# Phosphine

# General information

## Key Points

***Fire***

- Gas, extremely flammable and spontaneously flammable in air
- Reacts violently with air, oxygen, halogens and other oxidants causing fire and is an explosion hazard
- Decomposes on heating or burning, releasing toxic phosphorus oxides fumes
- In the event of a fire involving phosphine, use fine water spray and liquid-tight chemical protective clothing and breathing apparatus

***Health***

- Extremely flammable
- Very toxic by inhalation; symptoms usually occur within a few hours of exposure
- Phosphine is irritating to the mucous membranes of the nose, mouth, throat and respiratory tract
- Inhalation may result in weakness, chest tightness and pain, dry mouth, cough, sickness, vomiting, diarrhoea, chills, muscle pain, headache, dizziness, ataxia, confusion and lung damage. These symptoms may develop 2-3 days after exposure
- Severe poisoning may result in increased heart rate, low blood pressure, convulsions, coma, heart damage and death. These symptoms usually within 4 days but may be delayed up to 1-2 weeks
- Exposure to the eyes or skin may cause irritation
- Long-term exposure may cause anaemia, bronchitis, gastrointestinal disorders, speech and motor problems, toothache, weakness, weight loss, swelling and damage of the jaw bone and spontaneous fractures
- Phosphine has not been associated with cancer
- Phosphine is not likely to cause reproductive or developmental effects

***Environment***

- Dangerous for the Environment
- Inform Environment Agency of substantial release incidents

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**2007**
**Version 1**

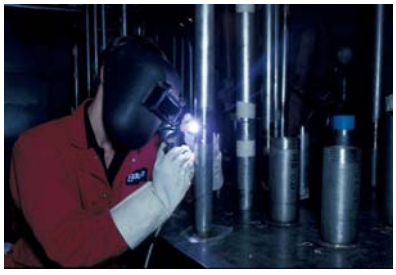
## Background

Phosphine is a colourless gas, which is slightly heavier than air. It usually smells of garlic or rotting fish due to the presence of contaminants but pure phosphine is odourless. Phosphine is extremely flammable and highly reactive with air, copper and copper-containing alloys.

Phosphine is rarely found in nature. Small amounts can be formed during the breakdown of organic matter, although it is rapidly degraded.

Phosphine is released into the air via emissions from various manufacturing processes and from the use of metal (magnesium, aluminium and zinc) phosphide fumigants and pesticides, which release phosphine on contact with water or acid.

The major uses of phosphine are as a fumigant during the storage of agricultural products such as nuts, seeds, grains, coffee and tobacco, and in the manufacture of semi-conductors. Phosphine is also used in the production of some chemicals and metal alloys and is an unintentional by-product in the illegal manufacture of the drug methamphetamine.



Phosphine is rapidly broken down in the environment and it is very unlikely that the general population will be exposed to sufficient levels of phosphine to cause health effects. However, people may be exposed to very small amounts of phosphine present in air, food and water.

Workers employed as fumigators, pest-control operators, transport workers and those involved in the production or use of phosphine and metal phosphides (welding, metallurgy, semi-conductors), may be exposed to higher levels of phosphine, although occupational incidents involving exposure to phosphine are rare, and safety levels are in place to protect employees.

Inhalation is the most likely route of exposure to phosphine, although ingestion of metal phosphides may also occur. Symptoms are non-specific and include irritation of the respiratory tract, headaches, dizziness, abdominal pain, sickness, and vomiting. Severe phosphine poisoning can cause convulsions, damage to the lungs, heart, liver and kidney, and death. Long-lasting effects of single dose exposure are unlikely, most symptoms clearing within a month.

Long-term exposure to phosphine, while unlikely to occur, can cause bronchitis, gastrointestinal, visual, speech and motor problems, toothache, swelling of the jaw, anaemia and spontaneous fractures.

Children exposed to phosphine will have the same symptoms of poisoning as adults.

Phosphine is not likely to cause harm to the unborn child as acute effects are not known to cause developmental effects.

Phosphine has not been associated with cancer and has not reviewed by the International Agency for Research on Cancer.

# Production and Uses

## Key Points

- Phosphine is present in emissions from some industrial processes such as the manufacture of some chemicals and metal alloys
- Phosphine is used as a chemical dopant, fumigant and as a rodenticide (in the form of metal phosphides) and as a catalyst and in the production of polymers

The main uses of phosphine are as a chemical dopant in the manufacture of semi-conductors for the electronics industry, and in the fumigation (in the form of metal phosphides) of stored agricultural products such as cereal grains and tobacco. Phosphine is also used as a condensation catalyst and in the manufacture of some polymers. Zinc phosphide is used as a rodenticide in the form of a pellet or as a paste mixed with food.

Small amounts of phosphine are produced in the production of chemicals such as phosphonium halide and acetylene gas.

# Frequently Asked Questions

*What is phosphine?*

Phosphine is a colourless gas which is highly flammable and explosive in air. Pure phosphine is odourless, although most commercially available grades have the odour of garlic or decaying fish. Small amounts of phosphine can occur naturally, formed during the anaerobic degradation of organic matter. Phosphine is corrosive towards metals, in particular copper and copper-containing alloys.

