in closed systems (Bayer Chemicals, 2004a), include

- Manufacturing processes: Synthesis of phosphorus trichloride and its conversion with oxygen to phosphoryl trichloride
- Processing: In chemical synthesis, e.g. production of organic phosphates.

In the Bayer industrial park in Leverkusen most of the phosphoryl trichloride is transported via pipeline. A minor amount (less than 10 %) of phosphoryl trichloride is transported in ISO-containers (20 feet-containers) or steel barrels with polyethylene inliner (Bayer Chemicals, 2004a).

Precautionary measures at the workplace

Surveys of the Bayer workplaces have been performed according to German Technical Guidance TRGS 402 (1997). This includes regular checks in the working area for any possible exposure to phosphoryl trichloride and appropriate control measures(Bayer Chemicals, 2004a).

To protect workers several precautionary and protective measures are taken. These measures include technical equipment like suction devices at filling and sampling stations as well as appropriate personal protection equipment as prescribed in detail for different work situations e.g.

during sampling, maintenance, and repair work. During sampling, for instance, gas filter masks, goggles, and rubber gloves have to be worn. Depending on the work to be done during maintenance, gas filter masks (classification ABEK) or a respirator with independent air supply have to be used as well as protective clothing (Bayer Chemicals, 2004a).

Down stream users of phosphoryl trichloride are informed by way of a material safety data sheet on the recommended safety measures (see above, Bayer Chemicals, 2004a).

Potential exposure at the workplace

The maximum admissible concentration of phosphoryl trichloride in the workplace air (MAK) is 1.3 mg/m^3 (0.2 ppm) in Germany. Workplace air measurements of phosphoryl trichloride were performed in the Bayer Chemicals processing plant. 18 total shift measurements and one short time measurement were done in the relevant areas between 1992 and 1996. Three values of these (0.03 - 0.1 mg/m^3) were above the detection limit (0.02 – 0.1 mg/m^3 depending on sampling conditions) (Bayer Chemicals, 2004a).

In the manufacturing plant, the precursor of phosphoryl trichloride, phosphorus trichloride was monitored. The maximum admissible concentration of phosphorus trichloride in the workplace air (MAK) is 2.8 mg/m^3 (0.5 ppm) in Germany. In the manufacturing unit, 13 total shift measurements were done in the relevant areas between 1987 and 1993. 6 values of these (0.009 – 0.7 mg/m^3) were above the detection limit (0.004 – 0.09 mg/m^3 depending on sampling conditions). Phosphorus trichloride was not detected in the other 7 samples. All results were below one third of the MAK value (Bayer Chemicals, 2004a).

Since there was no relevant exposure neither to phosphoryl trichloride nor to phosphorus trichloride, the monitoring program was modified to include all compounds which release hydrochloric acid upon hydrolysis. The MAK value of hydrochloric acid is 8 mg/m^3 (5 ppm). Between 1999 and 2003, eight hydrochloric acid measurements were performed in the manufacturing unit. All results were below the limit of detection (0.8 mg/m^3) (Bayer Chemicals, 2004a).

In general, the exposure of Bayer workers to phosphoryl trichloride, to its precursor phosphorus trichloride, and to the hydrolysis product hydrochloric acid, is negligible.

Phosphoryl trichloride (and also hydrochloric acid) is formed as a by-product from the reaction of organic free acids with phosphorus pentachloride. In 1972 - 1973, workplace air concentrations have been measured in a chemical plant in Switzerland where an organic acid chloride was produced from the free acid by reaction with phosphorus pentachloride. The following concentrations were measured: In the vicinity of a centrifuge during cleaning: 0.2 mg/m^3, during evacuation 0.9 mg/m^3, and after opening 7.9 mg/m^3 (Oltramare et al. 1975).

Biological monitoring

In the framework of the Bayer occupational health surveillance program, the level of an immunoglobin E (IgE) specific for phosphoryl trichloride (and phosphorus trichloride) was determined in the last 5 years (1999 - 2003) in about 900 workers routinely handling these substances. This specific IgE would indicate a possible sensitising effect of phosphoryl trichloride (and phosphorus chloride). With a detection limit of 0.35 kU, in the previous five years no specific IgE against phosphoryl trichloride (and phosphorus trichloride) was seen neither in the occupational surveillance program nor in any case of product contact. Phosphoryl trichloride (and phosphorus trichloride) had no sensitisation potential in the tested individuals (Bayer Industry Services, 2004).

Exposure information on other production and/or processing sites in Germany is not available.

2.3.2 Consumer Exposure

No direct use is known (Bayer Chemicals, 2004a). Phosphoryl trichloride is not listed in the Norwegian (SPIN 2004) and Swiss product registers (Swiss Product Register, 2003). In the Finnish and Swedish product registers, in total, there are about a dozen industrial preparations containing phosphoryl trichloride. Entries in the Danish Product Register are confidential. In the Finnish product register, there are 6 different preparations for industrial use, 5 with the specification of manufacture of chemicals and chemical products, and one for the manufacture of radio, television and communication equipment, all in the category with a non-dispersive use in closed systems (SPIN, 2004).

In products of the Sponsor company no phosphoryl trichloride could be detected. To cover all chloride containing compounds in products manufactured from phosphoryl trichloride, 8 organic phosphates were analysed for chloride with a determination limit of about 1 mg/kg. The products of the Sponsor company are virtually free of phosphoryl trichloride (Bayer Chemicals, 2004a).

The use of phosphoryl trichloride as a solvent in cryoscopy (Merck, 2001) respectively as an anhydrous solvent in general (Roempp, 2003) is limited to some scientific laboratories.

Phosphoryl trichloride can be converted by multistage chemical synthesis to nerve gases. Therefore the production and export of phosphoryl trichloride is stringently controlled under the International Chemical Weapons Convention (1993). The Chemical Weapons Convention lists phosphoryl trichloride as precursor to chemical weapons.

Thus, an exposure of consumers to phosphoryl trichloride is unlikely to occur.

3 HUMAN HEALTH HAZARDS

3.1 Effects on Human Health

3.1.1 Toxicokinetics, Metabolism and Distribution

Studies with phosphoryl trichloride were not identified in the available literature.

At low concentrations the free acids resulting from the hydrolysis of phosphoryl trichloride will be neutralised quickly by body fluids. The resulting phosphate and chloride ions are natural components of food and ubiquitously found in living tissues and are not expected to pose a hazard. At high concentrations, which exceed the buffer capacity of body fluids the acids will damage the tissue at the portal of entry dependent upon concentration and duration of exposure. A systemic availability of phosphoryl trichloride or the free acids is hence not expected.

Conclusion

Phosphoryl trichloride is hydrolyzed quickly in water or moist air. Studies on metabolism and toxicokinetics of the parent compound are not feasible. Distribution is limited due to hydrolysis.

3.1.2 Acute Toxicity

Studies in Animals

Inhalation

In a study by Monsanto Co (1978) 6 male Sprague-Dawley rats were exposed for 18 minutes to a concentration of 159 700 mg/m³. This exposure caused laboured breathing within less than 2 minutes, weakness, convulsions, collapse and death in 10 minutes. All animal died within 18 minutes.

An LC_{50} value of 48.4 ppm (308 mg/m³) was determined by Weeks et al. (1964) after whole body exposure of rats for 4 hours. Animals showed signs of irritation as agitation, pawing, scratching of head and nose and chromodakryorhea. Death occurred within 48 hours. Microscopic examination revealed desquamation of bronchial epithelium, oedema and haemorrhages in the lungs. Survivors recovered completely within 14 days.

A study by Mobil (1977) used 10 rats, which were exposed to an aerosol 20.47 mg/ml (3200 ppm) for an unspecified period. Mortality occurred in 7/10 animals. Signs of toxicity were bloody nasal discharge, salivation, nasal discharge, laboured respiration, corneal opacity, lacrimation, eye irritation, and tonic convulsions an LC_{50} could not be determined.

A LC_{50} of 200 mg/m³ (= 31.4 ppm) is cited in the rational of the German MAK report (MAK, 1984) from Marhold and Cizek (1957) without sufficient experimental detail.

In several publications Molodkina and Roshchin (Molodkina, 1971; 1974; Roshchin and Molodkina, 1977) reported an LC_{50} of 71 mg/m³ (= 11.1 ppm; LC_{16}: 56 mg/m³; LC_{84}: 89 mg/m³) for rats. Signs of intoxication were: agitation, pawing of the nose, signs of irritation (immediately) and later on nausea, disturbance of movement co-ordination, lateral position, fibrillar twitching, convulsions, slow and strained respiration, loss of weight, reduced food consumption, foamy discharge from nose and mouth, lacrimation, and corneal opacity. Weight loss and appetite loss were observed several days post exposure. Pathology revealed dose dependent necrosis of tracheal and bronchial mucosa, and alveolar oedema in the respiratory tract and dose dependent dystrophy of neurones as well as in liver and kidney tubuli.

The same authors also reported studies in guinea pigs and mice. No species specific or sex specific differences were detected.

Male guinea-pigs were exposed for 4 hours to vapours of the above compounds in varying concentrations. Animals were observed and deaths were recorded up to 14 days post exposure. Median lethal concentrations (LC_{50}) were computed. The LC_{50} of phosphoryl trichloride was 52.5 ppm (334 mg/m³) for guinea-pigs. Hydrolysis of phosphoryl trichloride was about 15 percent. Animals showed signs of irritation during exposure to phosphoryl trichloride, but not during exposure to neutralised products. All deaths occurred within 48 hours (Weeks et al., 1964).

Dermal

There are two studies in New Zealand White rabbits available.

Phosphoryl trichloride was applied undiluted to the skin at several dose levels. Signs of toxicity were weight loss, increasing weakness and collapse. Mortality was observed at 1000 mg/kg bw and above. At necropsy the lungs and livers were hyperaemic, the gall bladder enlarged, the kidneys discoloured and the intestinal tract showed inflammation. Survivors did not exhibit any changes after 14 days. Due to the low animal number an LD_{50} could not be derived. The LDlo was 1000 mg/kg bw. (Monsanto Co, 1978).

The second study consisted of a the range finding study using doses of 500 to 3000 mg/kg in one animal each. All doses produced necrosis, eschar, decreased locomotor activity and death. Based on the corrosive effects at these doses, 250 mg/kg was used in the main study. The main study included 12 animals, none of which died (LD_{50}: > 250 mg/kg bw). Signs of toxicity were decreased locomotor activity, necrosis and eschar. An LD_{50} value could not be determined (Mobil 1977b).

Oral

Two studies on the oral toxicity are available.

Molodkina and Roshchin (Molodkina, 1971, 1974; Roshchin and Molodkina, 1977) treated rats with phosphoryl trichloride in vegetable oil and determined a LD_{50} value of 380 mg/kg bw. The treatment produced nausea, disturbance of movement co-ordination, weakness, chromodakryorhea, and reduced respiratory frequency. At a lethal dose cyanosis, convulsion and dyspnea were detected.

Rats received various doses of the compound via stomach tube. Animals were observed for sex related susceptibility and adverse symptoms, weighed, and grossly examined for abnormalities. Threshold concentrations for single exposures were also determined.

Another study reported an LD50 of 36 mg/kg (95 % confidence limits: 31-41mg/kg). The dose mortality curve was very steep (Dose/Mortality: 25.1 mg/kg: 0/5; 31.6 mg/kg: 2/5; 39.8 mg/kg: 3/5; 50.1 mg/kg: 5/5). Signs of intoxication were weight loss (1 - 3 days in survivors), increasing weakness, collapse, and death. At necropsy haemorrhage of lungs, liver discoloration, and acute gastrointestinal inflammation were detected in dead animals (Monsanto Co, 1978).

Studies in Humans

No systemic toxicity studies in humans, but several case reports are available.

After single inhalation exposure wheezing respiration was observed. Additionally delayed symptoms were asthmatic fits after irritation by chemicals or cold (Rivoire et al., 1995).

Acute phosphoryl trichloride inhalation causes intense irritation of airways and conjunctivae, spastic bronchitis, broncho-pulmonia, pulmonary edema. After oral ingestion severe corrosion, stomach pain, vomiting, prostration, perforation of esophagus and stomach may occur. Dermal acute exposure produced severe corrosion (Parmeggiani, 1953).

Eight men and 3 women (22 to 56 years of age) accidently exposed to large amounts of a gaseous mixture of hydrogen chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride, and oxalic acid were studied both by clinical observation and laboratory analysis. The main symptoms included hoarseness, wheezing cough and shortness of breath. Fine crepitations and scattered rhonchi were heard diffusely over the lungs. Severe conjunctivitis was present in some individuals. Laboratory tests revealed leukocytosis in four of the patients, elevated lactic dehydrogenase in three and traces of albumin in the urine of one. The arterial oxygen pressure was reduced in seven and mixing efficiency impaired, suggesting disturbances in ventilation and perfusion. Hypoxemia was found in one patient without associated symptoms or abnormal physical findings but this disappeared with time. In four patients the vital capacity was low suggesting a broncho-spastic element. Follow up data showed that in most cases symptoms and disturbances cleared in a short time (Rosenthal et al., 1978)

Four workers aged 20 - 47 showed signs of ocular and respiratory irritation after exposure to phosphoryl trichloride. Signs were: irritation of conjunctivae and pharynx (hyperemia), cough, dyspnea, retro-sternal pain, neutrophilia, and pleutritis. Symptoms developed within minutes to

several hours. While two of the workers recovered within several days, the others developed lasting signs of obstructive respiratory disease (Scotti, 1967).

Conclusion

The 4-h-LC_{50} of phosphoryl trichloride is 48.4 ppm (308 mg/m³) to 11.1 ppm (71 mg/m³) for rats and 52.5 ppm (335 mg/m³) for guinea pigs. Clinical signs included severe respiratory irritation, nasal discharge and eye irritation. The oral LD_{50} was determined as 36 to 380 mg/kg bw for rats showing a very steep dose/mortality relation. After dermal exposure the LDlo was 1000 mg/kg bw in rabbits.

In humans intense irritation/corrosion at the site of contact, pulmonary edema of delayed onset and lasting respiratory hypersensitivity to irritants have been reported.

3.1.3 Irritation

Skin Irritation

Studies in Animals

Rabbit skin treated with undiluted phosphoryl trichloride (4 drops per 20 cm²) showed skin scales, hemorrhagic fissures and a slowly healing wound (Molodkina, 1971, 1974).

Studies in Humans

No studies in humans are available. Several reports of occupational exposure in workers describe severe irritation of skin, eyes and airways. These effects are reported under chapter 3.1.2 Acute Toxicity (Parmeggiani, 1953; Scotti, 1967; Molodkina, 1971,1974; Oltramare et al., 1975; Tati, 1988; Velsicol Chemical Corp., 1988; Rivoire et al., 1995; IPCS, 2000).

Eye Irritation

Studies in Animals

One drop of undiluted phosphoryl trichloride caused necrotic changes in the eye and complete blindness. (Molodkina, 1971, 1974)

Studies in Humans

No studies in humans are available. Several reports of occupational exposure in workers describe severe irritation of skin, eyes and airways (Parmeggiani, 1953; Scotti, 1967; Molodkina, 1971, 1974; Oltramare et al., 1975; Tati, 1988, Velsicol Chemical Corp., 1988; Rivoire et al., 1995; IPCS, 2000). These effects are reported under chapter 3.1.2 Acute Toxicity.

Respiratory Tract Irritation

Studies in Animals

All studies regarding toxicity after inhalation of phosphoryl trichloride showed severe irritation or corrosion of the respiratory tract including all parts from nose to alveoli. Most severe lesions were generally observed in the bronchi and bronchioli (see resp. Chapters 3.1.2, 3.1.5).

Studies in Humans

No studies in humans are available. Several reports of occupational exposure in workers describe severe irritation of skin, eyes, and airways (Parmeggiani, 1953; Scotti, 1967; Molodkina, 1971,

1974; Velsicol Chemical Corp., 1988; Oltramare et al., 1975; Tati, 1988; Rivoire et al., 1995). These effects are reported under chapter 3.1.2 Acute Toxicity.

Conclusion

Phosphoryl trichloride is corrosive to skin, eyes, and the respiratory tract.

3.1.4 Sensitisation

Studies with phosphoryl trichloride in experimental animals were not identified in the available literature.

The hydrolysis product hydrochloric acid was tested in a Guinea Pig Maximisation Test (concentration of 1 %) and also in a Mouse Ear Swelling Test (concentrations of up to 5 %). Both tests gave no indication for a sensitising potential (Gad et al., 1986).

Conclusion

Data for phosphoryl trichloride were not identified. The hydrolysis product hydrochloric acid gave no indication for a sensitising potential in humans and experimental animals. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected. At low concentrations the acid will be neutralized quickly and the resulting phosphates are ubiquitous necessary constituents of all living cells. Low concentrations of phosphate are considered as inocuous. At high concentrations the acidic nature of phosphoric acid will have similar effects as the change of pH by any other strong acid (irritation/corrosion).

3.1.5 Repeated Dose Toxicity

There are no studies available performed according to current OECD guidelines.

Studies in Animals

Inhalation

A Russian group has performed parallel studies in rats and guinea pigs. It is not possible to allocate the descriptions to one specific species. Animals were exposed for 4 months with a 1 month recovery period to concentrations of 0 (control), 0.48 or 1.34 mg/m³ (0.075 or 0.21 ppm). Treatment with 0.48 mg/m³ caused weight loss, changes of respiration frequency and oxygen consumption, respiratory irritation, and increased relative kidney weight. These effects had subsided after 1 month of recovery. In animals of the high dose group (1.34 mg/m³) the effects noted in the low dose group were significantly increased. Additionally, there was severe irritation of the mucous membranes of the respiratory tract and a chronic rhinitis, tracheitis, desquamating bronchial catarrh, hyperplasia of mucus cells and round cell infiltration of the submucosa. In liver and kidney protein dystrophy and small droplet fatty degeneration and altered urinary concentrations of hippuric acid and protein were noted. The excretion of phosphorus, chloride and calcium were altered. Bones showed degradation and reduction of the number of trabeculae and in cells of the bone marrow chromosomal anomalies were increased (5 of 9 animals affected; no quantitative data no experimental detail; no such effects at 0.48 mg/m³; effects only in combination with overt toxicity. The excess phosphate produced by hydrolysis of phosphoryl trichloride may play a role in the development of these effects on kidney bone and calcium levels).

In the brain degeneration of neurones occurred. In the testes calcification (mentioned as “substance”) of testicular tubuli was recorded and the motility of sperm was reduced (no influence on spermatogenesis). Even after four weeks after the end of exposure recovery was still incomplete

(especially the respiratory tract still showed significant alterations). The LOAEL was 0.48 mg/m³. (Molodkina, 1971; Molodkina and Tolgskaya, 1975; Roshchin and Molodkina, 1977)

As phosphoryl trichloride hydrolyzes quickly to form hydrochloric and phosphoric acids, chronic effects are expected mostly from exposure to these degradation products. Data are available only regarding hydrochloric acid/hydrogen chloride. To improve the evaluation of phosphoryl trichloride data of an inhalation study of the hydrolysis product hydrogen chloride are included.

In a 90-day inhalation study using B6C3F1 mice, Sprague-Dawley, and Fisher 344 rats groups of 31 males and 31 females of each species and strain were exposed (whole body) to HCl at 0, 10, 20 or 50 ppm (0, 15, 30, or 75 mg/m^3), 6 h/day, 5 days/week for 90 days. Several animals died during the study; however, the deaths did not appear to be exposure related. There was a slight, but significant decrease in body weight gain in male and female mice and male Fisher 344 rats in the high dose groups. There was no effect on hematology, clinical chemistry, and urinalysis. Histologic examination showed minimum to mild rhinitis in both strains of rats. Lesions occurred in the anterior portion of the nasal cavity and were concentration and time related. In mice exposed to 50 ppm, there was cheilitis and accumulation of macrophages in the peripheral tissues after 90 days. Mice in all exposure groups developed eosinophilic globules in the epithelial lining of the nasal tissues (CIIT, 1984).

All findings were confined to the site of first contact and can be explained by the irritating/corrosive properties of the acid. No signs of systemic effects were reported. Therefore systemic availability is unlikely. The local NOAEC is below 10 ppm (15 mg/m³). No statement is possible about a systemic NOAEC because of the severe irritation/corrosion effect occurring at the site of entry. Potential systemic effects are considered as consequences of these local effects.

Dermal/ Oral

No oral or dermal studies are available.

Studies in Humans

No studies are available regarding effects of phosphoryl trichloride in humans. After chronic inhalation chronic bronchitis, dermatitis and conjunctivitis were reported (Parmeggiani, 1953).

Inhalation

Inhalation of phosphoryl trichloride causes sore throat, cough, burning sensation, nausea, headache, unconsciousness, vomiting, weakness, and shortness of breath. Symptoms may be delayed (IPCS, 2000). Workers in phosphoryl trichloride producing facilities suffered from coughing, rhinitis, difficulties regarding the voice, angina, and lacrimation. After prolonged exposure sleeping disorders increased. The irritating effect of phosphoryl trichloride on mucous membranes appeared only after a latency period (Molodkina, 1971).

A review by the German MAK states that long term, low level exposure can produce liver and kidney changes, and changes in bone structure in animals. The validity of the studies, however, is not known (MAK, 1984).

Conclusion

From a 4 month inhalation study with phosphoryl trichloride in rats, a NOAEC could not be derived, since weight loss, respiratory irritation and increased kidney weights were still observed at the lowest exposure level of 0.48 mg/m^3 (= LOAEC). The evaluation of this study is limited as methodology and results were published in little detail. The LOAEC found in a 90-day study with hydrochloric acid was 15 mg/m³. Most findings were confined to the site of first contact and can

easily be explained by the irritating/corrosive properties of the compound and its degradation products. The long term effects observed in humans (asthma, angina, sleeping disorders) are considered as sequelae of the irritation in the lungs which after prolonged periods may lead to an impairment of lung function (i.e. oxygen availability). The excess phosphate produced by hydrolysis of phosphoryl trichloride may play a role in the development of effects on kidney, bone and calcium levels).

Also by other routes (oral, dermal) phosphoryl trichloride is expected to produce effects at the site of first contact (irritation, corrosion).

3.1.6 Mutagenicity

The only available mutagenicity study with phosphoryl trichloride is an Ames-Test with *Salmonella typhimurium* and with *Saccharomyces cerevisiae* D4.

Phosphoryl trichloride was not mutagenic to *S. typhimurium* TA 98, TA 100, TA 1535, TA 1537 and TA 1538 or *S. cerevisiae* D4 with and without metabolic activation. Dose range was 0.01 to 5.0 µl per plate; cytotoxicity occurred at 5 µl per plate (Mobil Co, 1977 c).

A Review by the German MAK states that long term, low level exposure can produce mutagenic effects in animals. The validity of the studies, however, is not known (MAK, 1984).

Hydrochloric acid was not mutagenic in an Ames test, both with and without metabolic activation and did not cause DNA damage in the rec-assay with *Escherichia coli* and *Bacillus subtilis* (Isquith, Matheson and Slesinski, 1988; McCarroll, Piper and Keech, 1981a, 1981b).

In 1 of 2 Chromosome aberration tests hydrochloric acid showed positive effects in Chinese hamster ovary K1 (CHO-K1) cells at concentrations of 10 or 14 mM (pH 5.8 or 5.5) with and without S9-mix. The effect in CHO cells was observed in the absence of rat liver S9 preparations at a nominal HCl concentration of 14 mM (pH 5.5) but was greater in the presence of S9, when a nominal HCl concentration of 10 mM (pH 5.8) was required. Similar results were obtained using sulphuric acid Chinese hamster ovary K1 (CHO-K1) cells cultured *in vitro* were used. (Morita et al. 1989).

The second chromosome aberration test in Fischer L5178Y mouse-lymphoma cells incubated with 0.1 - 0.8 µl/ml with and without metabolic activation resulted in no genotoxic effects (Isquith et al. 1988).

Conclusion

Phosphoryl trichloride as well as the hydrolysis product hydrochloric acid are not mutagenic in bacteria. As phosphoryl trichloride decomposes to acid in aqueous media the resulting acidity of the hydrolysis products may cause unspecific effects of low pH in in-vitro tests. The change in pH may induce chromosomal aberrations and other DNA damage. Specific effects of phosphoryl trichloride are not expected. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected.

In vivo, the hydrolysis products, phosphoric and hydrochloric acid, will be neutralized immediately in the physiologic medium at low concentrations. The resulting anions chloride and phosphate are essential components of every living tissue. They are not expected to produce mutagenic effects. The reduced pH levels could lead to chromosomal changes and DNA damage at the portal-of-entry of phosphoryl trichloride. However, it is unlikely that systemic changes in pH would occur after exposure to phosphoryl trichloride, that are sufficient in magnitude to induce this effect in distant tissues or organs. Due to the corrosive nature of phosphoryl trichloride the performance of studies in animals is not warranted.

3.1.7 Carcinogenicity

In vivo Studies in Animals

No carcinogenicity studies with phosphoryl trichloride in experimental animals were identified in the available literature. As phosphoryl trichloride hydrolyzes quickly to form hydrochloric and phosphoric acids, chronic effects are expected mostly from exposure to these degradation products. Data are available only regarding hydrochloric acid/hydrogen chloride.

Inhalation

Albert et al. (1982) reported data from a chronic whole body inhalation exposure study with HCl in rats, discussed in detail by Sellakumar et al. (1985). One hundred male Sprague-Dawley rats were exposed to 10 ppm hydrogen chloride (HCl) for 6 hours/day, 5 days/week (duration-adjusted concentration = 2.5 mg/m^3) for their lifetimes. All animals were observed daily, weighed monthly, and allowed to die naturally or killed when moribund. Complete necropsy was performed on all animals, with particular attention given to the respiratory tract. Histological sections were prepared from the nasal cavity (one lateral section from each side of the head), lung (one section from each lobe), trachea, larynx, liver, kidneys, testes, and other organs where gross pathological signs were present. However, Sellakumar et al. (1985) did not discuss histopathological events in organs other than the respiratory tract. HCl-exposed animals showed no differences in body weights or survival when compared with air controls. The data indicated 62/99 exposed animals with epithelial or squamous hyperplasia in the nasal mucosa (location not specified) vs. 51/99 in the concurrent control group. Incidence of squamous metaplasia was 9 and 5 in the exposed and control rats, respectively. There was increased hyperplasia of laryngeal-tracheal segments in HCl-exposed rats (larynx 22/99, trachea 26/99) vs. the controls (larynx 2/99, trachea 6/99). The authors did not make any comments concerning the severity of these changes. The tumour incidence in organs other than the respiratora tract was similar in the treated and control groups. The total incidences of tumours at various sites being 19/99, 25/99 and 24/99 in treated, air control and colony control animals, respectively.

Oral

The repeated oral application of hydrochloric acid in mice gave no indication for an increased tumor incidence and also did not promote the activity of a known carcinogen. However, possibly only the gastro-intestinal tract was examined (Dyer, Kelly and Dunn, 1946).

Studies in Humans

No data regarding carcinogenicity in humans were identified in the available literature.

Conclusion

No carcinogenicity studies with phosphoryl trichloride were identified. The hydrolysis product hydrochloric acid gave no clear indications for an increased tumour incidence after life-time exposure by inhalation in rats. Histopathological findings in organs other than the respiratory tract.were not discussed. A likely mechanism for tumour induction could be the constant stimulus to cell proliferation produced by prolonged local irritation at the site of entry. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected.

At low concentrations the hydrolysis products, phosphoric and hydrochloric acid, will be neutralised immediately in the physiologic medium. The resulting anions chloride and phosphate are essential components of every living tissue. They are not expected to produce mutagenic effects. The reduced pH levels could lead to chromosomal changes and DNA damage at the portal-of-entry of phosphoryl trichloride. However, it is unlikely that systemic changes in pH would occur after

exposure to phosphoryl trichloride, that are sufficient in magnitude to induce this effect in distant tissues or organs. Nevertheless prolonged irritation could give rise to a constant stimulus to cell proliferation.

Due to the corrosive nature of phosphoryl trichloride the performance of studies in animals is not warranted.

3.1.8 Toxicity for Reproduction

Valid studies in experimental animals performed with phosphoryl trichloride were not identified in the available literature.

In an insufficiently documented inhalation study with rats and guinea pigs Molodkina (1971) and Roshchin and Molodkina (1977) reported no morphologic differences of the spermatogenic epithelium between treated and control rats. The mobile period of sperm was reduced (for details see chapter 3.1.5).

In a second insufficiently documented study Pashkova (1973) reported that chronic exposure of female rats to phosphoryl trichloride decreased the number of primary follicles in the ovaries and intensified the process of atresia. Changes in the estral and ovarian cycles, caused by POCl3, were always accompanied by poisoning symptoms. The findings are considered as secondary consequences of general toxicity by the author.

There were also no studies identified for the hydrolysis products hydrochloric acid and phosphoric acid.

Phosphoryl trichloride is quickly hydrolysed on contact with water. It is therefore very unlikely that phosphoryl trichloride will reach tissues distant from the portal of entry and become systemically available. The products of hydrolysis, hydrochloric acid and phosphorous acid, also act at the portal of entry. After absorption they will be neutralised immediately and the resulting anions are essential components of every living tissue.

Therefore, it is very unlikely that phosphoryl trichloride could reach the reproductive organs or the embryo/fetus, and toxicity to reproduction or developmental toxicity in mammals are not likely to occur following exposure to phosphoryl trichloride by any route.

Additionally, due to the corrosive properties of the substance, exposure is limited to a degree that avoids irritation and therefore a condition of general toxicity, which might cause secondary effects on reproductive performance, is not anticipated to be attained.

Developmental Toxicity

Studies in experimental animals performed with phosphoryl trichloride were not identified in the available literature.

Because phosphoryl trichloride is a toxicant acting at the portal-of-entry, and because it is unlikely to reach the reproductive organs or the embryo/fetus, developmental effects in mammals are not likely to occur following exposure by any route.

Valid studies for the hydrolysis products hydrochloric acid and phosphoric acid were not identified in the available literature.

Conclusion

Data for phosphoryl trichloride were not identified. Because phosphoryl trichloride is a toxicant acting at the portal-of-entry, and because it is unlikely to reach the reproductive organs or the

embryo/fetus, toxicity to reproduction or developmental toxicity in mammals are not likely to occur following exposure to phosphoryl trichloride by any route.

3.2 Initial Assessment for Human Health

Phosphoryl trichloride is hydrolyzed quickly in water or moist air. Studies on metabolism and toxicokinetics of the parent compound are not feasible. Distribution is limited due to hydrolysis. Transfer of a substance, showing a halflife of less than 10 seconds in water at 23 °C, via the bloodstream seems very unlikely. Such a substance could reach e.g. the reproductive organs only if one supposed a very high concentration at the site of entry. High concentrations, however, produce corrosion and acute toxicity, that by itself would influence general condition of the exposed organism.

The 4-h-LC_{50} of phosphoryl trichloride is 48.4 ppm (308 mg/m³) to 11.1 ppm (71 mg/m³) for rats and 52.5 ppm (335 mg/m³) for guinea pigs. Clinical signs included severe respiratory irritation, nasal discharge and eye irritation. The oral LD_{50} was determined as 36 to 380 mg/kg bw for rats showing a very steep dose/mortality relation in individual studies. After dermal exposure the LDlo was 1000 mg/kg bw in rabbits.

In humans intense irritation/corrosion at the site of contact, pulmonary edema of delayed onset and lasting respiratory hypersensitivity to irritants have been reported.

Phosphoryl trichloride reacts with water, forming hydrochloric acid and phosphoric acid. Due to this hydrolytic reaction, phosphoryl trichloride is corrosive to the skin, eyes and respiratory tract.

Studies with phosphoryl trichloride concerning sensitising properties are not available. The hydrolysis product hydrochloric acid gave no indication for a sensitising potential in humans and experimental animals. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected.

From a 4 month inhalation study with phosphoryl trichloride in rats, a NOAEC could not be derived, since weight loss, respiratory irritation and increased kidney weights were still observed at the lowest exposure level of 0.48 mg/m^3 (= LOAEC). The evaluation of this study is limited as methodology and results were published in little detail. The LOAEC found in a 90-day study with hydrochloric acid was 15 mg/m³. Most findings were confined to the site of first contact and can easily be explained by the irritating/corrosive properties of the compound and its degradation products. The long term effects observed in humans (asthma, angina, sleeping disorders) are considered as sequelae of the irritation in the lungs which after prolonged periods may lead to an impairment of lung function (i.e. oxygen availability).

Systemic effects reported in some studies are considered to be secondary consequences of the irritation/corrosion by the compound and its degradation products, which give rise to systemic reactions to prolonged, severe, primary effects (i.e. severe inflammation, scar tissue formation e.g. in the lungs, irreversible effects on respiration). Additionally, the primary effects (corrosion/ irritation) facilitate resorption of phosphate and chloride through damaged mucous membranes and skin. This could cause a shift in phosphate, chloride and calcium metabolism leading to effects on bone and kidney and testes reported in individual studies. The excess phosphate produced by hydrolysis of phosphoryl trichloride may play a role in the development of effects on kidney, bone and calcium levels). Also by other routes (oral, dermal) phosphoryl trichloride is expected to produce effects at the site of first contact (irritation, corrosion).

Phosphoryl trichloride as well as the hydrolysis product hydrochloric acid are not mutagenic in bacteria. As phosphoryl trichloride decomposes to acid in aqueous media the resulting acidity of the hydrolysis products may cause unspecific effects of low pH in in-vitro tests . The change in pH may

induce chromosomal aberrations and other DNA damage. Specific effects of phosphoryl trichloride are not expected. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected.

In vivo, the hydrolysis products, phosphoric and hydrochloric acid, will be neutralized immediately in the physiologic medium at low concentrations. The resulting anions chloride and phosphate are essential components of every living tissue. They are not expected to produce mutagenic effects. However, it is unlikely that systemic changes in pH would occur after exposure to phosphoryl trichloride, that are sufficient in magnitude to induce this effect in distant tissues or organs. Due to the corrosive nature of phosphoryl trichloride the performance of studies in animals is not warranted. No carcinogenicity studies with phosphoryl trichloride were identified. The hydrolysis product hydrochloric acid gave no clear indications for an increased tumour incidence after life-time exposure. Histopathological findings in organs other than the respiratory tract were not discussed. A likely mechanism for tumour induction could be the constant stimulus to cell proliferation produced by prolonged local irritation at the site of entry. Data on phosphoric acid, the second hydrolysis product, are not available, but no specific effects are expected. At low concentrations the hydrolysis products, phosphoric and hydrochloric acid, will be neutralised immediately in the physiologic medium. The resulting anions chloride and phosphate are essential components of every living tissue. They are not expected to produce mutagenic effects. The reduced pH levels could lead to chromosomal changes and DNA damage at the portal-of-entry of phosphoryl trichloride. However, it is unlikely that systemic changes in pH would occur after exposure to phosphoryl trichloride, that are sufficient in magnitude to induce this effect in distant tissues or organs. Nevertheless prolonged irritation could give rise to a constant stimulus to cell proliferation.

Due to the corrosive nature of phosphoryl trichloride the performance of studies in animals is not warranted.

Studies with phosphoryl trichloride concerning effects on fertility and development were not available and there were also no data on fertility effects for the hydrolysis products phosphoric acid and hydrochloric acid. Because phosphoryl trichloride is a toxicant acting at the portal-of-entry, and because it is unlikely to reach the reproductive organs or the embryo/fetus, toxicity to reproduction or developmental toxicity in mammals are not likely to occur following exposure to phosphoryl trichloride by any route.

4 HAZARDS TO THE ENVIRONMENT

4.1 Aquatic Effects

In water, phosphoryl trichloride hydrolyzes to phosphoric acid and hydrochloric acid. The experimentally determined half-life is less than 10 seconds at 23 °C (*cf.* Chapter 2.2.3). Right from the start of the test, ecotoxicological measurements will cover the effects of the degradation products phosphoric acid and hydrochloric acid.

The hydrolysis product hydrochloric acid was tested with several aquatic species (OECD SIDS Hydrochloric Acid, 2002). Hydrochloric acid causes a pH shift in water (Table 2). The resulting pH determines the impact of hydrogen chloride on aquatic life as shown with buffered test substance solution. Thus toxic effects are not due to substance inherent properties but a function of the pH (OECD SIDS Hydrochloric Acid, 2002).

Some experiments with phosphoryl trichloride were performed in the presence of buffer to avoid the pH effects of the acids formed by hydrolysis of phosphoryl trichloride. Comparison of

experiments in the presence and absence of buffer (with and without neutralisation) confirmed the conclusions drawn from the OECD SIDS Hydrochloric Acid (2002; see below). Regarding natural systems, the impact of dissociated acids depends on the buffer capacity of the system. Buffer function is attributed to humic substances, alkaline earth carbonates, clay minerals, silicates, as well as amphoteric oxides.

Table 2 Theoretical pH-values of hydrochloric acid in non-buffered water

Hydrochloric acid concentration (mg/l)	Corresponding phosphoryl trichloride concentration (mg/l)	pH
0.036	0.051	6
0.36	0.51	5
3.6	5.1	4
36	51	3

The tolerance of water organisms towards pH is diverse. pH-values recommended in OECD guidelines for testing issues are compiled in Table 3.

Table 3 pH values recommended in OECD guidelines for testing issues

Group (Trophic level)	Recommendation
Fish	PH 6.0 to pH 8.5 is preferable
Daphnia	Within the range of pH 6 to pH 9
Algae	Approximately pH 8

Acute Toxicity Test Results

Short term tests on aquatic toxicity are available for each trophic level (Table 4).

Since the detrimental effects of unsuitable pH on fish are very well known, for animal protection, no fish test was conducted with phosphoryl chloride. However, this endpoint is covered by several substances:

- Phosphate (phosphoric acid) (Roempp, 2003) and chloride (hydrochloric acid) (OECD SIDS Hydrochloric Acid, 2002) are present in every environmental water and their effects on aquatic life are well-known (see above).
- Phosphorus trichloride hydrolyzes to hydrochloric acid and phosphonic acid. Phosphonic acid and phosphorus acid are tautomeric molecules. Phosphorus acid is slowly oxidised by oxygen (air) to phosphoric acid (Merck 2001). Thus, the data on phosphorus trichloride can be used to estimate ranges of aquatic toxicity of phosphoryl chloride (To verify this statement, the results of aquatic toxicity tests with phosphorus trichloride on *Daphnia magna* and *Desmodesmus subspicatus* are compiled also in Table 4)

  Acute toxicity of phosphorus trichloride to fish (*Danio rerio*) was tested in a static test system according to the method proposal of the German Environmental Protection Ageny “Lethal effects on Brachydanio rerio”. Phosphorus trichloride was not monitored because it hydrolyzes. A limit test was conducted with an adjusted pH (pH ca. 7.5) value at 1000 mg/l (nominal concentration). During 96 h no effects were observed at the tested concentration level, and a

LC_0 of ≥ 1000 mg/l was determined for phosphorus trichloride, which equals a LC_0 of ≥ 597 mg/l of (neutralized) phosphonic acid as the hydrolysis product (Bayer AG, 1991).

In contrast, acute toxicity was found in a study without adjustment of pH. This test was not conducted according to any guideline (Gurova, Krasnov and Mazmanidi, 1970). In the tests media (dechlorinated tap water and Wolga water) pH values are assumed to vary from 3.3 to 7 (information not given for the acute study but for the long-term study of the same authors performed with the same concentration range as described below) (*cf.* Table 3). The 3 d-NOEC (= LC_0) was found to be about 60 mg/l (LC_{100}: 75 mg/l) for sturgeon eggs (*Acipenser stellatus*). The hatching success of the fish larvae was reduced by about 10 % at 60 and 70 mg/l. Growth of hatchlings was not tested at 70 mg/l, as all hatchlings showed abnormalities at this concentration. With regard to length of the hatchlings after 5 days, a NOEC of 20 mg/l was observed. A small reduction (5 %) of fish larvae weight was observed at the lowest concentration tested (20 mg/l). In an insufficiently described experiment, dace (*Leuciscus leuciscus*) were more sensitive to phosphorus trichloride and its degradation products, respectively, and a 10 d-LC_{100} of 25 mg/l was observed However, from this study, no EC_{50} can be derived (Gurova, Krasnov and Mazmanidi, 1970).

A test on prolonged toxicity of phosphorus trichloride to 3 fish species was performed by Gurova, Krasnov and Mazmanidi (1970) with the same conditions as above. In 30 d tests with the 3 fish species *Carassius carassius, Perca fluviatilis*, and *Esox lucius*, NOEC values of 40 - 50 mg/l were found (Gurova, Krasnov and Mazmanidi, 1970) in non-buffered media.