*What is phosphine used for?*

A major use of phosphine is as a semi-conductor doping agent by the electronics industry. Metal (aluminium, magnesium and zinc) phosphides, which release phosphine on contact with moisture and acid, are used as rodenticides and fumigates during storage of agricultural commodities such as grain e.g. cereals, and tobacco. Phosphine is also used as a catalyst and in the production of polymers.

*How does phosphine get into the environment?*

Small amounts of phosphine occur naturally during the decomposition of phosphorous-containing organic matter e.g. in marsh gas. Emissions and effluents from the manufacture of some chemicals and metal alloys, as well the production or use of phosphine and metal phosphides (welding, metallurgy, semi-conductors, rodenticides and fumigants), release phosphine into the air.

*How will I be exposed to phosphine?*

It is unlikely that the general population will be exposed to significant amounts of phosphine, since it is degraded quickly in the environment; the half-life of phosphine in the air is about one day or less. However, people may be exposed to very small amounts by inhaling air, drinking water and eating food containing phosphine. Workers involved with industries and processes where phosphine is used, e.g. fumigation and pest control, may be exposed to higher levels of phosphine. People living nearby sites where phosphine is being used may also be exposed to small amounts of phosphine in the air. Phosphine gas does not present a risk of secondary contamination, although solid phosphides may pose some risk. Absorption though the skin is not considered a significant route of exposure.

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

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

Exposure to phosphine or metal phosphides can be irritating to the respiratory tract and can cause weakness, chest pain and tightness, dry mouth, cough, sickness, vomiting, diarrhoea, chills, muscle pain, headache, dizziness, ataxia and confusion. Severe cases may lead to lung damage, convulsions, damage to the heart, liver and kidney, and death.

Long-term exposure to low levels of phosphine can cause anaemia, bronchitis, gastrointestinal problems, visual, speech and motor problems, toothache, swelling of the jaw and spontaneous fractures.

### *Can phosphine cause cancer?*

The Governmental Committee on Mutagenicity recently reviewed the available data on carcinogenicity of phosphine and concluded that it did not cause cancer in animal studies.

Phosphine has not been reviewed by the International Agency for Research on Cancer (IARC), and the US Environmental Protection Agency (US EPA) considers phosphine as not classifiable as to human carcinogenicity, due to inadequate animal studies and a lack of human tumour data.

### *Does phosphine affect children or damage the unborn child?*

Children who ingest metal phosphides or inhale phosphine gas are expected to have similar symptoms as adults, e.g. sickness, vomiting, headache, dizziness, in severe cases leading to damage to the lungs, heart, liver and kidney and death.

There is no evidence to suggest that maternal exposure to phosphine affects the health of the unborn child.

### *What should I do if I am exposed to phosphine?*

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

This document from the HPA Centre for Radiation, Chemical and Environmental Hazards reflects understanding and evaluation of the current scientific evidence as presented and referenced in this document.

# Phosphine

# Incident management

## Key Points

### *Fire*

- Gas, extremely flammable and spontaneously flammable in air
- Reacts violently with air, oxygen, halogens and other oxidants causing fire and explosion hazard
- Decomposes on heating or burning, releasing toxic phosphorus oxides fumes
- In the event of a fire involving phosphine, use fine water spray and liquid-tight chemical protective clothing and breathing apparatus

### *Health*

- Very highly toxic by inhalation
- Symptoms usually occur within a few hours of exposure
- Irritating to the mucous membranes of the nose, mouth, throat and respiratory tract
- Inhalation may also cause weakness, chest pain and tightness, breathlessness, dry mouth, cough, headache, fever, tremor, palpitations, sinus tachycardia/bradycardia, hypotension, dizziness and ataxia
- Severe nausea, vomiting and diarrhoea can also occur
- Ocular exposure may result in irritation, diplopia, blurred vision and xanthopsia
- Dermal contact may cause sweating, irritation, and paraesthesiae.

### *Environment*

- Dangerous for the environment
- Inform the Environment Agency of substantial release incidents

**CRCE HQ, HPA**
**03/2012**
**Version 2**

# Hazard Identification

## *Standard (UK) Dangerous Goods Emergency Action Codes*[a]

| | | | | |
|---|---|---|---|---|
| **UN** | | **2199** | Phosphine | |
| **EAC** | | **2PE**[1] | Use fine water spray. Wear liquid-tight chemical protective suit in combination with breathing apparatus*. Danger that the substance can be violently or explosively reactive. Spillages and decontamination run-off may be washed to drain with large quantities of water. There may be a public safety hazard outside the immediate area of the incident**. | |
| **APP** | | **A(cf)** | Gas-tight chemical protective suit with breathing apparatus*** Liquefied flammable gas with a boiling point below -20°C. | |
| **Hazards** | **Class** | **2.3** | Toxic gas |   |
| | **Sub risks** | **2.1** | Flammable gas |   |
| **HIN** | | **-** | | |

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

[1] Not applicable to the carriage of dangerous goods under Regulations Concerning the International Carriage of Dangerous Goods by Rail (RID) and in the European Agreement Concerning the International Carriage Dangerous Goods by Road (ADR)

* Liquid-tight chemical protective clothing (BS 8428) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).
** People should stay indoors with windows and doors closed, ignition sources should be eliminated and ventilation stopped. Non-essential personnel should move at least 250 m away from the incident.
***Gas-tight chemical protective clothing (BS EN 943 part 2) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).