- Phosphorus pentachloride reacts vigorously with water and hydrolyzes to hydrochloric acid and phosphoric acid in two stages (Greenwood and Earnshaw, 1988):

  $PCl_5 + H_2O \rightarrow POCl_3 + 2\ HCl.$

  $POCl_3 + 3\ H_2O \rightarrow H_3PO_4 + 3\ HCl.$

  Since it is a precursur of phosphoryl trichloride and yields the same hydrolysis products (on a molar basis 67 % additional hydrochloric acid), its ecotoxicological data represent a worst case scenario for phosphoryl trichloride.

  The acute toxicity of phosphorus pentachloride to fish was examined in a study without adjustment of pH. This test was not conducted according to any guideline (Gurova, Krasnov and Mazmanidi, 1970). In the tests media (dechlorinated tap water and Wolga water) pH values varied from 3.3 to 7 (*cf.* Table 3). For sturgeon eggs (*Acipenser stellatus*) there is a steep effect curve: 3 d-LC_8 ca. 60 mg/l, 3 d-LC_{10} ca. 70 mg/l, and 3 d-LC_{100} ca. 75 mg/l. For the hatched fish larvae the 5 d-LC_0 was approximately 70 mg/l (highest concentration tested). Since there were some 30 % deformations in the high concentration, the 5 d-NOEC was 20 mg/l. At that concentration a small reduction of fish larvae weight (3 %) and length (8 %) was observed as compared to the controls (Gurova, Krasnov and Mazmanidi, 1970).

With the invertebrate *Daphnia magna* one acute test was performed with phosphoryl trichloride according to the European guideline 92/69/EEC, method C.2, equivalent to OECD TG 202. In non-buffered test solution the pH decreased from pH 7.9 in the controls to pH 6.7 at 25 mg/l, pH 3.7 at 50 mg/l, and pH 3.0 at 100 mg/l, each at the start of the incubation. For a test period of 24 h, an EC_0 (immobilisation) of 25 mg/l, an EC_{50} of 35.4 mg/l, and an EC_{100} of 50 mg/l were obtained. The same effect concentrations were measured after a test period of 48 hours. In buffered test solution (pH 7.9) no effect was observed at the highest tested concentration of phosphoryl trichloride (nominal 100 mg/l), suggesting that the effects in the non-buffered solutions were solely due to the pH decrease (Bayer AG, 2003b). The same results were obtained with phosphorus trichloride (Bayer AG, 2003c).

Algal toxicity was determined by a test with *Desmodesmus subspicatus* in the presence of phosphoryl trichloride and its hydrolysis products. In a growth inhibition test according the European guideline 92/69/EEC, method C.3, equivalent to OECD TG 201, in non-buffered solution, the pH depended on the nominal phosphoryl trichloride concentration and was pH 8.2 in the controls and pH 2.9 at 100 mg (nominal concentration at the start of the incubation period). In non-buffered solution, a 72 h-E_rC_{50} of 32 mg/l was determined for growth rate (population density) and a 72 h-E_bC_{50} of 28 mg/l for growth (biomass). The 72h-NOEC was 12.5 mg/l for both growth rate and biomass. In buffered solution no effect was observed at the highest phosphoryl trichloride concentration tested (nominal 100 mg/l). Thus, it can be concluded that the effects found in this study are caused by pH effects (Bayer AG, 2003d). Similar results were obtained with phosphorus trichloride (Bayer AG, 2003e).

The tests on aquatic toxicity (Table 4) demonstrate that ecotoxicological effects observed with phosphoryl chloride (and phosphorus trichloride and phosphorus pentachloride) were caused by low pH.

Chronic Toxicity Test Results

There are no result available on chronic toxicity.

Toxicity to Microorganisms

With phosphorus trichloride, a test with activated sludge with a duration of 3 h was conducted according to the ISO 8192 (Test for the Inhibition of Oxygen Consumption by Activated Sludge). The inoculum contained 6 g of dry matter per litre (the pH was not reported). An EC_{50} of 9450 mg/l and an EC_0 of 3520 mg/l were determined (Bayer AG, 1991).

Table 4 Aquatic toxicity of phosphorus trichloride and its hydrolysis products

Species	Test substance	Endpoint	Duration (exposure regime)	Effect concentration	Reference	IUCLID
Fish						
Danio rerio	PCl_3	Mortality	96 h-LC_{50} (static)	> 1000 mg/l (n)*	Bayer AG 1991	4.1
Acipenser stellatus, eggs	PCl_3	Mortality (hatching success)	3 d-NOEC (= LC_0) LC_{10} LC_{100}(semi-static)	60 mg/l (n) > 60 - 70 mg/l (n) 75 mg/l (n)	Gurova, Krasnov and Mazmanidi, 1970	4.1
Acipenser stellatus, hatchlings	PCl_3	Growth (weight, length)	5 d-LC_{10} (semi-static)	70 mg/l (n)	Gurova, Krasnov and Mazmanidi, 1970	4.1
Acipenser stellatus, eggs	PCl_5	Mortality	3 d-LC_{10} 3 d-LC_{100} (semi-static)	70 mg/l (n) ca. 75 mg/l (n)	Gurova, Krasnov and Mazmanidi, 1970	4.1
Acipenser stellatus, hatchlings	PCl_5	Growth (weight, length)	5 d-LC_{10} NOEC (semi-static)	70 mg/l (n) 20 mg/l (n)	Gurova, Krasnov and Mazmanidi, 1970	4.1
Leuciscus leuciscus	PCl_3	Mortality	10 d-LC_{100} (semi-static)	25 mg/l (n)	Gurova, Krasnov and Mazmanidi, 1970	4.1
Carassius carassius, Perca fluviatilis, and *Esox lucius*	PCl_3	Mortality and growth (weight)	30 d-NOEC (semi-static)	40 - 50 mg/l (n)	Gurova, Krasnov and Mazmanidi, 1970	4.1
Invertebrates						
Daphnia magna	$POCl_3$	Immobility	48 h-EC_0 48 h-EC_{50} 48 h-EC_{100} 48 h-EC_{50} (static)	25 mg/l (n) 35.4 mg/l (n) 50 mg/l (n) > 100 mg/l (n)*	Bayer AG, 2003b	4.2
Daphnia magna	PCl_3	Immobility	48 h-EC_0 48 h-EC_{50} 48 h-EC_{100} 48 h-EC_{50} (static)	25 mg/l (n) 35.4 mg/l (n) 50 mg/l (n) > 100 mg/l (n)*	Bayer AG, 2003c	
Algae						
Desmodesmus subspicatus	$POCl_3$	Growth	72 h-E_rC_{50} 72 h-E_bC_{50} 72 h-EC_{50} 72 h-NOEC (for both population growth and biomass) 72 h-NOEC	32 mg/l (n) 28 mg/l (n) > 100 mg/l (n)* 12.5 mg/l (n) > 100 mg/l (n)*	Bayer AG, 2003d	4.3

Table 4 (Cont.) Aquatic toxicity of phosphorus trichloride and its hydrolysis products

Species	Test substance	Endpoint	Duration (exposure regime)	Effect concentration	Reference	IUCLID
Desmodesmus subspicatus	PCl_3	Growth	72 h-E_rC_{50} 72 h-E_bC_{50} 72 h-EC_{50} 72 h-NOEC (for both population growth and biomass) 72 h-NOEC	33 mg/l (n) 30 mg/l (n) > 100 mg/l (n)* 12.5 mg/l (n) > 100 mg/l (n)*	Bayer AG, 2003e	4.3
Activated Sludge	PCl_3	Respiration inhibition	3 h-EC_{50}	9450 mg/l (n)	Bayer AG, 1991	4.4

(n) = nominal concentration; *buffered test medium

Determination of $PNEC_{aqua}$

The acute aquatic endpoints are covered by tests with phosphoryl trichloride on invertebrates and algae, and by tests with phosphorus trichloride and phosphorus pentachloride on fish. The lowest acute effect concentration (72 h-E_bC_{50} = 28 mg/l, nominal concentration in non-buffered medium) was found for the alga *Desmodesmus subspicatus* in a study with phosphoryl trichloride according to the European guideline 92/69/EEC, method C.3 (equivalent to OECD TG 201). As has been shown by several studies (Table 4), toxic effects were due to the pH which was far off from the pH range tolerated by fish, invertebrates, and algae (Table 2 and 3). The lowest acute effect concentration from tests with buffered test media, is a 48 h-EC_{50} of > 100 mg/l (n) of *Daphnia magna*.

Using the lowest acute test result (> 100 mg/l) and an assessment factor of 1000 (EU Technical Guidance Document), a

$$\mathbf{PNEC_{aqua} > 0.1}\ \text{mg/l}$$

is obtained. Due to the fast hydrolysis this $PNEC_{aqua}$ covers also the hydrolysis products hydrochloric acid and phosphoros acid.

4.2 Terrestrial Effects

No data available.

4.3 Other Environmental Effects

No data available.

4.4 Initial Assessment for the Environment

Phosphoryl trichloride is a moisture/water sensitive fluid with a melting point of 1.3 °C, a boiling point of 105.1 °C, and a density of 1.675 g/cm³ at 20 °C. The vapour pressure of the substance is 53.3 hPa at 27.3 °C. The log K_{ow}, the water solubility and several other parameters cannot be determined due to hydrolysis. Phosphoryl trichloride hydrolyzes completely in water within less than 10 seconds at 20 °C (via the hydrolysation intermediate phosphorodichloric acid), forming phosphoric acid and hydrochloric acid. Any emission into water, air, or the terrestrial compartment would be affected by humidity and also results in the formation of the hydrolysis products. Hydrochloric acid dissociates readily in water causing a pH shift which determines the impact of

phosphoryl trichloride on aquatic life. The tolerance of water organisms towards pH is diverse. Recommended pH values for test species listed in OECD guidelines are between 6 and 9.

Phosphoric acid is of medium acidity ($pK_a = 2.1$) and partly dissociates in water causing a pH shift. Phosphoric acid and phosphates may affect aquatic life due to their fertilizing effect. Several aquatic toxicity tests have been undertaken in non-buffered solution. The observed toxicity effects in these studies can be attributed to the acidity of the degradation products and are not used for the hazard assessment.Acute toxicity of phosphoryl trichloride to fish was evaluated by using fish tests with phosphorus trichloride and phosphorus pentachloride. Toxicity of phosphorus trichloride (buffered) on *Danio rerio* (tested according to the German guideline proposal "Lethal effects on Brachydanio rerio") yielded a 96 h-LC_0 (nominal concentration) ≥ 1000 mg/l.

Tests with invertebrates were done with phosphoryl trichloride and phosphorus trichloride, for proving the validity of the evaluation approach. With *Daphnia magna* an EC_{50} (48 h) of > 100 mg/l in buffered solution was determined for both substances (92/69/EEC, method C.2).

Algal toxicity was determined with phosphoryl trichloride and phosphorus trichloride. In a growth inhibition test with *Desmodesmus subspicatus* (92/69/EEC, method C.3) in buffered solution no effect was observed at 100 mg/l (nominal). For phosphorus trichloride, a 72 h-E_rC_{50} of 33 mg/l (nominal) was determined for growth rate (population density) and a 72 h-E_bC_{50} of 30 mg/l (nominal) for growth (biomass) in non-buffered media.

There is no result available on chronic toxicity. With activated sludge a 3 h-EC_{50} of 9450 mg/l (nominal) and an EC_0 of 3520 mg/l (nominal) were measured according to the ISO 8192 (pH not reported) for phosphorus trichloride.

There are test results available for acute testing from three trophic levels (all in buffered media) . Using the lowest acute test result (> 100 mg/l) and an assessment factor of 1000 (EU Technical Guidance Document), a $PNEC_{aqua}$ > 0.1 mg/l is obtained.

5 RECOMMENDATIONS

Environment

The chemical is currently of low priority for further work due to its low hazard profile. One of the degradation products, hydrochloric acid, has already been assessed within the OECD SIDS-Program.

Human Health

The chemical possesses properties indicating a hazard for human health (acute toxicity, corrosiveness). Based on data presented by the Sponsor country (relating to production by one producer which accounts for 5 - 25 % of global production and relating to the use pattern of several OECD countries), exposure is limited to the technically feasible extent in occupational settings in the sponsor country. There is no exposure of consumers. No recommendation for further testing within the context of the SIDS program is therefore warranted. Although there are no valid data regarding reproductive effects, due to the fast hydrolysis it is unlikely that $POCl_3$ could reach organs and tissues distant from the site of first contact, therefore, and due to the corrosive properties, studies in animals are not warranted. The chemical is currently of low priority for further work

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S I D S

Dossier

Existing Chemical	:	ID: 10025-87-3
CAS No.	:	10025-87-3
EINECS Name	:	phosphoryl trichloride
EC No.	:	233-046-7
TSCA Name	:	Phosphoric trichloride
Molecular Formula	:	Cl3OP

Producer related part

Company	:	Bayer AG
Creation date	:	01.12.2003

Substance related part

Company	:	Bayer AG
Creation date	:	01.12.2003
Status	:	
Memo	:	AKTUELL EG / ICCA / OECD
Printing date	:	20.01.2006
Revision date	:	01.12.2003
Date of last update	:	16.01.2006
Number of pages	:	80
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Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name :
Smiles Code :
Molecular formula : Cl3OP
Molecular weight : 153.33
Petrol class :

Flag : Critical study for SIDS endpoint
20.02.2004 (1)

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance
Substance type : inorganic
Physical status : liquid
Purity : ca. 99.5 % w/w
Colour : colourless
Odour : pungent

Flag : Critical study for SIDS endpoint
20.02.2004 (1)

Purity type : typical for marketed substance
Substance type : inorganic
Physical status : liquid
Purity : >= 99.7 % w/w
Colour : colourless
Odour : pungent

Remark : Information on purity from Bayer Chemicals, Performance Chemicals Business Group, technical informatiom bulletin, method CH-p ELS 32.91 GC-WLD
02.12.2003 (2)

Purity type : typical for marketed substance
Substance type : inorganic
Physical status : liquid
Purity : 99.9 % w/w
Colour : colourless
Odour : pungent

05.12.2003 (3)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Phosphoric trichloride

02.12.2003 (4) (5)

Phosphorus oxychloride

20.02.2004 (4) (5) (6)

Phosphorus oxytrichloride

17.06.2004 (6)

Phosphoryl chloride

Remark : CA index name
20.02.2004 (4) (5)

Phosphoryl oxychloride

02.12.2003 (5)

Phosphoryl trichloride

(4) (5) (6)

Trichlorophosphine oxide

(6)

Trichlorophosphorus oxide

17.12.2003 (6)

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No : 7719-12-2
EC-No : 231-749-3
EINECS-Name : phosphorus trichloride
Molecular formula : PCl3
Value :

Remark : Commercial POCl3 contains traces of PCl3. Technical phosphoryl trichloride has a purity of > 99.5 % w/w.
Flag : Critical study for SIDS endpoint
16.06.2004 (1)

Purity : typical for marketed substance
CAS-No : 7719-12-2
EC-No : 231-749-3
EINECS-Name : phosphorus trichloride
Molecular formula : PCl3
Value : <= .3 % w/w

Flag : Critical study for SIDS endpoint
20.02.2004 (2)

Purity : typical for marketed substance
CAS-No : 7439-89-6
EC-No : 231-096-4
EINECS-Name : iron
Molecular formula :
Value : <= .005 g/kg

Remark : Value given as <= 5 mg/kg
Flag : Critical study for SIDS endpoint
20.02.2004 (2)

Purity : typical for marketed substance
CAS-No : 7440-38-2
EC-No : 231-148-6
EINECS-Name : arsenic
Molecular formula :
Value :

Remark : Value given as <=0.02 mg/kg
Result : Arsenic = 0.000002 % w/w
(value given as <=0.02 mg/kg)
Flag : Critical study for SIDS endpoint
17.06.2004 (2)

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name : Destillation residue
Molecular formula :
Value : <= .3 % w/w

Flag : Critical study for SIDS endpoint
20.02.2004 (2)

Purity : typical for marketed substance
CAS-No : 7719-12-2
EC-No : 231-749-3
EINECS-Name : phosphorus trichloride
Molecular formula : PCl3
Value : .1 % w/w

20.02.2004 (3)

Purity : typical for marketed substance
CAS-No : 7439-89-6
EC-No : 231-096-4
EINECS-Name : iron
Molecular formula :

Value : .001 g/kg

Remark : Value given as 1 ppm
20.02.2004 (3)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : - tonnes in 1995

Result : In 1995 the phosphoryl trichloride manufacturing capacities were about 39,900 tonnes in the USA, 100,000 tonnes in Western Europe, and 30,000 tonnes in Japan. The phosphoryl trichloride consumption of the USA increased from 24,300 tonnes in 1983 to about 30,700 tonnes in 1994

Flag : Critical study for SIDS endpoint
21.07.2005 (7)

Result : The global production capacity of phosphoryl trichloride was estimated to be 0.2 million tonnes for about 15 producers in 2002. Approximately 0.15 million tonnes/year of the manufacturing capacity are in the OECD countries and 0.05 million tonnes/year in non-member countries

Flag : Critical study for SIDS endpoint
21.07.2005

1.6.1 LABELLING

Labelling : as in Directive 67/548/EEC
Specific limits :
Symbols : T+, C, ,
Nota : , ,
R-Phrases : (14) Reacts violently with water
(22) Harmful if swallowed
(26) Very toxic by inhalation
(29) Contact with water liberates toxic gas
(35) Causes severe burns
(48/23) Toxic: danger of serious damage to health by prolonged exposure through inhalation
S-Phrases : (1/2) Keep locked up and out of reach of children
(7/8) Keep container tightly closed and dry
(26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
(36/37/39) Wear suitable protective clothing, gloves and eye/face protection
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

05.12.2003 (8)

1.6.2 CLASSIFICATION

Classified : as in Directive 67/548/EEC

Class of danger : corrosive
R-Phrases : (35) Causes severe burns
Specific limits :

05.12.2003 (8)

Classified : as in Directive 67/548/EEC
Class of danger : harmful
R-Phrases : (22) Harmful if swallowed
Specific limits :

05.12.2003 (8)

Classified : as in Directive 67/548/EEC
Class of danger : other: Contact with water liberates toxic gas.
R-Phrases : (29) Contact with water liberates toxic gas
Specific limits :

05.12.2003 (8)

Classified : as in Directive 67/548/EEC
Class of danger : other: Reacts violently with water
R-Phrases : (14) Reacts violently with water
Specific limits :

05.12.2003 (8)

Classified : as in Directive 67/548/EEC
Class of danger : toxic
R-Phrases : (48/23) Toxic: danger of serious damage to health by prolonged exposure through inhalation
Specific limits :

05.12.2003 (8)

Classified : as in Directive 67/548/EEC
Class of danger : very toxic
R-Phrases : (26) Very toxic by inhalation
Specific limits :

05.12.2003 (8)

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : type
Category : Non dispersive use

26.05.2004 (9)

Type of use : type
Category : Use in closed system

Type of use : industrial
Category : Basic industry: basic chemicals

Type of use : industrial
Category : Chemical industry: used in synthesis

Type of use : use
Category : Intermediates

Result : Phosphoryl trichloride is used as an intermediate for the manufacturing of wide range of chemicals (percentages reported for the USA 2001):
· Plastics and elastomers additives (55 %)
· Functional fluids, e.g. phosphate ester hydraulic fluids (22 %)
· Pesticides (7 %)
· Lubricant oil additives (4 %)
· Surfactants and sequesterants (2 %)
· Miscellaneous (10 %)

21.07.2005 (10)

Type of use : use
Category : Intermediates

Remark : Use of phosphoryl trichloride as non aqueous solvent is pressumed to be a specialized, small-scale application limited to reseach and development

Result : Phosphoryl trichloride is a basic chemical which is used industrially as an intermediate. Because of its properties phosphoryl trichloride has a large number of chemical applications, e.g.
· Synthesis of alkyl- and arylphosphates by reaction with alcohols, phenols, or epoxides
· Production of carbonic acid halogenides
· Use as non aqueous solvent

21.07.2005 (11)

Type of use : use
Category : Solvents

Result : The use of phosphoryl trichloride as a solvent in cryoscopy (Merck, 2001) respectively as an anhydrous solvent in general (Roempp, 20034) is limited to some scientific laboratories

21.07.2005 (12) (13)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : MAK (DE)
Limit value : 1.3 mg/m3

Remark : 1 mg/m³=0.18 ml/m³ (ppm)
Ceiling limit: Category I (should not be exceeded)
MAK: 0.2 ppm
not assignable to any pregnancy risk group (MAK)
17.06.2004 (14)

Type of limit : TRK (DE)
Limit value : 1.3 mg/m3

Remark : TRGS 900 "Atmospheric Threshold Value":
0,2 ml/m³ (ppm) = 1,3 mg/m³
maximum limit of excess factor: 4
17.06.2004 (15)

Type of limit : TLV (US)
Limit value : .63 mg/m3

Remark : 0.63 mg/m³=0.1 ppm
17.06.2004 (6)

Type of limit : OES (UK)
Limit value : 1.2 mg/m3
Short term exposure limit value
Limit value : 3.6 mg/m3
Time schedule : 10 minute(s)
Frequency : times

17.06.2004 (6)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Classified by : other: VwVwS
Labelled by :
Class of danger : 1 (weakly water polluting)

Remark : Classification in accordance with the German Water Resources Act (in accordance with Annex 3 to the Directive on Water-Hazardous Substances). Official German Classification with identification number (Kenn-Nr.) 5171
18.06.2004 (16)

1.8.4 MAJOR ACCIDENT HAZARDS

Legislation : Stoerfallverordnung (DE)
Substance listed : yes
No. in Seveso directive : No. 1 (highly toxic)

21.07.2005 (17)

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

Type : degradation product in water
CAS-No : 7647-01-0
EC-No : 231-595-7
EINECS-Name : hydrogen chloride
IUCLID Chapter : 3.1.2

17.06.2004

Type : degradation product in water
CAS-No : 7664-38-2
EC-No : 231-633-2
EINECS-Name : orthophosphoric acid
IUCLID Chapter : 3.1.2

17.06.2004

Type : degradation product in water
CAS-No :
EC-No :
EINECS-Name : dichlorophosphoric acid
IUCLID Chapter : 3.1.2

Remark : Degradation intermediate, not stable
17.06.2004

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

Type of search : Internal and External
Chapters covered : 1
Date of search : 25.11.2002

10.02.2004

Type of search : Internal and External
Chapters covered : 2
Date of search : 25.11.2002

10.02.2004

Type of search : Internal and External
Chapters covered : 3, 4
Date of search : 25.11.2002

10.02.2004

Type of search : Internal and External
Chapters covered : 5
Date of search : 01.05.2003

10.02.2004

1.13 REVIEWS

2.1 MELTING POINT

Sublimation :
Method : other:no data
Year : 1989
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : 1.25 °C
Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
21.06.2004 (18)

Value : 1.2 °C
Sublimation :
Method : other: no data
Year : 1979
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
17.06.2004 (19)

Value : 1.3 °C
Sublimation :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
17.06.2004 (20)

Value : 2 °C
Sublimation :
Method : other: no data
Year : 1991
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
17.06.2004 (21)

Sublimation :
Method : other: no data
Year : 1988
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : 1.25 °C
Reliability : (4) not assignable
Data from handbook or collection of data, not peer-reviewed
21.06.2004 (22)

Sublimation :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : 1.25 °C
Reliability : (2) valid with restrictions
Data from handbook or collection of data
21.06.2004 (23)

Sublimation :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : 1.25 °C
Reliability : (2) valid with restrictions
Data from handbook or collection of data
21.06.2004 (1)

2.2 BOILING POINT

Value : 105.1 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
17.06.2004 (1)

Value : 105.1 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 1979
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.06.2004 (19)

Value : 105.1 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 1988
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (4) not assignable
Data from handbook or collection of data, not peer-reviewed
17.06.2004 (22)

Value : 105.3 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 1991
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
17.06.2004 (21)

Value : 105.8 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.06.2004 (18)

Value : 105.8 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
17.06.2004 (23)

Value : 108.7 °C at 1013 hPa
Decomposition :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.06.2004 (20)

Value : 137.5 °C at
Decomposition :
Method : other: no data
Year : 1962
GLP : no
Test substance : other TS: Phosphoryl trichloride, no purity reported, but cleanup reported

Remark : Clean up: Phosphoryl trichloride was boiled for 2 h in a slow stream of dry nitrogen and distilled several times
Reliability : (4) not assignable
Documentation insufficient for assessment
17.06.2004 (24)

2.3 DENSITY

Type : density
Value : 1.675 g/cm³ at 20 °C
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
18.06.2004 (1)

Type : density
Value : 1.685 g/cm³ at 15.5 °C
Method : other: no data
Year : 1979
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.06.2004 (19)

Type : density
Value : 1.675 at 20 °C
Method : other: no data
Year : 1988
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : Value relative to the density of water at 4°C
Reliability : (4) not assignable
Data from handbook or collection of data, not peer-reviewed
18.06.2004 (22)

Type : density
Value : 1.645 g/cm³ at 25 °C
Method : other: no data
Year : 2001
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
17.06.2004 (18)

Type : density
Value : 1.645 at °C
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : Value relative to the density of water at 4°C
Reliability : (2) valid with restrictions
Data from handbook or collection of data

18.06.2004 (23)

Type : density
Value : 1.675 g/cm³ at °C
Method : other: no data
Year : 1991
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.06.2004 (21)

Type : density
Value : 1.68 g/cm³ at °C
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.06.2004 (20)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : 53.3 hPa at 27.3 °C
Decomposition :
Method : other (measured): description of the method is not given
Year : 1979
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
17.06.2004 (19)

Value : 36 hPa at 20 °C
Decomposition :
Method : other (measured): description of the method is not given
Year : 1988
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Result : Further, the following values are reported:
vapour pressure at 30°C 60 hPa
vapour pressure at 50°C 150 hPa
Reliability : (4) not assignable
Data from handbook or collection of data, not peer-reviewed
17.06.2004 (22)

Value : 53 hPa at 27.3 °C
Decomposition :

Method : other (measured): description of the method is not given
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.07.2005 (23)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : at °C
pH value :
Method : other (calculated): Expert judgement
Year : 2003
GLP : no
Test substance : other TS: Phosphoryl trichloride

Result : "Endpoint Partition Coefficient" is not applicable because the substance is not stable in water due to hydrolysis
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
30.06.2004 (25)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: Expert judgement
Year : 1990
GLP : no
Test substance : other TS: Phosphoryl trichloride

Remark : Not stable in water due to hydrolysis
Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
30.06.2004 (26)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

Value : 1.112 - mPa s (dynamic) at 22 °C
Result :
Method : other: no data
Year : 2003
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported

Reliability : (4) not assignable
Manufacturer data without proof
17.06.2004 (27)

Test type : other: no data
Test procedure :
Value : 1.1119 - mPa s (dynamic) at 22 °C
Result :
Method : other: no data
Year : 1965
GLP : no data
Test substance : other TS: Phosphoryl trichloride, purity not given

Reliability : (2) valid with restrictions
Data from handbook or collection of data
18.07.2005 (28)

2.14 ADDITIONAL REMARKS

Memo : Conversion factors

Result : 1 ppm = 6.36 mg/m3
1 mg/m3 = 0.157 ppm
Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
20.02.2004 (29)

Memo : Conversion factors at 20°C and 1.013 bar

Result : 1 ppm = 6.37 mg/m3
1 mg/m³ = 0.157 ppm
Reliability : (4) not assignable
Data from handbook or collection of data
20.02.2004 (22)

Memo : Relative vapour density

Result : 5.3 (air = 1)
Reliability : (2) valid with restrictions
Data from handbook or collection of data
Flag : Critical study for SIDS endpoint
19.02.2004 (19)

Memo : pH value after hydrolysis

Result : ca. 1.0 at 5 g/l water
Reliability : (4) not assignable
Manufacturer data without proof
20.02.2004 (27)

3.1.1 PHOTODEGRADATION

Deg. product	:	
Method	:	other (calculated): expert judgement
Year	:	2004
GLP	:	
Test substance	:	other TS: Phosphoryl trichloride
Result	:	Photodegradation due to OH radicals in the atmosphere is not calculable with AOPWIN v. 1.90 (2000) (expert judgement). Direct photolysis of gaseous phosphoryl trichloride is not expected due to the lack of adsorption of light with a wavelength above 225 nm (Jan-Khan and Samuel 1936). Photodegradation in water cannot be calculated because the substance is not stable in water due to hydrolysis (Bayer Chemicals 2004).
Reliability	:	(2) valid with restrictions Accepted calculation method
Flag	:	Critical study for SIDS endpoint

18.07.2005 (25) (30)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Deg. product	:	yes
Method	:	other: pH monitoring
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Deg. products	:	7647-01-0 231-595-7 hydrogen chloride 7664-38-2 231-633-2 orthophosphoric acid
Method	:	The reaction of phosphoryl chloride and water was studied by bringing a small amount of phosphoryl chloride into contact with an excess of well stirred water and following the generation of acidic reaction products using a pH electrode. Quantitative analysis (redox titration with AgNO3 and pH titration) after completion of reaction confirmed that all reaction products have been captured by this method.
Result	:	The experimental set up could not distinguish the apparent reaction rate from, e.g., the mixing delay or the inertia of the measuring system. However, the half-life of phosphoryl chloride in water was estimated to be less than 10 seconds at 23 °C. Quantitative analysis (redox titration with AgNO3 and pH titration) after completion of reaction confirmed that all reaction products were captured by this method. In the chloride titrations with AgNO3 99 % of the chloride expected to be generated by hydrolysis of the phosphoryl chloride were recovered. In the pH titrations, 94 % of the expected total acidity were recovered (pKa values of phosphoric acid are 2.16, 7.21 and 12.33 for the first, second, and third dissociation step, respectively. Using phenolphthalein as the indicator for titration with NaOH, the third dissociation step of phosphoric acid will not be reached due to the indicator

transition range of pH 8.2 - 9.8)
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
21.07.2005 (25)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product : yes
Method : other: Conductometry, potentiometry
Year : 1962
GLP : no
Test substance : other TS: Phosphoryl trichloride, no purity given, but clean up described
Deg. products : phosphorodichloric acid
7647-01-0 231-595-7 hydrogen chloride
7664-38-2 231-633-2 orthophosphoric acid

Method : Examination of the intermediates of phosphoryl trichloride hydrolysis:
Conductometric measurement of acid formation
Potentiometric measurement of chloride at a silver-silver chloride electrode
Remark : Clean up: Phosphoryl trichloride was boiled for 2 h in a slow stream of dry nitrogen and distilled several times
Result : Initial hydrolysis of phosphoryl trichloride proceeds with a t1/2 of ca. 1/100 s, followed by slower degradation of the intermediate phosphorodichloric acid (t1/2 = ca. 250 s), which looses its chlorine atoms simultaneously in both acidic solution as well as basic solution. The hydrolysis of phosphorodichloric acid (synthesized by authors) in pure water, acidic and alkaline solution was followed by measurement. Rate constants are similar at pH 4, pH 7 and in alkaline solution.
It is also discussed that a dimerisation intermediate might be formed from each one molecule of phosphorodichloric acid (deprotonated form) and phosphoryl trichloride: Cl2PO-O-POCl2 (P2O3Cl4). This intermediate hydrolyzes rapidly to phosphorodichloric acid
Test substance : Boiling point is reported to be 137.5 °C (no pressure mentioned)
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
18.07.2005 (24)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product : not measured
Method : other: see test conditions
Year : 1942
GLP : no
Test substance : other TS: Phosphoryl trichloride, exact purity not reported

Result : At 20 °C the constant for the hydrolysis rate of phosphoryl trichloride was found to be k = 0.018 corresponding to a half-life of t1/2 = 39 s (for comparison: Phosphorus trichloride k = 0.093 corresponding to a half-life of t1/2 = 7 s).
At 35 °C the constant for the hydrolysis rate of phosphoryl trichloride was found to be k = 0.037 corresponding to a half-life of t1/2 = 19 s (for comparison: Phosphorus trichloride k = 0.13 corresponding to a half-life of t1/2 = 5 s).
Test condition : - Stock solution was prepared with 153.4 g of phosphoryl trichloride

dissolved in 1 l toluene
- An aliquot of 10 cm3 was added in 10 cm3 bidistilled, not buffered water and introduced in a reactor provided with a thermostat
- Two tests were performed at different temperatures: 20 °C and 35 °C. For each temperature 3 replicates were conducted (with slight different surface of reaction)
- Solution was analysed after up to 189 min (20 °C) and 101 min (25 °C)
- Analytical method: The sample was titrated with NaOH N/10. Phenolphthalein was used as an indicator

Reliability : (4) not assignable
Documentation insufficient for assessment
Flag : Critical study for SIDS endpoint
18.07.2005 (31)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method : other: Hydrolysis at low temperatures (-70-0 °C)
Year : 1959
GLP : no
Test substance : other TS: Phosphoryl trichloride, no purity reported
Deg. products : phosphorodichloric acid
7647-01-0 231-595-7 hydrogen chloride
7664-38-2 231-633-2 orthophosphoric acid

Method : Several important data not reported, e.g. pH and method of dissolution of POCl3.
Remark : The scope of the study was to prepare phosphorodichloric acid and to examine its properties. Several attempts were made to synthesize phosphorodichloric acid. The hydrolysis of phosphoryl trichloride was not very efficient for this purpose. The most efficient method started with P2O3Cl4.
Result : When POCl3 hydrolyzes at a temperature of 0 °C, the hydrolysis intermediate POCl2OH (phosphorodichloric acid) has a half-life of about 30 minutes.
Phosphorodichloric acid hydrolyzes rapidly at room temperature in the presence of water.
Reliability : (4) not assignable
Documentation insufficient for assessment
Flag : Critical study for SIDS endpoint
18.07.2005 (32)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product : yes
Method : other: Reaction with water in vapor and liquid phase
Year : 1958
GLP : no data
Test substance : other TS: Phosphoryl trichloride was obtained from Merck and cleaned by fractionated distillation
Deg. products : dichlorophosphoric acid
7647-01-0 231-595-7 hydrogen chloride

Remark : For gas phase tests, no test conditions reported, with the exception of the temperatures. E.g. duration of experiment, air humidity, and other essential data not reported.

In different systems with aerosol droplets, phosphoryl trichloride will be affected by humidity and hydrolyzes to hydrochloric acid and phosphoric acid

Result : Reaction in vapor phase at 20 °C was not observed. At 65 and 450 °C the conversion rate was very low and led to product mixtures. Reaction in water was conducted with varying amounts of water (max. 1:1.00) at low temperature with the aim to prepare HOP(O)Cl2.

Reliability : (4) not assignable
Documentation insufficient for assessment

Flag : Critical study for SIDS endpoint

20.07.2005 (33)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product : yes
Method : other: Computer modeling
Year : 2001
GLP : no
Test substance : other TS: Phosphoryl trichloride
Deg. products : 7647-01-0 231-595-7 hydrogen chloride
7664-38-2 231-633-2 orthophosphoric acid

Method : The dangers caused by accidental releases of phosphoryl trichloride (including spill behaviour) were examined using a computer model (REACTPOOL).

Remark : Not relevant for assessment

Result : The model suggests that effects of phosphoryl chloride spills depend on the amount of water available, surface roughness, and wind speed. In the presence of stoichiometric (3 moles water / mol phosphoryl chloride) or excess water the hydrolysis products are hydrochloric acid and phosphoric acid with 3 mol of hydrochloric acid forming for every mole of phosphoryl chloride.
The hydrolysis is highly exothermic, raising both the temperature and the vapor evolution rates. Hydrochloric acid vapor will be evolved due to its high volatility as well as phosphoryl trichloride vapor. The amount of phosphoric acid evolved is negligible due to its extremely low volatility.
When phosphoryl chloride is in excess of the stoichiometic amount of water essential for complete hydrolysis, P2O3Cl4 and hydrochloric acid are formed (P2O3Cl4 is a complex compound and no information could be found on its nature and properties).
Increasing roughness and wind speed results in increasing vapor evolution rates.

Reliability : (2) valid with restrictions
Basic data given

18.07.2005 (34)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Degradation : .2 % after 39 minute(s) at pH and 5 °C
Deg. product : yes
Method : other: non-homogeneous system according to Carrara and Zoppellari (1894)
Year : 1896
GLP : no

Test substance : other TS: Phosphoryl trichloride, no purity given
Deg. products : 7647-01-0 231-595-7 hydrogen chloride
7664-38-2 231-633-2 orthophosphoric acid

Result : Although authors observed that the reaction with water was very vigorous, they report that the degradation of only 0.2 % of phosphoryl chloride took about 39 min at 5 °C, and about 11 min at 10 °C under the experimental conditions applied
Test condition : Examination of the reaction of phosphoryl trichloride with water in non-homogeneous system according to Carrara and Zoppellari (1894).
Phosphoryl trichloride hydrolyzes according to
$POCl_3 + 3 H_2O > H_3PO_4 + 3HCl$
- Cylindrical recipient with a thermostate
- Constant temperature (5 or 10 °C)
- The amount of acid released was determined with alkali
- Test period: 180 min at 5 °C, 90 min at 10 °C
Reliability : (3) invalid
Documentation insufficient for assessment

18.07.2005 (35) (36)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product :
Method : other: alcoholysis
Year : 1992
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity reported in abstract

Remark : Alcohols (instead of water) used as reactants lead to the formation of esters from phosphoryl trichloride. Rice starch can be cross-linked with phosphoryl trichloride; this cross-linking is improved by addition of sodium sulfate to the cross-linking liquid. The authors discuss whether this effect is due to inhibition of phosphoryl trichloride hydrolysis by low concentrations of sodium sulfate.
Results not relevant for assessment.
Study in Chinese. Only short abstract available
Reliability : (4) not assignable
Original reference not translated

18.06.2004 (37)

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C
Deg. product : yes
Method : other: Experiment to prepare dichlorophosphric acid
Year : 1943
GLP : no data
Test substance : other TS: Phosphoryl trichloride, no purity given
Deg. products : dichlorophosphoric acid
7647-01-0 231-595-7 hydrogen chloride
7664-38-2 231-633-2 orthophosphoric acid

Remark : It is not clear how phosphoryl trichloride was dissolved in the water. No effort was undertaken to measure or control the pH decrease which occured right from the start of the experiment
Result : Author describes an experimentel procedure to prepare dichlorophosphoric

acid. Due to the rapid hydrolysis of the product it is not possible to isolate the free acid but only poorly soluble derivates e.g. the nitron salt (nitron CAS No. 578-95-0).

Reliability : (4) not assignable
Documentation insufficient for assessment

18.07.2005 (38)

3.1.3 STABILITY IN SOIL

Type	:	other: expert judgement
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Deg. product	:	
Method	:	other: expert judgement
Year	:	1990
GLP	:	no
Test substance	:	other TS: Phosphoryl trichloride

Remark : Not stable, hydrolysis with moisture in soil
Reliability : (2) valid with restrictions
Data from handbook or collection of data

18.07.2005 (26)

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	adsorption
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other: Expert judgement
Year	:	2003

Result : Models of fate and behaviour in the environment require values for Kow, water solubility and vapor pressure. Since the substance is highly unstable in water, environmental distribution modelling of either the substance itself or its hydrolysis products (mineral acids, the anions of which are ubiquitous in the environment) is not relevant in this case
Test substance : Phosphoryl trichloride
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
20.07.2005 (39)

3.3.2 DISTRIBUTION

Media : air - biota - sediment(s) - soil - water
Method : other (calculation): Expert judgement
Year : 2003

Result : Models of fate and behaviour in the environment require values for Kow, water solubility and vapour pressure. Since the substance is highly unstable in water, environmental distribution modelling of ei-ther the substance itself or its hydrolysis products (mineral acids, the anions of which are ubiquitous in the environment) is not relevant in this case
Test substance : Phosphoryl trichloride
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
20.07.2005 (39)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum :
Deg. product :
Method : other: expert judgement
Year : 2004
GLP : no
Test substance : other TS: Phosphoryl trichloride

Remark : "Endpoint Biodegradation" not applicable to inorganics.
Since phosphoryl trichloride hydrolyzes rapidly in water (Bayer chemicals 2004), no biodegradation can be measured. The hydrolysis products chloride, phosphate and hydrogen ions, are inorganic end products of biodegradation.
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
18.06.2004 (25)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Elimination :
Method : other: expert judgement
Year : 2004
GLP : no
Test substance : other TS: Phosphoryl trichloride

Result : No potential for bioaccumulation.
Since phosphoryl trichloride hydrolyzes rapidly in water (Bayer Chemicals

2004), no BCF can be measured for phosphoryl trichloride. Since the hydrolysis products chloride, phosphate and hydrogen ions, are generally present in the natural environment, and can be excreted by physiological mechanisms, no bioaccumulation is expected

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint

18.06.2004 (25)

3.8 ADDITIONAL REMARKS

Memo : Investigation of vapor phase hydrolysis of non-metallic chlorides

Remark : The author describes an experimental design for investigating the hydrolysis of inorganic covalent halides in the vapor phase refering to the known fact that several organic compounds which readily hydrolyze in solution do not undergo vapor phase hydrolysis. POCl3 did not hydrolyze appreciably when two jets delivering water vapor and POCl3 vapor were arranged so that the vapors met in space, but a wall reaction was noted further along the tube, when a film of phosphoric acid gradually formed.