[a] Dangerous Goods Emergency Action Code List 2011. National Chemical Emergency Centre (NCEC). The Stationary Office, London.

## *Chemical Hazard Information and Packaging for Supply Classification*[a]

| | | | |
|---|---|---|---|
| **Classification** | **F+** | Extremely flammable |  |
| | **T+** | Very toxic |  |
| | **C** | Corrosive |  |
| | **N** | Dangerous for the environment |  |
| **Risk phrases** | **R12** | Extremely flammable | |
| | **R17** | Spontaneously flammable in air | |
| | **R26** | Very toxic by inhalation | |
| | **R34** | Causes burns | |
| | **R50** | Very toxic to aquatic organisms | |
| **Safety phrases** | **S1/2** | Keep locked up and out of reach of children | |
| | **S28** | After contact with skin, wash immediately with plenty of....(to be specified by the manufacturer) | |
| | **S36/37** | Wear suitable protective clothing and gloves | |
| | **S45** | In case of accident or if you feel unwell seek medical advice immediately (show the label where possible) | |
| | **S61** | Avoid release to the environment. Refer to special instructions/safety data sheet | |
| | **S63** | In case of accident by inhalation: remove casualty to fresh air and keep at rest | |

[a] Annex VI to Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures- Table 3.2.
http://esis.jrc.ec.europa.eu/index.php?PGM=cla (accessed 03/2012)

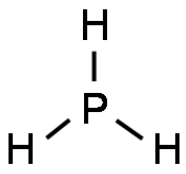
## *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*[a]

| | | | |
|---|---|---|---|
| **Hazard Class and Category** | Flam. Gas 1 | Flammable gas, category 1 |  |
| | Press. Gas | Gas under pressure |  |
| | Acute Tox. 2 | Acute toxicity (inhalation), category 2 |  |
| | Skin Corr. 1B | Skin corrosion, category 1B |  |
| | Aquatic Acute 1 | Acute hazard to the aquatic environment, category 1 |  |
| **Hazard Statement** | **H220** | Extremely flammable gas | |
| | **H330** | Fatal if inhaled | |
| | **H314** | Causes severe skin burns and eye damage | |
| | **H400** | Very toxic to aquatic life | |
| **Signal Words** | DANGER | | |

Implemented in the EU on 20 January 2009.

[a] Annex VI to Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures- Table 3.1.
http://esis.jrc.ec.europa.eu/index.php?PGM=cla (accessed 03/2012)

## Physicochemical Properties

| | |
|---|---|
| **CAS number** | 7803-51-2 |
| **Molecular weight** | 34 |
| **Empirical formula** | $PH_3$ |
| **Common synonyms** | - |
| **State at room temperature** | Gas |
| **Volatility** | Vapour pressure 4186 kPa at 20°C |
| **Specific gravity** | 1.17 (air = 1) |
| **Flammability** | Extremely flammable. Spontaneously flammable in air due to presence of phosphorus hydrides in most commercial preparations. Gives off irritating or toxic fumes (or gases) in a fire. |
| **Lower explosive limit** | 1.8 % |
| **Upper explosive limit** | Data not available |
| **Water solubility** | 26 ml per 100 ml at 20°C |
| **Reactivity** | Reacts violently with air, oxygen, oxidants such as chlorine and nitrogen oxides, metal nitrates and halogens causing fire and explosion hazard. Attacks many metals |
| **Reaction or degradation products** | Decomposes on heating or burning producing toxic fumes including phosphorus oxides. Liberates hydrogen when passed over heated metal. Forms phosphonium salts when bought into contact with halogen acids |
| **Odour** | Pure phosphine is odourless. Commercial grade phosphine has the odour of garlic or decaying fish |
| **Structure** |  |

References[a,b]

[a] The Merck Index (14th Edition). Entry 7338: Phosphine, 2006.
[b] International Programme on Chemical Safety: International Chemical Safety Card entry for phosphine (0694), 2005.

## Threshold Toxicity Values

| EXPOSURE VIA INHALATION | | | |
|---|---|---|---|
| **ppm** | **mg $m^{-3}$** | **SIGNS AND SYMPTOMS** | **REFERENCES** |
| 7 | 10 | No serious effects after 30 – 60 minutes | a |
| 100 – 190 | 140 – 260 | Serious effects after 30 – 60 minutes | a |
| 290 – 430 | 400 – 600 | Dangerous to life after 30 – 60 minutes | a |
| 400 – 600 | 560 – 840 | Death after 30 – 60 minutes | a |
| 2000 | 2800 | Short exposure rapidly fatal | a |

[a] International Programme on Chemical Safety (IPCS) (1988). Environmental Health Criteria 73, Phosphine and selected metal phosphides. World Health Organisation. Geneva

# Published Emergency Response Guidelines

## *Emergency Response Planning Guideline (ERPG) Values*[(a)]

| | Listed value (ppm) | Calculated value (mg $m^{-3}$) |
|---|---|---|
| **ERPG-1*** | NA† | NA† |
| **ERPG-2**** | 0.5 | 0.7 |
| **ERPG-3***** | 5 | 7 |

NA† = Not appropriate
* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odour.
** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.
*** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects.