Test substance : Phosphoryl trichloride, no purity reported, but clean up described

Reliability : (3) invalid
Unsuitable test system

18.07.2005 (40)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	>= 1000
Limit test	:	
Analytical monitoring	:	no
Method	:	other: UBA-Verfahrensvorschlag "Letale Wirkung beim Zebrabaerbling Brachydanio rerio" (LC 0, LC 50, LC 100; 48-96 Stunden) (Mai 1984)
Year	:	1991
GLP	:	yes
Test substance	:	other TS: Phosphorus trichloride, purity 99.98 %
Remark	:	Although not explicitly mentioned in the original report, the test was conducted with pH-neutralized medium. LC0 >= 1000 mg/l PCl3 corresponds to a LC0 of >= 597 mg/l of (neutralized) phosphonic acid as the hydrolysis product The accepted scientific name for Brachydanio rerio is Danio rerio.
Test condition	:	- Brachydanio rerio from West-Aquarium (Bad Lauterberg) - pH: 7.3-7.7 adjusted - Temperature: 22 °C - Oxygen: 7.8-8.6 mg/l - Test concentration: 1.000 mg/l (nominal concentration) - 5 l test medium, 10 fish/tank - No carrier, control: synthetic tap water, hardness 14.8 °dH - No analytical monitoring because test substance hydrolyzes rapidly yielding hydrochloric acid and phosphonic acid
Reliability	:	(1) valid without restriction Test procedure in accordance with national standard methods
Flag	:	Critical study for SIDS endpoint

18.07.2005 (41)

Type	:	semistatic
Species	:	other: species name not stated, it is assumed to be Acipenser stellatus (eggs)
Exposure period	:	3 day(s)
Unit	:	mg/l
NOEC	:	ca. 60
LC100	:	ca. 75
LC30	:	ca. 70
Limit test	:	
Analytical monitoring	:	no data
Method	:	other: As described by the authors
Year	:	1970
GLP	:	no data
Test substance	:	other TS: Phosphorus trichloride, purity ot given
Remark	:	Original reference in Russian, cited according to German translation
Result	:	LC0 ca. 60 mg/l LC100 ca. 75 mg/l
Test condition	:	Test was performed under the following conditions: -Test species: eggs of Acipenser stellatus -Test vessel: enamelled basins of 1 l -Dilution water: water from the river Wolga

-Test temperature: 20.2 - 24.2°C
-Oxygen concentration: 5.9 - 8.14 mg/l
-Concentration of test substance: 20, 60, 70, 74, 80, 100, 150 mg/l
-Test duration: 3 days
-pH 3.3-7 (depending on initial concentration of phosphorus trichloride)
-Endpoint: hatching

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint

18.07.2005 (42)

Type : semistatic
Species : other: species name not stated, it is assumed to be Acipenser stellatus
Exposure period : 5 day(s)
Unit : mg/l
NOEC : ca. 20
LC100 : ca. 70
EC1 (length) : ca. 20
EC5 (body weight) : ca. 20
Limit test :
Analytical monitoring : no data
Method : other: As described by the authors
Year : 1970
GLP : no data
Test substance : other TS: Phosphorus trichloride, Purity not given

Remark : Original reference in Russian, cited according to German translation
Result : 70 mg/l (highest concentration tested): 100 % malformation of larvae, death after 3d (LC100)
60 mg/l: 15 % reduction of length, 30 % reduction of body weight, slight pigmentation
20 mg/l (lowest concentration tested): 1.2 % reduction of length (EC1), 5.4 % reduction of body weight (EC5). EC1 and EC5 were used as NOEC (20 mg/l).
Test condition : Test was performed under the following conditions:
- Test species: larvae of Acipenser stellatus
- Test vessel: enamelled basins of 1 l or aquaria of 10 l
- Dilution water: water from the river Wolga
- Test temperature: 20.2 - 24.2°C
- Oxygen concentration: 5.9 - 8.14 mg/l
- Concentration of test substance: 20, 60, 70 mg/l
- Test duration: 5 days
- pH 3.3-7 (depending on initial concentration of phosphorus trichloride)
- Endpoint: Mortality

Reliability : (2) valid with restrictions
Basic data given

Flag : Critical study for SIDS endpoint

22.07.2004 (42)

Type : semistatic
Species : other: Acipenser stellatus (eggs)
Exposure period : 3 day(s)
Unit : mg/l
LC100 : ca. 75
LC8 : ca. 60
LC10 : ca. 70
Limit test :
Analytical monitoring : no data
Method : other: As described by the authors
Year : 1970

GLP : no
Test substance : other TS: Phosphorus pentachloride, purity not given

Remark : Original reference in Russian, cited according to German translation
Test condition : Test was performed under the following conditions:
-Test species: eggs of Acipenser stellatus
-Dilution water: water from the river Wolga
-Test temperature: 20.2 - 24.2°C
-Oxygen concentration: 5.9 - 8.14 mg/l
-Concentration of test substance: 20, 60, 70, 74, 80, 100, 150 mg/l
-Test duration: 3 days
-pH 3.3-7 (depending on initial concentration of phosphorus pentachloride)
-Endpoint: Hatching
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
18.07.2005 (42)

Type : semistatic
Species : other: Acipenser stellatus
Exposure period : 5 day(s)
Unit : mg/l
NOEC : 20
LC0 : ca. 70
Limit test :
Analytical monitoring : no data
Method : other: As described by the authors
Year : 1970
GLP : no
Test substance : other TS: Phosphorus pentachloride, purity not given

Remark : Original reference in Russian, cited according to German translation
Result : For the hatched fish larvae the 5 d-LC0 was approximately 70 mg/l (highest concentration tested). Since there were some 30 % deformations in the high concentration, the 5 d-NOEC was 20 mg/l. At that concentration a small reduction of fish larvae weight (3 %) and length (8 %) was observed as compared to the controls
Test condition : Test was performed under the following conditions:
-Test species: larvae of Acipenser stellatus
-Dilution water: water from the river Wolga
-Test temperature: 20.2 - 24.2°C
-Oxygen concentration: 5.9 - 8.14 mg/l
-Concentration of test substance: 20, 60, 70 mg/l
-Test duration: 5 days
-pH 3.3-7 (depending on initial concentration of phosphorus pentachloride)
-Endpoint: Mortality
Reliability : (2) valid with restrictions
Basic data given
Flag : Critical study for SIDS endpoint
22.07.2004 (42)

Type : semistatic
Species : Leuciscus sp. (Fish, fresh water)
Exposure period : 10 day(s)
Unit : mg/l
LC100 : ca. 25
Limit test :
Analytical monitoring : no data
Method : other: As described by the authors
Year : 1970

GLP : no data
Test substance : other TS: Phosphorus trichloride, purity not given

Remark : Original reference in Russian, cited according to German translation
The pH was presumably pH 3-4, which is not tolerated by several fish species (compare OECD-SIDS Hydrochloric Acid (2002)). The recommended for fish tests is pH 6.0 to pH 8.5 according to OECD Guidelines
Result : 5d-LC100 = 30 mg/l
10d-LC100 = 25 mg/l
Test condition : Tests were performed under the following conditions:
-Test species: Leuciscus leuciscus
-Dilution water: dechlorinated tap water
-Test temperature: 22 - 24 °C
-Oxygen concentration: 5.8 - 7.8 mg/l
-Concentration of test substance: 10, 20, 30, 40 mg/l
-Test duration: 5-10 days
Reliability : (2) valid with restrictions
Study acceptable for assessment
Flag : Critical study for SIDS endpoint
22.07.2004 (42)

Type : semistatic
Species : other: species name not stated, it is assumed to be Esox lucius and Perca fluviatilis
Exposure period : 30 day(s)
Unit : mg/l
LC0 : > 40
Limit test :
Analytical monitoring : no data
Method : other: As described by the authors
Year : 1970
GLP : no data
Test substance : other TS: Phosphorus trichloride, purity not given

Remark : Original reference in Russian, cited according to German translation
Result : No mortality and no deviations from normal appearence of fish observed at 40-50 mg/l
Reliability : (4) not assignable
Documentation insufficient for assessment
Flag : Critical study for SIDS endpoint
22.07.2004 (42)

Type : semistatic
Species : Carassius carassius (Fish, fresh water)
Exposure period : 30 day(s)
Unit : mg/l
NOEC : ca. 40
Limit test :
Analytical monitoring : no data
Method : other: As described by the authors
Year : 1970
GLP : no data
Test substance : other TS: Phosphorus trichloride, purity not given

Remark : A NOEC of ca. 40 mg/l was derived from EC0
Original reference in Russian, cited according to German translation
Test cannot be used to derive a PNECaqua, because it is not clear, whether early life stages have been covered

Result : 10-40 mg/l: Continuous increase of body weight during whole test period, no difference in comparison to control
50-58 mg/l: Decrease in body weight up to day 15, than increase of body weight
60 mg/l: No increase of body weight up to day 30, than decrease to 0.35 mg body weight
65 mg/l: 100 % death after 2 days
data of body weight development of control are not given

Test condition : Tests were performed under the following conditions:
- Test vessel 10 l aquarium
- Semistatic incubation with change of incubation solution every 24 h
- Dilution water: dechlorinated tap water
- Test temperature: 22 - 24 °C
- Oxygen concentration: 5.8 - 7.8 mg/l
- pH 3.3- 7.0
- Concentration of test substance and corresponding values for HCl and HP(O)(OH)2:

PCl3 (mg/l)	HCl (mg/l) cal	HP(O)(OH)2
10	2.7	6.0
20	5.3	11.9
30	8.0	18.0
40	10.6	23.9
50	13.3	29.9
55	14.3	32.8
58	15.4	34.6
60	16.0	35.8
65	17.3	38.8

- Fish were weighthed every five days
- Fish were fed with earthworms and gammarids
- Prior to incubation, fish were acclimated to test conditions for 10-15 days in dechlorinated tap water

Reliability : (2) valid with restrictions
Study acceptable for assessment

Flag : Critical study for SIDS endpoint

22.07.2004 (42)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC0 : 25
EC50 : 35.4
EC100 : 50
Analytical monitoring : no
Method : Directive 92/69/EEC, C.2
Year : 2003
GLP : yes
Test substance : other TS: Phosphoryl trichloride, purity not given

Method : Method is in most parts equivalent to the OECD TG 202 Daphnia sp., Acute immobilisation test and reproduction test, Part I -The 24h EC50 Acute immobilisation test. Unpublished report.

Remark : The following values were determined in non-buffered media:
24h-EC0 = 25 mg/l
24h-EC100 = 50 mg/l
48h-EC0 = 25 mg/l

48h-EC100 = 50 mg/l
Geometric mean (EC0/EC100) = 35.4 mg/l
Under pH-adjusted conditions no immobilisation of the daphnids has been observed at a nominal concentration up to 100 mg/l.
Measured pH-values:

concentration	0h	48h
control	7.8	7.9
25 mg/l	6.2	7.3
50 mg/l	3.7	3.7 (24 h)
100 mg/l	2.9	3.0 (24 h)
50 mg/l	7.9	7.9 (with adjusted pH)
100 mg/l	7.8	7.5 (with adjusted pH)

The results of the experiments in buffered solutions clearly demonstrate that immobilisation was caused by pH-effects.

Test condition : - 50 ml glass beakers holding 10 neonates in 20 ml of test medium
- Dilution water: reconstituted water total hardness, measured at test start: 14.8°dH
- 10 neonates per vessel, 2 replicates per concentration/control
- Temperature during the test: 18 - 22°C
- pH and oxygen values measured at the end of the test
- Experimental design: 5 test concentrations plus 1 control
- No feeding during the exposure period
- Lighting: 16h light to 8h dark
- Nominal test concentrations: 25, 50 and 100 mg/l without adjustment of pH-value, additionally 50 and 100 mg/l with adjustment of the pH-value, since extreme pH-decreases were observed due to inherent properties of the test substance
- Criteria of effects: item-induced alteration of the normal mobility behaviour and loss of locomotory actions of the neonates, observed at 24 and 48 hours
- No chemical analysis has been performed, as the test substance phosphorus trichloride hydrolyses rapidly in aqueous medium

Reliability : (1) valid without restriction
GLP guideline study

Flag : Critical study for SIDS endpoint

24.05.2004 (43)

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC0 : 25
EC50 : 35.4
EC100 : 50
Analytical monitoring : no
Method : Directive 92/69/EEC, C.2
Year : 2003
GLP : yes
Test substance : other TS: Phosphorus trichloride, purity not given

Method : Method is in most parts equivalent to the OECD TG 202 Daphnia sp., Acute immobilisation test and reproduction test, Part I -The 24h EC50 Acute immobilisation test. Unpublished report.

Result : The following values were determined in non-buffered media:
24h-EC0 = 25 mg/l
24h-EC100 = 50 mg/l
48h-EC0 = 25 mg/l
48h-EC100 = 50 mg/l
Under pH-adjusted conditions no immobilisation of the daphnids was been observed at a nominal concentration of up to 100 mg/l.

Geometric mean (EC0/EC100) = 35.4 mg/l
Measured pH-values:

concentration	0h	48h
control	7.9	7.8
12.5 mg/l	6.7	7.7
25 mg/l	6.1	7.2
50 mg/l	3.6	3.7*
100 mg/l	2.9	2.9*
50 mg/l	7.9	7.9 (with adjusted pH)
100 mg/l	8.0	7.8 (with adjusted pH)

The results of the experiments in buffered solutions clearly demonstrate that immobilisation was caused by pH-effects

Test condition : - 50 ml glass beakers holding 10 neonates in 20 ml of test medium
- Dilution water: reconstituted water total hardness, measured at test start: 14.8°dH
- 10 neonates per vessel, 2 replicates per concentration/control
- Temperature during the test: 18 - 22°C
- pH and oxygen values measured at the end of the test
- Experimental design: 5 test concentrations plus 1 control
- No feeding during the exposure period
- Lighting: 16h light to 8h dark
- Nominal test concentrations: 25, 50 and 100 mg/l without adjustment of pH-value, additionally 50 and 100 mg/l with adjustment of the pH-value, since extreme pH-decreases were observed due to inherent properties of the test substance
- Criteria of effects: item-induced alteration of the normal mobility behaviour and loss of locomotory actions of the neonates, observed at 24 and 48 hours
- No chemical analysis has been performed, as the test substance phosphorus trichloride hydrolyses rapidly in aqueous medium

Reliability : (1) valid without restriction
GLP guideline study

Flag : Critical study for SIDS endpoint

20.07.2005 (44)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	12.5
LOEC	:	25
EC50	:	32.12
Limit test	:	yes
Analytical monitoring	:	no
Method	:	Directive 92/69/EEC, C.3
Year	:	2003
GLP	:	yes
Test substance	:	other TS: Phosphoryl trichloride, purity not given
Method	:	Method is in most parts equivalent to the OECD TG 201 Alga, Growth inhibition test
Remark	:	Accepted new scientific name for Scenendesmus subspicatus: Desmodesmus subspicatus
Result	:	-Effect concentrations based on biomass growth (b): EC 10 = 19.37 mg/l EC 50 = 27.91 mg/l

NOEC = 12.5 mg/l
LOEC = 25 mg/l
-Effect concentrations based on population density growth rate (r):
EC 10 = 23.22 mg/l
EC 50 = 32.12 mg/l
NOEC = 12.5 mg/l
LOEC = 25 mg/l
Under pH-adjusted conditions no inhibition of the algae growth has been observed at a nominal concentration of 100 mg/l.
Measured pH-values:

concentration	0h	72h	av.growth rate
control	8.2	10.5	1.12
3.13	7.8	10.5	1.17
6.25	7.7	10.4	1.19
12.5	7.3	9.8	1.15
25	6.8	9.0	0.95
50	3.5	3.5	0.0
100	2.9	2.9	0.0
100 mg/l	8.0	10.7	1.30 (with adjusted pH)

The results clearly demonstrate that the inhibitory effects were caused by low pH.

Test condition : - Static conditions
- Algal inoculum about 10E+04 cells/ml initial cell density
- 300 ml Erlenmeyer flasks with stoppers as test vessels
- Temperature during the test: 21 - 25 °C
- Lighting 60 to 120 µE/m²/s
- pH is measured at the beginning of the test and after 72 hours
- Experimental design: 6 test concentrations plus 1 control, 3 replicates per concentration, 6 replicates per control, highest test concentration without algae
- Nominal test concentrations: 3.13, 6.25, 12.5, 25, 50 and 100 mg/l without adjustment of pH-value
- As extreme pH-decreases were observed due to inherent properties of the test substance additional replicates of the highest test concentration (100 mg/l) were investigated after pH-adjustment.
- Cell densities measured at 24 hours intervals using a microcell counter
- Inhibition of algal population measured as reduction in growth and growth rate, relative to control cultures under identical conditions
- The 72 hour EC50 values are calculated or read from the concentration/percebtage response curve
- No chemical analysis has been performed, as the test substance phosphoryl trichloride hydrolyses rapidly in aqueous medium

Reliability : (1) valid without restriction
GLP guideline study

Flag : Critical study for SIDS endpoint

18.07.2005 (45)

Species : Scenedesmus subspicatus (Algae)
Endpoint : growth rate
Exposure period : 72 hour(s)
Unit : mg/l
NOEC : 12.5
LOEC : 25
EC50 : 33.41
Limit test : yes
Analytical monitoring : no
Method : Directive 92/69/EEC, C.3
Year : 2003
GLP : yes
Test substance : other TS: Phosphorus trichloride, purity not given

Method : Method is in most parts equivalent to the OECD TG 201 Alga, Growth inhibition test

Remark : Accepted new scientific name for Scenendesmus subspicatus: Desmodesmus subspicatus

Result : The following results were observed:
-Effect concentrations based on biomass growth (b):
EC 10 = 21.30 mg/l
EC 50 = 30.24 mg/l
Determined NOEC and LOEC-values based on biomass growth (b):
NOEC = 12.5 mg/l
LOEC = 25 mg/l
Under pH-adjusted conditions no inhibition of the algae growth has been observed at a nominal concentration of 100 mg/l.
-Effect concentrations based on population density growth rate (r):
EC 10 = 24.89 mg/l
EC 50 = 33.41 mg/l
Determined NOEC and LOEC values based on population density growth rate (r):
NOEC = 12.5 mg/l
LOEC = 25 mg/l
Under pH-adjusted conditions no inhibition of the algae growth has been observed at a nominal concentration of 100 mg/l.
Measured pH-values:

concentration	0h	72h	av.growth rate
control	8.2	10.5	1.12
3.13 mg/l	7.8	10.4	1.17
6.25 mg/l	7.6	10.3	1.16
12.5 mg/l	7.3	10.0	1.17
25 mg/l	6.9	9.2	1.02
50 mg/l	3.5	3.5	0.0
100 mg/l	2.9	2.9	0.0
100 mg/l	8.0	10.7	1.31 (with adjusted pH)

The results of the respective replicates clearly demonstrate that the inhibitory effects observed were caused by pH-effects.