## *Acute Exposure Guideline Levels (AEGLs)*[(b)]

| | ppm | | | | |
|---|---|---|---|---|---|
| | **10 min** | **30 min** | **60 min** | **4 hr** | **8 hr** |
| **AEGL-1**† | NR | NR | NR | NR | NR |
| **AEGL-2**†† | 4.0 | 4.0 | 2.0 | 0.5 | 0.25 |
| **AEGL-3**††† | 7.2 | 7.2 | 3.6 | 0.9 | 0.45 |

NR = Not recommended due to insufficient data
† The level of the chemical in air at or above which the general population could experience notable discomfort.
†† The level of the chemical in air at or above which there may be irreversible or other serious long-lasting effects or impaired ability to escape.
††† The level of the chemical in air at or above which the general population could experience life-threatening health effects or death.

[a] American Industrial Hygiene Association (AIHA). 2011 Emergency Response Planning Guideline Values. http://www.aiha.org/insideaiha/GuidelineDevelopment/ERPG/Documents/2011erpgweelhandbook_table-only.pdf (accessed 03/2012).
[b] U.S. Environmental Protection Agency. Acute Exposure Guideline Levels, http://www.epa.gov/oppt/aegl/pubs/chemlist.htm (accessed 03/2012).

# Exposure Standards, Guidelines or Regulations

## *Occupational standards*

| | |
|---|---|
| **WEL**[(a)]<br>http://www.hse.gov.uk/ | LTEL (8 hour reference period): 0.1 ppm (0.14 mg $m^{-3}$) |
| | STEL (15 min reference period): 0.2 ppm (0.28 mg $m^{-3}$) |

## *Public health guidelines*

| | |
|---|---|
| **DRINKING WATER QUALITY GUIDELINE** | No guideline value specified |
| **AIR QUALITY GUIDELINE** | No guideline value specified |
| **SOIL GUIDELINE VALUE AND HEALTH CRITERIA VALUES** | No guideline value specified |

WEL – Workplace exposure limit; LTEL - Long-term exposure limit; STEL – Short-term exposure limit

[a] EH40/2005 Workplace Exposure Limits (second edition, published 2011). http://www.hse.gov.uk/pubns/priced/eh40.pdf (accessed 01/2012)

# Health Effects

## *Major route of exposure*[(a)]

- Very highly toxic by inhalation.

## *Immediate signs or symptoms of acute exposure*[(b)]

- Inhalation can cause irritation of the mucous membranes of the nose, mouth throat and respiratory tract.
- Nausea, vomiting and diarrhoea may be so striking that poisoning from phosphine may be confused with acute gastroenteritis.
- Weakness, chest pain and tightness, breathlessness, dry mouth, cough, headache, fever, tremor, palpitations, sinus tachycardia/bradycardia, hypotension, dizziness and ataxia have been observed.
- Electrolyte abnormalities may occur but are thought to be secondary to vomiting. Methaemoglobinaemia has also been reported as a rare complication.
- Dermal exposure may result in sweating, irritation, and paraesthesiae.
- Ocular exposure can cause irritation, diplopia, blurred vision and xanthopsia.

TOXBASE - http://www.toxbase.org (accessed 03/2012)
[a] TOXBASE: Phosphine – 2012
[b] TOXBASE: Phosphine – features and management, 2012.

# Decontamination and First Aid

## *Important Notes*

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

## *Dermal exposure*[(a)]

- Remove patient from exposure.
- Contaminated clothing should be removed, double-bagged, sealed and stored safely.
- Decontaminate open wounds first and avoid contamination of unexposed skin.
- Any particulate matter adherent to skin should be removed and the patient washed with soap and water under low pressure for at least 10 - 15 minutes.
- Pay particular attention to mucous membranes, moist areas such as skin folds, fingernails and ears.
- Following decontamination, apply a soothing cream if there is any residual skin irritation.

## *Ocular exposure*[(a)]

- If symptomatic, immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10-15 minutes.
- If symptoms persist check for corneal damage by instillation of fluorescein and refer for ophthalmological assessment if necessary.
- Other measures as indicated by the patient's clinical condition.

## *Inhalation*[(a)]

- Remove patient from exposure.
- Ensure a clear airway and adequate ventilation.
- Give oxygen to symptomatic patients.
- Monitor pulse, blood pressure and cardiac rhythm. In the presence of methaemoglobinaemia pulse oximetry is unreliable.
- Perform a 12 lead ECG and measure the QRS duration and QT interval.
- Symptomatic patients should be admitted to hospital. Asymptomatic patients do not necessarily require hospitalisation but should be observed for 12 hours and advised to seek medical help immediately should symptoms develop.
- Other measures as indicated by the patient's clinical condition.

## *Ingestion*

- Not applicable

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TOXBASE - http://www.toxbase.org (accessed 03/2012)
[a] TOXBASE: Phosphine – features and management, 2012.

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# Phosphine

# Toxicological overview

## Key Points

### *Kinetics and metabolism*

- Inhaled phosphine is absorbed rapidly from the lungs and distributed round the body
- Inhaled or ingested zinc, aluminium and magnesium phosphides release phosphine into the respiratory tract and stomach; zinc phosphide can be absorbed intact from the gut
- Dermal absorption of phosphine or phosphides is not considered a significant route of exposure
- The majority of absorbed phosphine is excreted in exhaled air; minor amounts are metabolised and excreted in urine as hypophosphite and phosphate

### *Health effects of acute exposure*

- Phosphine is acutely toxic; exposure to high levels cause immediate effects
- Early symptoms of acute phosphine or phosphide exposure are non-specific and include respiratory problems, cough, headaches, dizziness, numbness, general fatigue and gastrointestinal disturbance (pain, nausea, vomiting and diarrhoea)
- Effects of exposure to higher levels of phosphine, the onset of which may be delayed by several days or more, include pulmonary oedema, convulsions, damage to the kidney, liver and heart, and death

### *Health effects of chronic exposure*

- Symptoms of chronic exposure include: anaemia, bronchitis, gastrointestinal disorders, speech and motor disturbances, toothache, weakness, weight loss, swelling of the jaw, mandibular necrosis and spontaneous fractures
- Phosphine is genotoxic *in vitro* but is not considered to be mutagenic *in vivo* and has not been associated with cancer
- Phosphine is unlikely to cause reproductive or developmental effects
- Repeated exposure may lead to cumulative effects

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**2007**
**Version 1**

# Toxicological Overview

## *Summary of Health Effects*

Phosphine is rapidly absorbed and distributed throughout the body and is acutely toxic. The onset of symptoms is rapid following phosphine inhalation or the ingestion/inhalation of metal phosphides, which release phosphine on contact with moisture or stomach acid. Dermal absorption of phosphine or phosphides is not considered a significant route of exposure.

Exposure to low doses of phosphine causes non-specific symptoms such as headache, dizziness, numbness, general fatigue, breathing difficulties (tightness around the chest, pain in the region of the diaphragm and cough) and gastrointestinal disturbance (pain, nausea, vomiting and diarrhoea). At higher doses, subjects may experience lung irritation, persistent coughing, tremors and convulsions, leading to pulmonary oedema, myocardial injury, kidney damage and coma, and sometimes death due to cardiovascular failure, usually within the first a few hours or after a delay of up to two weeks in the case of liver failure.

Chronic exposure to phosphine is unlikely to occur in the general population but may occur in an occupational setting. Symptoms of chronic exposure may include anaemia, bronchitis, gastrointestinal disorders, speech and motor disturbances, weakness, weight loss, toothache, swelling of the jaw, mandibular necrosis, and spontaneous fractures. Some chronic effects can be confused with symptoms of acute poisoning.

Several studies indicate that phosphine is genotoxic *in vitro*, however the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM) considered that since the available data on *in-vivo* mutagenicity and carcinogenicity was negative and given the very low potential exposure, this provided sufficient reassurance regarding its *in-vivo* mutagenic potential. Phosphine can be assumed to have no *in-vivo* mutagenicity. Phosphine has not been reviewed by the International Agency for Research on Cancer (IARC).

The limited data available indicate that phosphine is unlikely to cause reproductive or developmental effects, since no gross teratogenic effects have been recorded. However, a study on mice reported an increase in the number of foetal resorptions following exposure to low concentrations of phosphine, suggesting possible foetal toxicity.

Children exposed to phosphine will have the same symptoms of toxicity as adults.

## *Kinetics and metabolism*

Although there are no formal experimental animal or human studies on the absorption, distribution and elimination of phosphine, inhaled phosphine is generally considered to be rapidly absorbed [1, 2]. Inhalation of aluminium, magnesium and zinc phosphides may result in the internal release of phosphine, and subsequent inhalation, following contact of the phosphides with the moist surfaces of the respiratory tract or, in the case of ingested zinc phosphide, gastric acid [1, 3, 4]. Inhaled zinc phosphide particles may also be absorbed and hydrolysed in surrounding tissues and may be transferred to the intestinal tract by particulate clearance mechanisms, where hydrolysis by gastric acids would release phosphine [1].

Detection of acid-hydrolysable phosphides in rat and human liver indicates that ingested zinc and aluminium phosphides can be absorbed intact from the gut [1]. Absorption of phosphine or metal phosphides through the skin is not considered a significant exposure pathway [1].

Following acute phosphine or phosphide exposure, phosphine is rapidly absorbed and distributed throughout the body leading to possible effects on the respiratory, circulatory and nervous system, liver, kidney and gastrointestinal tract [4].

The majority of absorbed phosphine is excreted in exhaled air [1]. Minor amounts are slowly and incompletely oxidised and excreted in the urine as hypophosphite and phosphate [1].