Test condition : - Static conditions
- Algal inoculum about 10E+04 cells/ml initial cell density
- 300 ml Erlenmeyer flasks with stoppers as test vessels
- Temperature during the test: 21 - 25 °C
- Lighting 60 to 120 µE/m²/s
- pH is measured at the beginning of the test and after 72 hours
- Experimental design: 6 test concentrations plus 1 control, 3 replicates per concentration, 6 replicates per control, highest test concentration without algae
- Nominal test concentrations: 3.13, 6.25, 12.5, 25, 50 and 100 mg/l without adjustment of pH-value
- As extreme pH-decreases were observed due to inherent properties of the test substance additional replicates of the highest test concentration (100 mg/l) were investigated after pH-adjustment.
- Cell densities measured at 24 hours intervals using a microcell counter
- Inhibition of algal population measured as reduction in growth and growth rate, relative to control cultures under identical conditions
- The 72 hour EC50 values are calculated or read from the concentration/percebtage response curve
- No chemical analysis has been performed, as the test substance phosphoryl trichloride hydrolyses rapidly in aqueous medium

Reliability : (1) valid without restriction
GLP guideline study

Flag : Critical study for SIDS endpoint

24.05.2004 (46)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	activated sludge
Exposure period	:	3 hour(s)
Unit	:	mg/l
EC50	:	9450
EC05	:	3520
Analytical monitoring	:	no
Method	:	ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year	:	1991
GLP	:	yes
Test substance	:	other TS: Phosphorus trichloride, purity 99.7 %
Test condition	:	- Inoculum: Activated sludge from laboratory waste water treatment plant, inoculum contained 6 g/l dry matter - Test concentrations of phosphorus trichloride: 1000, 1800, 3200, 5600, and 10000 mg/l (The report does not contain any reference to pH adjustment. Given the very high EC50 it can be assumed that pH was adjusted) - Reference substance: 3,5-dichlorophenol - No analytical monitoring because test substance hydrolyses into hydrochloric acid and phosphonic acid
Reliability	:	(1) valid without restriction Test procedure in accordance with national standard methods
Flag	:	Critical study for SIDS endpoint

18.06.2004 (41)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 380 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	other: vegetable oil
Doses	:	
Method	:	other: no data
Year	:	1974
GLP	:	no data
Test substance	:	other TS: OPCl3
Remark	:	This study was also reported by Molodkina NN (1971) and Roshchin AV, Molodkina NN (1977)
Result	:	LD50: 380 mg/kg (304-475)
Reliability	:	(2) valid with restrictions Short report; detailed desription of signs of toxicity
Flag	:	Critical study for SIDS endpoint

16.09.2004 (47)

Type	:	LD50
Value	:	= 36 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Method	:	other: no data
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	No further data given
Reliability	:	(4) not assignable Secondary literature, poor documentation

16.09.2004 (48) (49)

Type	:	LD50
Value	:	= 36 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle	:	other: undiluted
Doses	:	25.1 -31.6- 39.8 - 50.1
Method	:	other: no data
Year	:	1978
GLP	:	no
Test substance	:	other TS: OPCl3

Result	:	Mortality: 25.1 mg/kg: 0/5 31.6 mg/kg: 2/5 39.8 mg/kg: 3/5 50.1 mg/kg: 5/5 LD50: 36 mg/kg (95% confidence limits: 31-41mg/kg) Signs of intoxication: weight loss (1-3 days in survivors) increasing weakness, collapse, death Necropsy: hemorage of lungs, liver discoloration, acute gastrointestinal inflammation; no findings in survivors after 14 d
Reliability	:	(2) valid with restrictions Tabular report available. It should be noted that this summary is not all inclusive. Therefore, it may not highlight all adverse effects that EPA may judge to meet T8CA 8(e) reportability
Flag	:	Critical study for SIDS endpoint

16.09.2004 (50)

Type	:	LD50
Value	:	380 mg/kg bw
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	6
Vehicle	:	other: vegetable oil
Doses	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	This study was also reported by Molodkina NN (1971) and Roshchin AV, Molodkina NN (1977)
Result	:	LD50: 380 mg/kg (304-475) LD16: 250 mg/kg LD84: 580 mg/kg Signs of intoxication: nausea, disturbance of movement co-ordination, fatigue, weakness, chromodakryorhea, respiratory frequency: 50-80 per minute. 20 to 40 minutes after application of the LD50: cyanosis, weakness, convulsions, short-windedness. Necropsy: lungs of deceased animals were intensly red discolored. The livers were dark-gray, the stomach was distended and hemorhagic
Reliability	:	(2) valid with restrictions Short report; detailed desription of signs of toxicity
Flag	:	Critical study for SIDS endpoint

16.09.2004 (51)

Type	:	LD50
Value	:	110 mg/kg bw

Species : rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 50
Vehicle : other: corn oil
Doses : 50, 100, 200, 300, 400 mg/kg bw
Method : other: no data
Year : 1977
GLP : no data
Test substance : other TS: OPCl3

Remark : report is sufficient for evaluation
Result : Mortality
50 2/10
100 4/10
200 9/10
300 9/10
400 10/10

All but 2 deaths (1 from each of 50 and 100 mg/kg groups) occurred on day of dosing.

LD50: 110 ± 19 mg/kg bw
LD16: 54 mg/kg
LD84: 224 mg/kg

Signs of toxicity:
Decreased locomotor activity, piloerection, ptosis, suspected blood around the eyes, loss of righting reflex and death. Normal body activity returned within 7 days in all surviving animals.
Necropsy:
Lung fused to rib cage at 50 mg/kg. At 100 mg/kg lung fused to rib cage and filled with white mass and irrgular thickening of cardiac mucosa. Chronic pulmonary disease was revealed at 50, 100 and 200 mg/kg bw
Test condition : Male and female rats were fasted for 24 hours before administration of the test substance. The test material was administered orally, by intubation, as a 10% solution in corn oil. Animals were observed at 1, 3, 6, 24, 48, 72 hours then daily up to 14 days. The oral LD50 was calculated. All surviving animals were killed, autopsied and observed for gross pathological organ changes.
Reliability : (2) valid with restrictions
Short report, detailed description
Flag : Critical study for SIDS endpoint
16.01.2006 (52)

Type : LD50
Value : 380 mg/kg bw
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Method :
Year :
GLP :
Test substance : other TS: OPCl3

Remark : This study was also reported by Molodkina NN (1974) and Molodkina NN (1974)

Reliability : (2) valid with restrictions
Short notice of LD50 only
16.09.2004 (53)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC100
Value	:	< 159700 mg/m³
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male
Number of animals	:	6
Vehicle	:	
Doses	:	
Exposure time	:	18 minute(s)
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	other TS: OPCl3
Result	:	Mortality: 6/6 within 18 minutes Signs of intoxication: < 2 min: laboured breathing; eyes closed; FOG IN CHAMBER 10 min: In creasing weakness, convulsion, collapse, death 18 min: all animals dead Necropsy: lung congestion
Test condition	:	Concentration: 159700 mg/m³ Exposure: 18 Min Temperature: 25 C Humidity: 85 % Air flow: 4 l/min Vaporized sample: 11.5 g
Reliability	:	(2) valid with restrictions Tabular report available
Flag	:	Critical study for SIDS endpoint

16.09.2004 (54)

Type	:	LC50
Value	:	= 307.82 mg/m³
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	other TS: OPCl3
Remark	:	No further data given
Result	:	LC50s of POCl3 was 48.4 micromoles per mole of air (~308 mg/m³) for rats. The slope of the dose response curve was 10.8 +- 1.7.

Hydrolysis of POCl3 was about 15 percent. Animals showed signs of irritation (pawing, scratching of head and nose, chromodakryorhea) during exposure to POCl3.
All deaths occurred within 48 hours. Histopathology revealed effects in the trachea and bronchi of dead rats (desquamation of bronchial epithelium with plugging of airways, edema, hemorrhage).
Signs abated within 14 days in survivors. These rats did not show microscopic changes.

Test condition : 20 female rats per group; whole body
Animals were observed and deaths were recorded up to 14 days post exposure. Median lethal concentrations (LC50) were computed

Reliability : (2) valid with restrictions
Few details reported, number of groups and dose regimen missing

16.09.2004 (55)

Type : LC50
Value : = 200 mg/m³
Species : rat
Strain :
Sex :
Number of animals : 20
Vehicle :
Doses : 0,14 - 0,16 - 0,21 - 0,30
Exposure time : 4 hour(s)
Method : other: no data
Year :
GLP : no data
Test substance : other TS: OPCl3

Remark : 1273 ppm = 0.2 mg/L = 200 mg/m³;
no further data given

Reliability : (4) not assignable
Original article in Czech language. No detail given, summary of toxicity data, faulty printout, secondary literature

16.09.2004 (56) (57)

Type : LC50
Value : 71 mg/m³
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time :
Method :
Year : 1974
GLP : no
Test substance : other TS: OPCl3

Remark : This study is also reported by Molodkina NN (1974) and Roshichin (1977)
Result : LC16: 56 mg/m³
LC50: 71 mg/m³ (62 - 80)
LC84: 89 mg/m³

Signs of intoxication:
immediately: agitation, signs of irritation
later: nausea, slow and strained respiration, foamy discharge from nose and mouth, lacrimation,

Pathology:
irritation of respiratory tract: necrosis of
tracheal and bronchial mucosa, alveolar edema,
dystrophy of neurons, liver, and kidney tubuli,
No species specific or sex specific differences

Reliability : (2) valid with restrictions
It ist not possible to allocate specific results to the different species (rat, mouse, guinea pig and rabbit)

Flag : Critical study for SIDS endpoint

27.09.2004 (47)

Type	:	LC50
Value	:	
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3

Remark : This study is also reported by Molodkina NN (1971)

Result : LC16: 56 mg/m³
LC50: 71 mg/m³ (52-80)
LC84: 89 mg/m³
Signs of intoxication:
immediately: agitation, pawing of the nose, signs of irritation
later: nausea, disturbance of movement co-ordination, lateral position, fibrillar twitching, convulsions, slow and strained respiration, loss of weight, reduced food consumption, lacrimation, corneal opacity.
No species specific or sex specific differences.

Reliability : (2) valid with restrictions
Short report; few experimental details

The report does not contain further details. The LD50 is stated for rats but it is not completely clear whether the other findings relate to rat or other species.

14.09.2005 (51)

Type	:	LC50
Value	:	< 20470 mg/m³
Species	:	rat
Strain	:	no data
Sex	:	
Number of animals	:	10
Vehicle	:	other: none
Doses	:	20.47 mg/l
Exposure time	:	1 hour(s)
Method	:	other: no data
Year	:	1977
GLP	:	no data
Test substance	:	other TS: OPCl3

Remark : No further information available

Result : Mortality

20.47 7/10
Signs of toxicity:
Bloody nasal discharge, salivation, nasal discharge, laboured respiration, corneal opacity, lacrimation, eye membrane irritation, tonic convulsions

Test condition : 20.47 mg/ml = 3200 ppm = nominal concentration

10 rats were exposed to an aerosol of the test material. Observation period not given.

Reliability : (2) valid with restrictions
Short report, limited description

Flag : Critical study for SIDS endpoint

16.01.2006 (58)

Type : other: Limit of irritation
Value : .8 mg/m³
Species : rat
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method :
Year : 1973
GLP :
Test substance : other TS: OPCl3

Result : The Limir (min. irritating) value of
phosphoryl chloride for rats was about 2.6-fold higher than established for human subjects, when the animals were exposed to the poison-contg. air for 4 hr.
Changes in the frequency of respiration and degree of
neutral red accumulation in the lung tissue were recorded

Test condition : Irritation was determined by life staining of rat lungs
after 4 h exposure

Reliability : (4) not assignable
No experimental details given

16.09.2004 (59)

Type : LC50
Value : = 52.5 ppm
Species : guinea pig
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method : other: no data
Year :
GLP : no data
Test substance : other TS: OPCl3

Remark : Acute inhalation toxicity was determined in guinea-pigs for phosphorus-oxychloride (POCl3), phosphorus-trichloride (PCl3), methyl-phosphonic-dichloride (MPD), and the products of their neutralization by ammonia. Male guinea-pigs were exposed for 4 hours to vapors of the above compounds in varying concentrations. Animals were observed and deaths were recorded up to 14 days postexposure. Median lethal concentrations (LC50) were computed. LC50s of POCl3 and its ammonia neutralization

products were 52.5 and 41.3 micromoles per mole for guinea-pigs.
Hydrolysis of POCl3 was about 15 percent.
Animals showed signs of irritation during exposure to POCl3, but not during exposure to neutralized products. All deaths occurred within 48 hours.
The authors conclude that the degree of hydrolysis occurring in the phosphorus compound is related to the decrease in toxicity caused by ammonia neutralization. Although ammonia neutralization appears to lessen sensory effects, such a decrease is not necessarily related to a decrease in pathological effects.

Test condition : 52,5 ppm = 333,9 mg/m³
Reliability : (2) valid with restrictions
Limited documentation; few experimental details reported, numbers of animal and groups not stated

16.09.2004 (55)

Type : LC50
Value : 71 mg/m³
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Doses :
Exposure time :
Method :
Year :
GLP :
Test substance : other TS: OPCl3

Remark : This study is also reported by Molodkina NN (1971)
Reliability : (2) valid with restrictions
Tabular statement of LC50; no further data

16.09.2004 (53)

5.1.3 ACUTE DERMAL TOXICITY

Type : LD50
Value :
Species : rabbit
Strain : New Zealand white
Sex : male/female
Number of animals : 5
Vehicle : other: undiluted
Doses : 398-631-1000-1580 mg/kg
Method :
Year :
GLP : no
Test substance : other TS: OPCl3

Result : Mortality:
398 mg/kg: 0/1 male
631 mg/kg: 0/1 female
1000 mg/kg: 1/2 male+female; female died
1580 mg/kg: 1/1 male; died

LD50:
Male: 1000<LD50<1580
Female: 631<LD50<1000

Signs of intoxication:
weight loss (2-3 days in survivors) increasing weakness, collapse, death

Necropsy:
lungs and liver: hyperemia; enlarged gall bladder, kidney: discoloration; gastrointestinal inflammation; normal viscera in survivors after 14 days

Reliability : (2) valid with restrictions
Tabular report available; low animal number
Flag : Critical study for SIDS endpoint
16.09.2004 (50)

Type : LD0
Value : > 250 mg/kg bw
Species : rabbit
Strain : New Zealand white
Sex : male
Number of animals : 12
Vehicle : other: none
Doses : Main study: 250 mg/kg
Range-finder: 500, 1000, 2000, 3000 mg/kg bw

Method : other: no data
Year : 1977
GLP : no data
Test substance : other TS: OPCl3

Remark : No further information available
Result : Mortality (range finder)
500 1/1
1000 1/1
2000 1/1
3000 1/1
Based on the corrosive effects at these doses, 250 mg/kg was used in the main study.
Main Study:
250 0/12
LD50: > 250 mg/kg bw
Signs of toxicity:
In the range finding study all doses produced necrosis, eschar, decreased locomotor activity and death.
In the main study, the animals exposed to 250 mg/kg showed decreased locomotor activity, necrosis and eschar.
Test condition : Range finder:
Four animals were used, one at each of 500, 1000, 2000 and 3000 mg/kg bw
Main study:
The test material was administered undiluted to intact skin of 6 animals and to abraded skin of the other 6 animals. Animals were observed at 1, 3, 6, 24, 48, 72 hours then daily up to 14 days
Reliability : (2) valid with restrictions
Short report, detailed description
Flag : Critical study for SIDS endpoint
16.01.2006 (60)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	other TS: OPCl3
Result	:	Effects: wound (protracted healing)
Test condition	:	Shaved dorsal skin of rabbits treated
Reliability	:	(2) valid with restrictions Short report, non-standard test
Flag	:	Critical study for SIDS endpoint

16.09.2004 (47) (51)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	no data
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	
Method	:	
Year	:	1978
GLP	:	
Test substance	:	other TS: OPCl3
Test condition	:	0.5 ml undiluted, exposure: 24 h scoring: 24 + 72 h
Reliability	:	(2) valid with restrictions Tabular report without detail
Flag	:	Critical study for SIDS endpoint

16.09.2004 (50)

Species	:	rabbit
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3

Result	:	A correlation between the inhalation irritation threshold for humans and rats on one hand, and skin irritation for rabbits on the other, was assessed for POCl3 and other chemicals. The degree of hyperemia following the dermal application to rabbits was correlated with an increase in the thickness of the skin fold. The skin irritation was concn.-dependent. The inhalation toxicity may be approx. assessed from skin irritation tests
Test condition	:	8 animals per concentration; Concentration: 1-10 % in unknown vehicle
Reliability	:	(4) not assignable non standard evaluation and comparison scheme; no experimental data Literature review;
16.09.2004		(61)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	corrosive
Classification	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: OPCl3

Result	:	Effects: skin scales, deep hemorhagic fissures, wound
Test condition	:	4 drops per 4 x 5 cm2 of shaved dorsal skin of rabbits
Reliability	:	(2) valid with restrictions Short report, non-standard test
Flag	:	Critical study for SIDS endpoint
16.09.2004		(51)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	
Exposure time	:	24 hour(s)
Number of animals	:	6
Vehicle	:	other: none
PDII	:	
Result	:	corrosive
Classification	:	
Method	:	other: no data
Year	:	1977
GLP	:	no data
Test substance	:	other TS: OPCl3

Remark	:	No further information available
Result	:	Application of the test material caused immediate tissue destruction. Due to the severity of tissue destruction, a primary irritation index could not be calculated.
Test condition	:	New Zealand White rabbits were used. The test material was administered undiluted to abraded skin. Animals were observed for signs of dermal irritation on removal of dressing and at

72 hours.
Reliability : (2) valid with restrictions
Short report, detailed description
Flag : Critical study for SIDS endpoint
16.01.2006 (62)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : corrosive
Classification :
Method : other: no data
Year :
GLP : no data
Test substance : other TS: OPCl3

Remark : This study has been reported also by Molodkina NN (1974)
Result : Effects:
nekrotic changes and complete blindness
Test condition : 1 drop, undiluted,
Reliability : (2) valid with restrictions
Limited documentation
Flag : Critical study for SIDS endpoint
16.09.2004 (47)

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 24 hour(s)
Comment :
Number of animals : 6
Vehicle :
Result : corrosive
Classification :
Method :
Year : 1978
GLP : no
Test substance : other TS: OPCl3

Result : Immediate findings: severe discomfort with pawing, squealing, thrashing about the stocks, eye tightly closed
1 minute: corrosive
Test condition : 0.1 ml undiluted
Animals: New Zealand White rabbits
Reliability : (2) valid with restrictions
Tabular report available
Flag : Critical study for SIDS endpoint
16.09.2004 (50)

Species : rabbit
Concentration : undiluted
Dose :

Exposure time	:	
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	corrosive
Classification	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: OPCl3
Remark	:	This study is also reported by Molodkina NN (1971)
Result	:	Effects: nekrotic changes and complete blindness
Reliability	:	(2) valid with restrictions Limited documentation
Flag	:	Critical study for SIDS endpoint

16.09.2004 (51)

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	6
Vehicle	:	none
Result	:	corrosive
Classification	:	
Method	:	other: no data
Year	:	1977
GLP	:	no data
Test substance	:	other TS: OPCl3
Remark	:	No further information available
Result	:	Scoring could not be done due to irreversible damage to eye tissue on contact
Test condition	:	New Zealand White rabbits were used. The test material was instilled undiluted into the conjunctival sac of one eye of each rabbit. Ocular reactions were graded at 1, 24, 48, 72 hours, 4 and 7 days.
Reliability	:	(2) valid with restrictions Short report, detailed description
Flag	:	Critical study for SIDS endpoint

16.01.2006 (63)

Species	:	rat
Concentration	:	
Dose	:	
Exposure time	:	
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	
Classification	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3

Remark	:	Abstract: Sperman rank correlation values between the inhalation irritation threshold for humans and rats on one hand, and skin irritation for rabbits on the other, were 0.91 and 0.96, resp., for Et 6-hydroxy-8-chlorooctanate [1070-65-1], Et 6,8-dichlorooctanate [1070-64-0], Et adipate [141-28-6], tert-Bu hydroperoxide [75-91-2], morpholine [110-91-8], Et 6-keto-8-chlorooctanoate [50628-91-6], S2Cl2, chloroacetic acid [79-11-8], 2-chloroethanesulfochloride [1622-32-8], Br, PCl3, and POCl3. The degree of hyperemia following the dermal application to rabbits was correlated with an increase in the thickness of the skin fold. The skin irritation was concn.-dependent. The inhalation toxicity may be approx. assessed from skin irritation tests. Evaluation of mucous membrane reaction in the respiratory tract
Test condition	:	Literature review
Reliability	:	(4) not assignable Non standard evaluation and comparison scheme; no experimental data

16.09.2004 (61)

5.3 SENSITIZATION

Type	:	Guinea pig maximization test
Species	:	guinea pig
Number of animals	:	
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other:
Year	:	1986
GLP	:	no data
Test substance	:	other TS: 1% hydrochloric acid in 70% ethanol
Remark	:	Sensitization was not induced in 15 guinea pigs that were given two intradermal injections and a covered application (48-hr) of 1% HCl (in ethanol of undefined concentration) and challenged 2 weeks later by a similar 24-hr covered exposure. No. of animals with skin reaction at challenge: Treated: 0/15 Control group: 0/6
Reliability	:	(2) valid with restrictions Detailed publication
Flag	:	Critical study for SIDS endpoint

16.09.2004 (64)

Type	:	Mouse ear swelling test
Species	:	mouse
Number of animals	:	
Vehicle	:	
Result	:	not sensitizing
Classification	:	
Method	:	other:
Year	:	1986
GLP	:	no data
Test substance	:	other TS: 1% hydrochloric acid in 70% ethanol
Remark	:	Number of animals with skin reactions at challenge not stated
Result	:	4 consecutive daily uncovered applications of 1 % HCl solution in 70 % ethanol to the abdominal skin were followed 7 days later by a challenge

with 5% uncovered application to the ear.
No evidence of sensitisation was seen.