## *Sources and route of exposure*

It is likely that the general population will be exposed to only low levels of phosphine in air, drinking water and food [3]. Phosphine and the metal phosphides have only been detected in the general environment in relation to recent localised use of metal phosphides in industrial pest control and fumigation, such as during storage of agricultural grains (cereals) and tobacco, and certain industrial activities [5]. Most reported measurements of phosphine/phosphide residues in fumigated foodstuffs are below the World Health Organisation (WHO) recommended level of 0.1 mg phosphine $kg^{-1}$ for raw cereals or 0.01 mg phosphine $kg^{-1}$ for other stored products [5].

Phosphine rarely occurs naturally although it can be formed during the breakdown of phosphorus-containing organic matter, e.g. in marsh gas, but is rapidly degraded in the environment [1, 5].

Workers involved in the production of phosphine or metal phosphides are likely to be exposed to higher levels of phosphine than the general public. The main route of occupational exposure is direct inhalation of phosphine gas or metal phosphide dust, or inhalation of phosphine released from metal phosphide dust on clothes, skin or hair in the presence of water or moisture [4]. Phosphine gas does not present a risk of secondary contamination, although solid phosphides may pose some risk. Absorption though the skin is not considered a significant route [1].

Accidental inhalation of phosphine or accidental/intentional ingestion of metal phosphides may also occur. The majority of cases of acute poisoning from metal phosphides are attempted suicides [1].

Children exposed to phosphine will have the same symptoms of toxicity as adults but may be at a greater risk of phosphine poisoning due to a higher lung surface area to body weight

ratio, an increased ventilation rate and shorter stature (phosphine gas is slightly heavier than air) [4].

In the UK, the current occupational short-term exposure limit (STEL; 15-minute reference period) is 0.42 mg $m^{-3}$ (0.3 ppm; 1 mg $m^{-3}$ = 0.72 ppm) [6]. The Health and Safety Executive (HSE) has proposed an 8 hour time weighted exposure (TWA) limit of 0.14 mg $m^{-3}$ (0.1 ppm), and a reduced STEL of 0.28 mg $m^{-3}$ (0.2 ppm), in line with the European Commission occupational exposure limit. These values are awaiting formal approval by the Health and Safety Commission [7].

There are no biological indicators for exposure to phosphine [8].

# Health Effects of Acute / Single Exposure

## *Human Data*

### General toxicity

Inhalation is the most common route of phosphine exposure and intoxication. Accidental or intentional (suicidal) ingestion of metal phosphides also occurs resulting in the release of phosphine on contact with moisture or gastric acid [1, 4]. Dermal absorption is not considered a significant route of exposure.

Phosphine gas is highly toxic and has a very steep concentration-response curve [9]. Symptoms usually occur within the first few hours of exposure [1, 2] and most phosphine-related deaths occur within 12-24 hours of exposure, usually as a result of cardiovascular damage resulting in collapse, cardiac arrest and heart failure [4]. Deaths after 24 hours are usually as a result of liver or renal failure [4].

Acute exposure to phosphine affects the respiratory, nervous and gastrointestinal systems, heart, liver and kidneys [9]. In *in-vitro* studies, phosphine has been found to react with haemoglobin in the presence of oxygen, and in isolated mitochondria, phosphine inhibits cytochrome c oxidase and mitochondrial oxygen uptake; however, these findings have not been confirmed in *in-vivo* studies [10].

### Inhalation

Initial symptoms of phosphine inhalation are non-specific and may include headaches, dizziness, numbness, general fatigue, breathing difficulties (tightness around the chest, pain in the region of the diaphragm and cough), and gastrointestinal disturbance (pain, nausea, vomiting and diarrhoea). In cases of severe poisoning, patients may experience lung irritation, persistent coughing, tremors and convulsions, leading to pulmonary oedema, myocardial injury, liver and kidney damage, cardiovascular collapse, coma and death [1, 2, 4].

Exposure to 7-14 mg $m^{-3}$ (5-10 ppm) of phosphine for several hours may cause serious effects [2]. The severity of the toxic effects of phosphine in humans, following inhalation of various concentrations of phosphine, are given in table 1.

Several cases of acute phosphine poisoning have been documented following accidental or occupational exposure. A review of 26 deaths resulting from phosphine poisoning reported the most common post-mortem finding as congestion of the lung with pulmonary oedema [1]. In a fatal incident, concentrations of phosphine were estimated as 1.2 mg $m^{-3}$ (0.9 ppm) inside a house sharing a wall with a granary that was being fumigated. Symptoms were initially non-specific with subsequent effects noted at autopsy comprising congestion of all organs, pulmonary oedema with focal emphysema, and liver vacuolation [1]. Metal workers at a large shipyard in Norway were reported to experience nausea, dizziness, chest tightness, dyspepsia and disturbances of smell and taste when concentrations of phosphine were 1.4 mg $m^{-3}$ (1 ppm) in the worker's breathing zone [1]. Installation of ventilation systems reduced phosphine to undetectable levels and relieved symptoms.