Test substance : 1% hydrochloric acid in 70% ethanol
Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
22.07.2004 (64)

5.4 REPEATED DOSE TOXICITY

Type : Sub-chronic
Species : rat
Sex :
Strain :
Route of admin. : inhalation
Exposure period : 4 m
Frequency of treatm. : 4h*5d*4m
Post exposure period : 1 month
Doses : 0 - 0.5-1.0 mg/m³
Control group : yes
Method :
Year : 1975
GLP : no
Test substance : other TS: OPCl3

Result : Concentrations of phosphorus and calcium in urine and blood were determined
P:
urine: high dose initial decrease (month 1), then increase (month 2) and decrease again (month 4), increase after the recovery period.
low dose: constant increase during treatment and return to normal thereafter
blood/serum: no changes after 4 months

Ca:
urine: increase in both groups; low dose at control level at the end of treatment
blood/serum: no changes

pH-Value: (4 hours acute exposure)
blood: decrease
urine: decrease

Pathology:
Bone: high dose:thining and reductioon of trabeculae, homogenuos material beneath the periosteum
low dose: similar but less pronounced findings

Reliability : (2) valid with restrictions
Short report, only results regarding phosphorus, calcium and pH reported
Flag : Critical study for SIDS endpoint
16.09.2004 (65)

Type : Chronic
Species : rat
Sex :
Strain :
Route of admin. : inhalation
Exposure period : 4 months

Frequency of treatm.	:	
Post exposure period	:	1,4 months
Doses	:	0 - 0.48 - 1.34 mg/m³
Control group	:	yes
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	Due to the chemical properties of OPCl3 (fast hydrolysis, corrosion) it is hard to imagine a significant exposure and an effect in the bone marrow after inhalation exposure. An effect of the degradtation products, phosphoric acid and hydrochloric acid, exceding the effect of low pH is also not plausible. This study is also reported by Roshchin AV and Molodkina NN (1977)
Result	:	Reduction of weight gain, respiration frequency and oxygen comsumption during all of the treatment period, (groups affected not specified) Altered urinary concentrations of hippuric acid and protein were noted. There was a severe irritation of the mucous membranes of the respiratory tract and a chronic rhinitis, tracheitis, desquamating bronchial katharsis, hyperplasia of mucus cells and round cell infiltration of the submucosa. In liver and kidney protein dystrophy and small droplet fatty degeneration were recorded. In the testes foreign material was detected in testicular tubuli and the motility of sperm was reduced (no influence on spermatogenesis). In cells of the bone marrow of high dose animals chromosomal anomalies were increased, while the mitotic index was significantly reduced (no quantitative data; no experimental detail). Even 1 month after the end of exposure recovery was still incomplete in the high dose group. LOAEL = 0.48 mg/m³
Test condition	:	Aninmal species is not clearly stated. Probably the rat has been used. Guinea pigs cannot be excluded.
Reliability	:	(2) valid with restrictions Summary only: Studies on rats and guinea pigs are reported. A differentiation between the study on guinea pigs and the study on rats is not possible, probably the study was performed in rats
Flag	:	Critical study for SIDS endpoint

14.09.2005 (47)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	other: F-344/ Crl-Br and Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	90 days
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	10-20-50 ppm (nominal)
Control group	:	yes, concurrent vehicle
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: HCl
Result	:	At the high dose tepmoraryly reduced food consumption and body weight were observed. Inflammatory changes were observed in all dose group in the nasal cavity No effects were reported in other organs examined histopathologically

(adrenal, brain, duodenum, eyes + optic nerve, heart, kidney, lung, liver, mesenteric lymph node, testes + epididymides + prostate, ovaries + oviducts + uterus, gross lesions, + several other tissues (total of 44 organs))

Test condition : Animals: age at study initiation: 6-7 weeks
Number of animals: 10 male + 10 female per dose
Parameters:
clinical signs, mortality, weight, food, urinalysis, hematology (10 parameters), clinical chemistry (7 parameters), necropsy, organ weights (5 organs), histopathology (~50 tissues)

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

14.09.2005 (66)

Type : Sub-chronic
Species : mouse
Sex : no data
Strain :
Route of admin. : inhalation
Exposure period : 90 days
Frequency of treatm. :
Post exposure period :
Doses : 0 - 10 - 20 - 50 ppm
Control group : yes
Method :
Year :
GLP : yes
Test substance : other TS: HCl

Result : Cheilitis with accummulating hemosiderin-laden macrophages and eosinophilic globules in epthelium of nasal turbinates were observed in exposed mice
No effects were reported in other organs examined histo-pathologically (adrenal, brain, duodenum, eyes + optic nerve, heart, kidney, lung, liver, mesenteric lymph node, testes + epididymides + prostate, ovaries + oviducts + uterus, gross lesions, + several other tissues (total of 44 organs))

Reliability : (2) valid with restrictions

Flag : Critical study for SIDS endpoint

14.09.2005 (66)

Type : Chronic
Species : guinea pig
Sex :
Strain :
Route of admin. :
Exposure period :
Frequency of treatm. :
Post exposure period :
Doses :
Control group : yes
Method :
Year :
GLP :
Test substance : other TS: OPCl3

Remark : Data are reported for rats and guinea pigs. A differentiation between both species is not possible.
For details see under: Molodkina NN (1971)
This study is also reported by Roshchin AV and Molodkina NN (1977)

Reliability	:	(4) not assignable
17.09.2004		(47)
Type	:	Chronic
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	4 months
Frequency of treatm.	:	
Post exposure period	:	
Doses	:	0.48 - 1.34 mg/m³
Control group	:	yes
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	This study is also reported by Molodkina NN (1971)
Result	:	reduction of weight gain, respiration frequency and oxygen comsumption (groups affected not specified) altered urinary concentrations of hippuric acid and protein were noted in rats. There was a severe irritation of the mucous membranes of the respiratory tract and a chronic rhinitis, tracheitis, desquamating bronchial katharsis, hyperplasia of mucus cells and round cell infiltration of the submucosa. In liver and kidney protein dystrophy and small droplet fatty degeneration were recorded. in bones osteoporosis was detected. Most severe changes at the side of first contact. In the testes calcification of testicular tubuli was recorded and the motility of sperm was reduced (no influence on spermatogenesis). In cells of the bone marrow of high dose animals chromosomal anomalies were increased, while the mitotic index was significantly reduced (no quantitative data; no experimental detail). Even 4 months after the end of exposure recovery was still incomplete. 0.48 mg/m³ caused irritation of the airways with rhinitis and catarrhal bronchitis. In rats additionally an increase of relative kidney weight was seen. No changes remained after a recovery period (duration not specified) After 1.34 mg/m³ cytogenetic effects in bone marrow were observed (increase in chromosomal aberrations and cytostatic activity). 5 of 9 animals showed these effects while the other 4 remained normal. (This effect ocurred only in connection with general toxicity and is considered by the authors as unspecific and secondary to general toxicity) LOAEL = 0.48 mg/m
Test condition	:	Animal species not specified; presumably: rat
Reliability	:	(2) valid with restrictions Species not specified; as the study is reported also by Molodkina (1971), the species is probably the rat
Flag	:	Critical study for SIDS endpoint
16.09.2004		(53)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	S. typhimurium TA1535, TA100, TA1537, TA1538, TA98 S. cerevisiae D4
Test concentration	:	0.001 to 5.0 µl per plate
Cycotoxic concentr.	:	5.0 µl per plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	other TS: OPCl3
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

16.01.2006 (67)

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Test concentration	:	0.001- 5 uL/plate
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS:hydrochloric acid
Remark	:	Method: According to Ames BN et al. (1975). Mutat. Res. 31, 347-364. Procedure: Plate. Plates/test: Not stated Activation system: Liver S-9 fraction from Aroclor 1254 pretreated rats with NADPH-generating system Media: Histidine selective No. of replicates: Not stated
Reliability	:	(2) valid with restrictions Detailed publication
Flag	:	Critical study for SIDS endpoint

17.09.2004 (68)

Type	:	other: DNA damage and repair assay , 'rec' assay
System of testing	:	Escherichia coli WP2, WP2uvrA, WP67, CM611, W3110 (pol A+), P3478 (pol A-)
Test concentration	:	Not stated
Cycotoxic concentr.	:	not stated
Metabolic activation	:	with and without
Result	:	ambiguous
Method	:	
Year	:	1981
GLP	:	
Test substance	:	other TS: hydrochloric acid
Remark	:	HCl showed inhibitory activity in the WP2uvrA stain; while this response was reproducible, it was not considered adequate evidence of DNA-damaging activity since the remaining WP2 deficient strains which also carried the uvrA mutation gave no indication of preferential kill at all.
Test condition	:	Plates/test: Not stated Activation system: Liver S-9 fraction from Aroclor 1254 pretreated rats with NADPH-generating system No. of replicates: 1

Reliability : (2) valid with restrictions
Detailed publication
17.09.2004 (69)

Type : other: DNA damage and repair assay , 'rec' assay
System of testing : B. subtillis H17 arg- try- rec+ and M45 arg- try- rec-
Test concentration : not stated
Cycotoxic concentr. : Not stated
Metabolic activation : with and without
Result : negative
Method :
Year : 1981
GLP :
Test substance : other TS: hydrochloric acid

Remark : Plates/test: Not stated
Activation system: Liver S-9 fraction from Aroclor 1254 pretreated male SD rats with NADPH-generating system
No. replicates: Not stated
Reliability : (2) valid with restrictions
Detailed publication
17.09.2004 (70)

Type : Cytogenetic assay
System of testing : Chinese hamster ovary K1 (CHO-K1) cells
Test concentration : 10 or 14 mM (pH 5.8or 5.5)
Cycotoxic concentr. : Cytotoxicity conc:
With metabolic activation: pH 5.3
Without metabolic activation: pH 5.5
Metabolic activation :
Result : positive
Method :
Year : 1989
GLP : no
Test substance : other TS: hydrochloric acid

Remark : The effect in CHO cells was observed in the absence of rat liver S9 preparations at a nominal HCl concentration of 14 mM (pH 5.5) but was greater in the presence of S9, when a nominal HCl concentration of 10mM (pH 5.8) was required. Similar results obtained using sulphuric acid
Chinese hamster ovary K1 (CHO-K1) cells cultured in vitro were used
Result : Positive: Cytogenetic effects (chromatid breaks) seen +/- S9

Genotoxic effects:	+	?	-
With metabolic activation:	[X]	[ ]	[ ]
Without metabolic activation:	[X]	[ ]	[ ]

Test condition : Fixation time: not stated
Dose levels: not stated
Plates/test: not stated
Activation system: S-9 fraction from the liver of Phenobarbital and 5,6-benzoflavone-induced rats with NADPH-generating system
Media: Ham's F12 medium supplemented with 10% foetal calf serum, sodium bicarbonate (16.7 mM) and Kanamycin (60 ug/mL)
No. replicates: not stated
Reliability : (2) valid with restrictions
17.09.2004 (71)

Type : Cytogenetic assay
System of testing : Fischer L5178Y mouse-lymphoma cells
Test concentration : Incubated with 0.1-0.8 uL/mL

Cycotoxic concentr.	:	not stated
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	1988
GLP	:	
Test substance	:	other TS: Hydrochloric acid
Method	:	Method: according to Clive, D. and Spector, J.F.S., Mutat. Res., 31, 17 (1975); Lebowitz H. et al., 8th Ann. Meet. Mut. So. (1977).
Result	:	Precipitation conc: not stated Genotoxic effects: + ? - With metabolic activation: [ ] [ ] [X] Without metabolic activation: [ ] [ ] [X]
Test condition	:	Mouse-lymphoma cells cultured in vitro were used. Plates/test: not stated Activation system: S-9 fraction from the liver of CD-1 mice with NADPH-generating system Media: Fischer's medium supplemented with 10% horse serum, sodium pyruvate and penicillin-streptomycin No. replicates: not stated
Reliability	:	(2) valid with restrictions

17.09.2004 (68)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	other: anatelophase analysis
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	4 months
Doses	:	1,34 - 0,48 - 0 mg/m³
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	Due to the chemical properties of OPCl3 (fast hydrolysis, corrosion) it is hard to imagine a significant exposure and an effect in the bone marrow after inhalation exposure. An effect of the degradation products, phosphoric acid and hydrochloric acid, exceding the effect of low pH is also not plausible. These results have also been described by Roshchin and Molodkina (1977)
Result	:	Anatelophase analysis of bone marrow cells showed statistical significant (group 1) increase of chromosome aberrations (7,26+-0,65 - group 1; 5,58+-0,52 - group 2; 4,19+-0,41 control). The mitotic index was significantly reduced (1% - group 1; 1,25% - group 2; 1,61% control) Effects were seen in presence of overt toxicity only.
Test condition	:	Evaluation of the bone marrow of animals from a 4 months inhalation study
Reliability	:	(4) not assignable Study design unclear; no data on animal number, preparation and evaluation technique

14.09.2005 (47)

Type	:	other: chromosomal aberration
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	
Exposure period	:	
Doses	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Result	:	The exposure to POCL3 at a concentration of 0,00134 mg/l caused a cytogenetic effect which was manifest in an increased number of chromosomal anomalies and in cytostatic activity. At a lower concentration (0,00048 mg/l), the number of chromosomal anomalies was increased but did not differ significantly from the controls. It should be noted that in 5 out of 9 animals of the given group, the number of chromosomal aberrations was increased whereas in the remaining 4 animals, the number of chromosomal anomalies was within the limits of spontaneous occurence.
Reliability	:	(4) not assignable No experimental details given; limited documentation; secondary literature

16.09.2004 (53)

5.7 CARCINOGENICITY

Species	:	mouse
Sex	:	male/female
Strain	:	
Route of admin.	:	dermal
Exposure period	:	25 - 46 weeks
Frequency of treatm.	:	The applications were repeated at intervals of 1 to 2 days till the first appearance of macroscopic lesions, and renewed on the average twice weekly later on
Post exposure period	:	not described
Doses	:	Average concentration of 3-5% hydrochloric acid (the volume was not specified)
Result	:	
Control group	:	no
Method	:	other:
Year	:	1925
GLP	:	no data
Test substance	:	other TS: Hydrochloric acid, no data
Method	:	Fifty-two male and forty-seven female mice including 4 different strains were treated and the skin on the dorsum int the sacral region was painted without any previous epilation. The applications were repeated for about 4 to 6 weeks from the time of the first appearance of papillary growths and then discontinued. The total period of applications ranged from 25 to 46 weeks
Remark	:	This experiment was conducted on the basis of the assumption that any chemical substance able to cause irritation of the skin can lead tothe formation of cancer after prolonged and repeated applications. Crude coal tar (Ol. Lithanthracis) was used as tumor producing or carcinogenic agents.
Result	:	Hydrochloric acid treatment failed to produce malignant tumor growth.

Repeated applications resulted in production of papillomatous lesion in 15 animals (7 males and 8 females).
In 29 percent of mice treated with hydrochloric acid, the treated area assumed the appearance of chronic eczema; superficial ulceration, excoriations and formation of scabs and crusts were observed.

Reliability : (3) invalid
Main features of study reported

24.09.2004 (72)

Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : inhalation
Exposure period : Maximum, 128 weeks (for life)
Frequency of treatm. : 6 hours/day, 5 days/week
Post exposure period : No
Doses : 10.0 ppm (14.9 mg/m³)
Result :
Control group : yes
Method : other:
Year : 1985
GLP : no data
Test substance : other TS: hydrogen chloride, purity: 99,0% grade, Matheson Gas Products

Remark : Method: Three groups of 100 male rats, nine weeks old, were unexposed (colony controls), exposed by inhalation to air (air control) or exposed to 10 ppm of hydrogen chloride. Complete necropsy was performed on each animal and particular attention was given to the respiratory tract.
Comparable to the guideline study with acceptable restrictions

Result : There were no statistical differences between the mortality of the hydrogen chloride and air control groups. No preneoplastic or neoplastic nasal lesion was observed in any group, but hyperplasia ot the larynx and trachea was observed in treated animals (22/99 and 26/99, respectively).
Tumour responses were similar in the treated and control groups, the total incidences of tumours at various sites being 19/99, 25/99 and 24/99 in treated, air control and colony control animals, respectively. (No further details)

Observation		HCl	Air	Colony
No. animals examined		99	99	99
Larynx	Hyperplasia	22	2	2
	Squamous metaplasia	0	0	0
Trachea	Hyperplasia	26	6	2
	Squamous metaplasia	0	0	0
	Rhinitis	81	72	70
	Epithelial of squamous hyperplasia	62	51	45
	Squamous metaplasia	9	5	6
	Polyps or papillomas	0	0	0
Nasal mucosa	Squamous cell carcinoma	0	0	0
	Adenocarcinoma	0	0	0
	Mixed carcinoma	0	0	0
	Fibrosarcoma	0	0	0
	Esthesioneuroepithelioma	0	0	0
Total No. of tumors in organs other than the respiratory tract		19	25	24

No effects were reported in other organs examined histopathologically (lung, liver, kidney, testes, gross lesions)

Reliability : (2) valid with restrictions
Main study details reported

Flag : Critical study for SIDS endpoint

14.09.2005 (73)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	588 days (19.4 months)
Frequency of treatm.	:	6 hours/days, 4.7 days/week or two-hirds of each week
Post exposure period	:	No
Doses	:	average concentration: 10.2 ppm
Result	:	
Control group	:	yes
Method	:	other:
Year	:	1982
GLP	:	no data
Test substance	:	other TS: hydrogen chloride, purity: 99,0% grade, Matheson Gas Product

Remark : Method: 20 rats were treated (whole body) with hydrogen chloride gas or air sham-exposed as control. Complete necropsy was performed on each animal and particular attention was given to the respiratory tract.

Result : No loss of body weight
No excess mortality
No nasal cancer

Test condition : Animals: 20 rats per group
Treatment: whole body hydrogen chloride gas or air sham-exposed as control.
Duration: 6h*5d/w for lifetime
Observation: All animals were observed daily and weighed monthly
Complete necropsy was performed on each animal and particular attention was given to the respiratory tract

Reliability : (2) valid with restrictions
Publication, main features of study reported

Flag : Critical study for SIDS endpoint

16.09.2004 (74)

Species	:	mouse
Sex	:	no data
Strain	:	no data
Route of admin.	:	oral unspecified
Exposure period	:	11 months
Frequency of treatm.	:	5 to 10 times/week
Post exposure period	:	no
Doses	:	90-360 mg kg bw
Result	:	
Control group	:	no data specified
Method	:	other: not specified
Year	:	1946
GLP	:	no
Test substance	:	other TS:HCl

Remark : HCl was given to 58 mice. A known carcinogen was additionally given to another 40 mice. Probably, only the gastrointestinal tract was examined.

Result : The treatment did not apparently increase the incidence of tumours. The treatment lead to stomach damage. Probably no other tissue examined.