***Table 1. Time taken for symptoms or death to occur following inhalation of phosphine in humans [2, 5]***

| Dose | | Severity of Effects |
|---|---|---|
| **ppm** | **mg $m^{-3}$** | |
| 7 | 10 | No serious effects after 30-60 min |
| 100-190 | 140-260 | Serious effects after 30-60 min |
| 290-430 | 400-600 | Dangerous to life after 30-60 min |
| 400-600 | 560-840 | Death after 30-60 min |
| 2000 | 2800 | Death after 30-60 min |

Pure phosphine is odourless, although the presence of impurities in most commercial preparations of phosphine results in an odour of garlic or decaying fish. The odour threshold for phosphine is 0.14-0.28 mg $m^{-3}$ (0.1-0.2 ppm) [1]. However, odour is not a reliable indicator of phosphine levels [4] since impurities may be absorbed by stored products during fumigation, resulting in a loss of odour, even at toxic levels of phosphine [1].

### Ingestion

Metal phosphide ingestion causes non-specific symptoms within a few hours, similar to those observed following acute phosphine inhalation [1, 4]. These include effects on the respiratory and nervous system, heart, kidney and liver. In severe poisoning, gastrointestinal haemorrhage, jaundice, cardiac arrhythmias, pulmonary oedema, liver and kidney damage, convulsions, coma and death may occur [1, 2].

The majority of documented cases of metal phosphide ingestion relate to attempted suicides, which are common in countries without restrictions on these compounds [1, 4]. The lethal dose of ingested zinc phosphide varies. Most reported fatalities have occurred following ingestion of >20 g zinc phosphide, although some deaths have been reported at doses as low as 4.5 g. Recovery generally occurs at doses below 20 g [5] although this may occur at doses above 50 g [1].

### Dermal / ocular exposure

Adverse effects have not been reported following dermal exposure to phosphine gas, although skin contact with compressed, liquefied phosphine may cause frostbite [4]. Exposure to metal phosphides via broken skin can cause systemic toxicity similar to that resulting from inhalation [4].

There are no data on the effects of phosphine gas or metal phosphides on the eyes, although significant effects are not expected [1, 4].

### Delayed effects following an acute exposure

Long-term effects following acute exposure to phosphine are unusual, with most non-specific symptoms occurring within several hours of exposure and in the majority of cases clearing within 30 days of exposure [11]. However, the onset of pulmonary oedema and liver damage,

resulting in jaundice, enlarged liver, elevated serum transaminases and increased blood bilirubin, may be delayed by 48-72 hours or more [4]. Most patients that survive acute phosphine poisoning do not suffer any permanent damage, although brain and heart injury due to reduced blood supply to these organs has been reported [4]. Subacute poisoning resulting from exposure to phosphine for several days, may lead to reactive airways dysfunction syndrome [4].

## *Animal and In-Vitro Data*

### Inhalation

Rats exposed to 80 mg $m^{-3}$ (58 ppm) or 800 mg $m^{-3}$ (575 ppm) of phosphine exhibited initial signs of respiratory irritation followed by death after 4 and 1 hours, respectively, due to pulmonary oedema; bronchiolitis and atelectasis were noted in the lungs, and all organs were hyperaemic. Fatty infiltration of the liver and cloudy swelling of kidney tubular cells were also reported [1]. In another acute inhalation study on male and female rats exposed to 28 - 56 mg $m^{-3}$ (20-40 ppm) phosphine (1% in nitrogen) for 4 hours, no evidence of phosphine-related neuropathological changes was noted, although the acute Lowest Observed Effect Level (LOEL) of 28 mg $m^{-3}$ (20 ppm) was based on a decrease in body temperature and motor activity in both sexes. It is not known whether other endpoints were studied. Since no systemic toxicity was reported, the No Observed Effect Level (NOEL) for systemic toxicity was 56 mg $m^{-3}$ (40 ppm) [12]. Inhalation exposure of rabbits to 140 or 700 mg $m^{-3}$ (100 or 500 ppm) of phosphine caused death in 2.5-3 hours and 25-30 minutes, respectively [5].

Median lethal concentrations ($LC_{50}$) values are given in table 2.

***Table 2. Acute inhalation toxicity of phosphine in rats [1, 12, 13].***

| Test animal | Exposure duration | $LC_{50}$ (mg $m^{-3}$) |
|---|---|---|
| Rat | 35-50 min | 1470 |
| Rat | 65-75 min | 680 |
| Rat | 4 h | 15 |
| Rat (F) | 4 h | 55 |

An inhalation $LC_{50}$ of 19.6 mg $L^{-1}$ in rats for 10% zinc phosphide powder was reported by the US National Pest Control Association, although it was not clearly stated whether the value was for pure zinc phosphide or 10% dilution, and no indication of exposure duration was given [5].

### Ingestion

In a study on the Kit fox, an oral $LD_{50}$ of 93 mg kg $bw^{-1}$ was noted for zinc phosphide, while in a study on wild Norway rats given 20-80 mg kg $bw^{-1}$ orally, an $LD_{50}$ of 40.5 ± 2.9 mg kg $bw^{-1}$ was recorded [1, 5]. The purity of the zinc phosphide compounds used in these studies was not given. A study on rats reported an oral $LD_{50}$ of 27 mg kg $bw^{-1}$ for 94% pure zinc phosphide [5].