Reliability : (2) valid with restrictions

Short notice, few details

16.09.2004 (75) (76)

Species	:	mouse
Sex	:	male/female
Strain	:	other: A, I, C3H, hybrid LA
Route of admin.	:	other: p.o.
Exposure period	:	11 months
Frequency of treatm.	:	First 5 months of the experiment injections were made 5 days/week. Because of the great mortality among the treated mice, the number of injections was decreased to 3 days/week on alternate days.
Post exposure period	:	No
Doses	:	90-360 mg/kg bw
Result	:	negative
Control group	:	yes
Method	:	other:
Year	:	1946
GLP	:	no
Test substance	:	other TS: hydrochloric acid
Remark	:	Method: Hydrochloric acid was orally given to mice with (40 mice) or without (58 mice) 1,2,5,6-dibenzanthracene, which was administered once a week during a later period. Probably, only the gastrointestinal tract was examined
Reliability	:	(2) valid with restrictions Short notice, few details

22.07.2004 (76)

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

Type	:	other: 4 months rat inhalation
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	4 months
Frequency of treatm.	:	
Duration of test	:	
Doses	:	0 - 0,48 - 1,34 mg/m³
Control group	:	yes
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	Due to the chemical properties of OPCl3 (fast hydrolysis (t1/2 = 12 sec in water at pH 7), corrosion) it is hard to imagine a significant exposure and an effect in the gonades after inhalation exposure. An effect of the degradtation products, phosphoric acid and hydrochloric acid, exceeding the effect of low pH is also not plausible

Result	:	Treatment with phosphorus oxychloride affects the motility of spermatozoids though it does not influence spermatogenesis. This suggests that POCl3 influences biochemical processes determining the motility of spermatozoids but does not disturb the morphological structures of the spermatogenic epithelium
Reliability	:	(4) not assignable Secondary literature

16.09.2004 (53)

Type	:	other:
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	female
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	
Frequency of treatm.	:	
Duration of test	:	4 months
Doses	:	
Control group	:	yes
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	Due to the chemical properties of OPCl3 (fast hydrolysis (t1/2 = 12 sec in water at pH 7), corrosion) it is hard to imagine a significant exposure and an effect in the gonades after inhalation exposure. An effect of the degradtation products, phosphoric acid and hydrochloric acid, exceeding the effect of low pH is also not plausible
Result	:	Chronic exposure of female rats to POCl3 decreased the no. of primary follicles in the ovaries and intensified the process of atresia. Changes in the estral and ovarian cycles, caused by POCl3, were always accompanied by poisoning symptoms and were considered as secondary to general toxicity by the author
Test condition	:	Inhalation: 0 - 0.4 - 1.0 mg/m³ for 4 months 6 animals examined no further data
Reliability	:	(4) not assignable No experimental detail given, documentation limited

16.09.2004 (77)

Type	:	
In vitro/in vivo	:	In vivo
Species	:	rat
Sex	:	male
Strain	:	
Route of admin.	:	
Exposure period	:	
Frequency of treatm.	:	
Duration of test	:	
Doses	:	
Control group	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Result	:	No morphologic differences between treated and control rats The mobile period of sperm was reduced in both treated groups (255+-14

Min - high dose, 146+-28 Min - low dose 311+-16 Min control)
At the end of the recovery period the values were as follows (157+-20 Min. high dose; 235+-53 Min. - low dose; 270+-60 Min control)

Reliability : (2) valid with restrictions
No experimental detail; observations in a repeated dose inhalation study in combination with overt systemic toxicity

16.09.2004 (47)

5.9 SPECIFIC INVESTIGATIONS

Endpoint	:	other: in-life staining of lungs
Study descr. in chapter	:	
Reference	:	
Type	:	
Species	:	rat
Sex	:	
Strain	:	
Route of admin.	:	inhalation
No. of animals	:	750
Vehicle	:	
Exposure period	:	
Frequency of treatm.	:	
Doses	:	0.8 - 4 - 8 mg/m³
Control group	:	
Observation period	:	
Result	:	
Method	:	
Year	:	1973
GLP	:	
Test substance	:	other TS: OPCl3

Remark : Abstract: Changes in the respiration frequency and degree of neutral red (2 mg/kg, i.v.) accumulation in the lung tissue permitted detn. of the Limir values (min. irritating values) of phosphoryl chloride [10025-87-3] for rats. The animals were exposed to the poison-contg. air for 4 hr. An equation is presented for calculating the max. permissible concns. of the poisons in the air.

Result : Lung weight: increase after high dose 8 mg/m³
Respiratory frequency: decrease after 4 h exposure in all dose groups
Life staining of lung tissue with neutral red: Non-dose-dependent effects
Inconsistent information about extent and direction of alterations

Test condition : Rats were exposed via inhalation for 4 hours, additionally they were injected with neutral red dye via tail vein to produce an in-life-stain of the lungs. Lung weights and respiratory frequency were determined

Reliability : (2) valid with restrictions
Few experimental details reported, non standard method, reliability of method unknown, toxicologic significance of findings unclear

Flag : Critical study for SIDS endpoint

16.09.2004 (78)

Endpoint	:	Endocrine System Modulation
Study descr. in chapter	:	
Reference	:	
Type	:	
Species	:	rat
Sex	:	female
Strain	:	
Route of admin.	:	inhalation

No. of animals	:	
Vehicle	:	
Exposure period	:	
Frequency of treatm.	:	
Doses	:	0 - 0.4 - 1.0 mg/m³
Control group	:	other: yes, concurrent
Observation period	:	chronic
Result	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	other TS: OPCl3
Remark	:	No further data given
Result	:	Chronic exposure of female rats to POCl3 (0.5-1.0 mg/m3) prolonged the estral period and shortened the rest period. POCl3 decreased the no. of primary follicles in the ovaries and intensified the processes of atresia. Changes in the estral and ovarian cycles, caused by POCl3, were always accompanied by poisoning symptoms.
Test condition	:	General toxicity: examinations of liver, kidneys, mineral homeostasis, reflexes, hematology, choline esterase in plasma and erythrocytes, protein fractions, respiratory frequency, body weight, organ weights, histopathology of lungs, liver, kidney, heart, brain ovarian toxicity: determination of estrus cycle, microscopic evaluation, pituitary function was determined in juvenile female mice
Reliability	:	(4) not assignable No experimental details given

16.09.2004 (77)

Endpoint	:	Neurotoxicity
Study descr. in chapter	:	
Reference	:	
Type	:	
Species	:	mouse
Sex	:	male
Strain	:	Swiss Webster
Route of admin.	:	ip
No. of animals	:	
Vehicle	:	other: corn oil
Exposure period	:	
Frequency of treatm.	:	
Doses	:	
Control group	:	
Observation period	:	
Result	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS: OPCl3
Remark	:	Abstract: Phosphorus oxychloride (POCl(3)) is an intermediate in the synthesis of many organophosphorus insecticides and chemical warfare nerve gases that are toxic to insects and mammals by inhibition of acetylcholinesterase (AChE) activity. It was therefore surprising to observe that POCl(3), which is hydrolytically unstable, also itself gives poisoning signs in ip-treated mice and fumigant-exposed houseflies similar to those produced by the organophosphorus ester insecticides and chemical warfare agents. In mice, POCl(3) inhibits serum butyrylcholinesterase (BuChE) at a sublethal dose and muscle

but not brain AChE at a lethal dose. In houseflies, POCl(3)-induced brain AChE inhibition is correlated with poisoning and the probable cause thereof. POCl(3) in vitro is selective for AChE (IC(50) = 12-36 microM) compared with several other serine hydrolases (BuChE, carboxylesterase, elastase, alpha-chymotrypsin, and thrombin) (IC(50) = 88-2000 microM). With electric eel AChE,
methylcarbamoylation of the active site with eserine reversibly protects against subsequent irreversible inhibition by POCl(3). Most importantly, POCl(3)-induced electric eel AChE inhibition prevents postlabeling with [(3)H]diisopropyl phosphorofluoridate; i.e., both compounds phosphorylate at Ser-200 in the catalytic triad.
Pyridine-2-aldoxime methiodide does not reactivate POCl(3)-inhibited AChE, consistent with an anionic phosphoserine residue at the esteratic site. The actual phosphorylating agent is formed within seconds from POCl(3) in water, has a half-life of approximately 2 min, and is identified as phosphorodichloridic acid [HOP(O)Cl(2)] by (31)P NMR and derivatization with dimethylamine to HOP(O)(NMe(2))(2). POCl(3) on reaction with water and HOP(O)Cl(2) have the same potency for inhibition of AChE from either electric eel or housefly head as well as the same toxicity for mice. In summary, the acute toxicity of POCl(3) is attributable to hydrolytic activation to HOP(O)Cl(2) that phosphorylates AChE at the active site to form enzymatically inactive [O-phosphoserine]AChE.

Result : Serum but not brain AChE was inhibited in vivo 1 h after exposure
ED50 : 12 mg/kg
Mortality: 30-60 mg/kg

Test condition : Dose: 0-100 mg/kg ip in corn oil
Tissue samples were removed for AChE determination 1 or 24 hours after treatment or at death. blood, sceletal muscle, diaphragma, and brain were examined.
The in vivo experiments were supplemented by in vitro studies using different sources of AChE

Reliability : (4) not assignable
Irrelevant route of exposure (i.p.); only few experimental details

16.09.2004 (79) (80)

Endpoint : Neurotoxicity
Study descr. in chapter :
Reference :
Type :
Species : other: house fly
Sex :
Strain :
Route of admin. :
No. of animals :
Method :
Year :
GLP :
Test substance : other TS: OPCl3

Result : ED 50 : 6000-20 000 mg/m³
IC 50 : 6000 mg/m³ (brain)
Mortality was associated with > 90% inhibition

Test condition : adult house flies were exposed to vapors of POCl3 in a 120 ml glas chamber. The inability to walk or fly was recorded and at 15 minutes mortality was determined. Animals were frozen on dry ice, heads removed and AChE activity assayed.

Reliability : (4) not assignable
Species not relevant for mammalian toxicity determination; insufficient documentation

16.09.2004 (79) (80)

5.10 EXPOSURE EXPERIENCE

Type of experience : Direct observation, poisoning incidents

Result : OPCl3 was irritating to the eyes of a worker
Reliability : (2) valid with restrictions
Short case report, one person injured

08.01.2004 (81)

Type of experience : Human

Result : OPCl3 causes corrosion of the skin, swelling and hyperemia of the face, necrosis of conjunctivae and corena, blepharospasm, try cough, dyspnea, cyanosis, lung edema, and heart weakness
Reliability : (4) not assignable
No source of these observations given

09.01.2004 (51)

Type of experience : Human

Remark : Abstract: The characteristics of the biological action of phosphorus oxychloride (POCl3) are described. POCl3 possesses well-pronounced irritating properties. When introduced into the stomach it produces necrotic changes in the gastro-intestinal tract, and with acute exposure to inhalation--necrotic alterations of the respiratory passages. POCl3 application to the skin results in the development of a lingering ulcer, while instillation into the conjunctival sac of the experimental rabbit's eye ends with a complete loss of sight. The compound is highly toxic (Cl50=0.071 mg/l) and extremely dangerous in causing both acute (a narrow zone of acute action), and chronic poisoning (broad zone of chronic action). With an exposure to low POCl3 concentrations in chronic tests changes of integral indices were parallelled by disturbed mineral metabolism in test animals and by changes in the structure of the osseous tissue, taking the shape of osteoporosis. During chronic poisoning one could see an intensive elimination from the organism of inorganic phosphorus, calcium salts, and chlorides. (Russian)
Result : Workers in OPCl3 producing facilities suffered from coughing, rhinitis, difficulties regarding the voice, angina, lacrimation. After prolonged exposure sleeping disorders increased. The irritating effect of OPCl3 on mucous membranes appeared only after a latency period
Reliability : (4) not assignable
Summary case reports; limited documentation; no source given

27.05.2004 (47)

Type of experience : Human - Epidemiology

Result : a) after exposure to OPCl3 the respiratory performance is altered
b) the alterations intensify with duration of exposure
c) after the end of exposure complete recovery is achieved regarding peak flow (PFR), forced exspiratory volume (FEV1)

and vital capacity (CV)
d) intensity and incidence of effects are increased by repeated exposure
e) the clinical signs disappeared immediately after the end of exposure

Reliability : (2) valid with restrictions
Short report only

Flag : Critical study for SIDS endpoint

27.05.2004 (82)

Type of experience : Human

Result : Symptoms caused by OPCl3:
inhalation acute: intesive irritation of airways and conjunctivae, spastic bronchitis, broncho-pulmonia, pulmonary edema
oral acute: severe corrosion, stomach pain, vomiting, prostration, perforation of esophagus and stomach
dermal acute: severe corrosion
chronic inhalation: chronic bronchitis, dermatitis and conjunctivitis

Reliability : (2) valid with restrictions
Review, Summary

06.02.2004 (83)

Type of experience : Human

Remark : Case report; one female patient; OPCl3

Result : Acute sypmtoms after single inhalation exposure: wheezing respiration
Delayed sypmtoms after single inhalation exposure: asthmatic fits after irritation by chemicals or cold

Reliability : (2) valid with restrictions

16.01.2006 (84)

Type of experience : Human

Remark : Abstract:
Eight men and 3 women (22 to 56 years of age) accidently exposed to large amounts of a gaseous mixture of hydrogen chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride, and oxalic acid were studied both by clinical observation and laboratory analysis. The main symptoms included hoarseness, wheezing cough and shortness of breath. Fine crepitations and scattered rhonchi were heard diffusely over the lungs. Severe conjunctivitis was present in some. Laboratory tests revealed leukocytosis in four of the patients, elevated lactic dehydrogenase in three and traces of albumin in the urine of one. The arterial oxygen pressure was reduced in seven and mixing efficiency impairment suggesting disturbances in ventilation and
perfusion. Hypoxemia was found in one patient without associated symptoms or abnormal physical findings but this disappeared with time. In four patients the vital capacity was low suggesting a bronchospastic element. Followup data showed that in most cases symptoms and disturbances cleared in a short time

Reliability : (4) not assignable
Exposure to a mixture of several irritating agents

23.01.2004 (85)

Type of experience : Human - Medical Data

Remark : Abstract:
The toxicometric indices of phosphorus oxychloride, trichloride and pentachloride were determined and the peculiarities of the toxic effect of these compounds were investigated in experiment. Comparative characteristics of the irritant and resorptive effects of the substances were presented. The highest admissible concentrations (HAC) in the air of the working place were set at 0.05 mg/m sup(3), 0.2 mg/m sup(3) and 0.2 mg/m sup(3) for phosphorus oxychloride, phosphorus trichloride and phosphorus
pentachloride, respectively. Some prophylactic measures are recommended.

Result : Acute intoxication causes photophobia, lacrimation, burning in the eyes and throat, dyspnea, try cough, rhinitis, loss of voice, difficult swallowing, constriction in the chest, reddening of conjunctivae and mucous mebranes of the throat, tracheitis, bronchitis, bronchopneumonia, raised temperature. increased sensitivity of the bronchi may last for a long time.
Serious acute intoxications are observed at concentrations of 10 - 20 mg/m³. Acute exposure often results in chronic disorders of the respiratory tract.
Symptoms reported by exposed worker were: respiratory tract and eye irritation, cough, asthma, loss of voice

Reliability : (2) valid with restrictions
Limited documentation

27.05.2004 (53)

Type of experience : Human - Medical Data

Remark : Published in Italian

Result : 4 case reports;
workers age 20 - 47 showed signs of ocular and respiratory irritation after exposure to OPCl3.
Signs were: irritation of conjunctivae and pharynx (hyperemia), cough, dyspnea, retrosternal pain, neutrophilia, pleutritis.
Symptoms developed within minutes to several hours.
While two of the workers recovered within several days, the others developed lasting signs of obstructive respiratory disease.

Reliability : (2) valid with restrictions
Case report; exposure concentration and duration not defined

Flag : Critical study for SIDS endpoint

27.05.2004 (86)

Type of experience : Human

Result : POCl3 is mentioned as the cause of skin injury in 1 case in Japan (1966 - 1985)

Reliability : (4) not assignable
Secondary literature

26.01.2004 (87)

Type of experience : Human

Result : Inhalation:
sore throat, cough, burning sensation, nausea, headache, unconsiousness, vomiting, weakness, shortness of breath, symptoms may be delayed

Skin:
pain, redness, blisters, skin burns
Eyes:
pain, redness, severe deep burns, loss of vision
Ingestion:
burning sensation, abdominal pain, shock or collapse, (see inhalation)

Test substance : OPCl3
Reliability : (2) valid with restrictions
Official statement prepared in co-operation of IPCS and EU
Flag : Critical study for SIDS endpoint
16.01.2006 (88)

Type of experience : Human

Result : Symptoms reported by exposed worker were: respiratory tract and eye irritation, cough, asthma, loss of voice
Test substance : OPCl3
Reliability : (4) not assignable
Summary case report, exposure duration and concentration not defined
16.01.2006 (89)

Type of experience : Human

Result : The Limir (min. irritating) value: 1 mg/m³
The Limir (min. irritating) value of phosphoryl chloride for rats was about 2.6-fold higher than established for human subjects, when the animals were exposed to the poison-contg. air for 4 hr.
Changes in the frequency of respiration and degree of neutral red accumulation in the lung tissue were recorded
Test condition : Determination of respiratory irritation by subjective evaluation of volunteers
No details given
Test substance : OPCl3
Reliability : (4) not assignable
No details given
16.01.2006 (59)

Type of experience : Human

Result : A maintainance worker was exposed to 4mg/m³ of POCl3 for 25 minutes while wearing a gas mask. Pulmonary function tests were normal.
The authors conclude that there are intermittent exposures to POCl3 which may cause acute respiratory symptoms and they recommend air purifying, respiratory protection and the use of acid type gas masks.
Test condition : OPCl3
Reliability : (2) valid with restrictions
Detailed report available; actual exposure not known
16.01.2006 (90)

Type of experience : other: human sensitisation

Result : IgE specific for Phosphoryl chloride was determined in an occupational surveilance program for 5 years
No specific IgE against phosphoryl cloride was seen, neither in the surveilance program nor in any case of product contact
19.07.2004 (91)

5.11 ADDITIONAL REMARKS

Type : other: ADME

Result : Phosphorus oxychloride reacts with the water componoent of tissue it first contacts. The resulting acid ions, if absorbed, join the body pools of these ions. Phosphate, chloride and hydrogen are easily excreted by the kidneys by normal physiological mechanisms.

Reliability : (4) not assignable
Secondary literature

03.06.2004 (92)

Type : other: Review

Result : LC50 values (4h)
guinea pigs: 332 mg/m³
rats: 301 mg/m³
The LC 50 should be interpreted with caution because of the difficulty of measuring the concentration.
Effects: causes severe chemical burns; vapor and liquid are irritant to corrosive to eyes and respiratory tract depending on concentration. Permanent or delayed effects, other than scarring at the site of contact are unlikely. Repeated exposures to levels that are not high enough to cause severe immediate symptoms may cause progressive impairment of lung function.

Test substance : $OPCl_3$

Reliability : (4) not assignable
Secondary literature

16.01.2006 (92)

Type : other: Review

Remark : Distinction between the three compounds: PCl_3, PCl_5, and $POCl_3$ is not always possible in the report. All three are evaluated together

Result : $POCl_3$ is irrtant/corrosive to mucous membranes (eyes, respiratory tract) human as well as animal data are reviewed

Reliability : (4) not assignable
Secondary literature

03.06.2004 (93)

Type : other: Risk assessment: MAK rational

Remark : $POCl_3$ is a severely corrosive, colorless liquid of pungent odor. In contact with water, humid air or water containing liquids $POCl_3$ reacts to produce heat, phosphoric acid, and hydrochloric acid. A marked irritation to mucous membranes of eyes and respiratory tract is the most pronounced effect. The moderate solubility in water may cause a delay of the start of reaction and enable $POCl_3$ to reach the deeper parts of the respiratory tract. Additionally irritation is only weak at the beginning and sign of intoxication develop within several hours. These properties produce little warning at the start of exposure and severe, long-lasting effects can arise.
Symptom after acute exposure are: reddening of mucous membranes, inflammation of eyes, lacrimation, dry cough, dyspnea, corrosion of airways, lung edema. Additionally headache, nausea, fatigue, vomiting were reported. Long term effects: obstructive lung disease, increased sensitivity to irritants and infection.
Long term, low level exposure can produce liver and kidney changes, changes in bone structure and mutagenic effects in animals.

Direct skin contact causes all stages of irritation and corrosion depending on duration and the presence of water at the site of exposure. Similar effects occur in the digestive tract after ingestion.
Preliminary MAK- Value: 0.2 ml/m³ ~ 1 mg/m³

Reliability : (2) valid with restrictions
Secondary literature; peer reviewed literature review

15.07.2004 (29)

Type : other: dermal penetration/irritation

Result : Already after 1 minute severe hyperemia and hemorhages were observed
Test condition : The tails of mice were immersed into the undiluted fluid for 7-10 minutes
Test substance : OPCl3

16.01.2006 (47) (51)

Type : other: irritation/corrosion

Result : POCl3 is mentioned as a corrosive agent and advise on first aid is given
Reliability : (4) not assignable
No specific data given

03.06.2004 (94)

Type : other: respiratory irritation

Result : POCl3 is mentioned as a respiratory irritant that may cause tracheobronchitis, alveolitis, pulmonary edema and death (possibly via its degradation products H3PO4 and HCl).
A TLV of 0.1 ppm is given

Reliability : (4) not assignable
Secondary literature

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