**Dermal / ocular exposure**

An acute dermal $LD_{50}$ of 2000-5000 mg kg $bw^{-1}$ for zinc phosphide (94% purity) in rabbits was reported by the US National Pest Control Association [1].

No data are available on the effects of phosphine on the eyes.

# Health Effects of Chronic / Repeated Exposure

## *Human Data*

### General Toxicity

Published data on the effects of long-term exposure to phosphine and metal phosphides are limited and are generally confined to case studies following occupational exposure.

The chronic effects of phosphine exposure can be complicated by acute poisoning but are generally distinct and may include anaemia, bronchitis, gastrointestinal disorders, speech and motor disturbances, toothache, swelling of the jaw, mandibular necrosis, weakness, weight loss and spontaneous fractures [1].

Repeated exposure to low levels of phosphine 0.11-0.42 mg $m^{-3}$ (0.08-0.3 ppm) has been associated with mild headaches [11].

### Inhalation

No long-term studies have been reported on the effects of chronic phosphine inhalation. A review of 59 poisonings suggests that the minimum lethal concentration of phosphine in air is 7-14 mg $m^{-3}$, 2-4 h $day^{-1}$ for several days [13].

### Ingestion

No data available.

### Genotoxicity

In 1997 the COM expressed the opinion in relation to the use of phosphine in grain fumigation and rodenticides, that there was limited evidence to suggest that phosphine was an *in-vivo* mutagen. This was based on cytogenetic studies on a small group of pesticide applicators in Minnesota USA. However following a review of additional information, in 2002 the Committee noted that while it should be assumed that phosphine is genotoxic *in vitro*, the available data on *in-vivo* mutagenicity and carcinogenicity was negative and, together with the very low potential exposure arising from pesticide use, this provided sufficient reassurance regarding its *in-vivo* mutagenic potential [14].

In a follow-up study on the same population of pesticide applicators in Minnesota, no significant difference in genotoxic endpoints was noted, and the authors suggested that the use of personal protective equipment against phosphine exposure (not worn when the first study was carried out) or changes in work practices may have been responsible for the lack of observed effects [15].

### Carcinogenicity

Phosphine has not been reviewed by IARC, and the EPA considers phosphine as not classifiable as to human carcinogenicity, due to inadequate animal studies and a lack of human cancer data [10].

### Reproductive and developmental toxicity

No data available.

## *Animal and In-Vitro Data*

### Inhalation

Repeated exposure to phosphine causes death, with fatalities reported in several rat studies following repeated exposure to above ~ 7 mg $m^{-3}$ (5 ppm) [9, 16]. For example, in one study on rats exposed to 14 mg $m^{-3}$ (10 ppm) for 6 h $day^{-1}$, four of the ten females, but no males, died on the third day, the remaining animals were sacrificed on this day. Minor decreases in body weight gain (~7% for males and 4% for females) and renal tubular necrosis were reported, and congested lungs were noted in the four females that died [10]. During the same study, rats were exposed to 0.42, 1.4 or 4.2 mg $m^{-3}$ (0.3, 1 or 3 ppm) phosphine for 6 h $day^{-1}$, 5 days $week^{-1}$ for 13 weeks. No deaths were reported, although a significant decrease in haemoglobin, haemocrit and erthyrocytes in males exposed to 4.2 mg $m^{-3}$ (3 ppm) was reported at the end of the 13 week study period [9].

Repeat inhalation studies on rabbits and guinea pigs exposed to various concentrations of phosphine found that exposure to 28 mg $m^{-3}$ (20 ppm) phosphine for 4 h per day, was fatal for rabbits and guinea pigs, during or after the second exposure [5]. Rabbits exposed to 14 mg $m^{-3}$ (10 ppm) survived 7 -14 successive exposures and showed no signs of intoxication until 30 min prior to death, when animals became stuporous and showed signs of diminished reactivity and shallow respiration. Animals died during coma, and pulmonary oedema was noted at necropsy [5]. Rabbits exposed for 5 days to 7 mg $m^{-3}$ (5 ppm) for 4 h, died when exposed to 20 mg $m^{-3}$ (14 ppm) on the sixth day. The authors concluded that pre-treatment of animals to sub-lethal concentrations of phosphine reduces resistance to near-lethal concentrations [5]. In another study, rats were exposed to 681 mg $m^{-3}$ (490 ppm) phosphine for 10-20 min per day for 6 days, died on the seventh day when exposed for 22 -35 min [5]. The concentration x time product for lethality after exposure for 6 days was approximately 20 mg min $L^{-1}$, and was one third of that of the first exposure (48-87 mg min $L^{-1}$). It was suggested that the effects of exposure were cumulative [5].

A study on cats, guinea pigs and rats exposed to 1.4 and 3.5 mg $m^{-3}$ (1 and 2.5 ppm) phosphine for more than 800 hours found no evidence of haemolysis of red blood cells or the formation of methemoglobin, and no signs of cumulative poisoning [13, 16].

A sub-chronic repeat dose study on rats found that exposure for 13 weeks, did not adversely affect behaviour or result in any clinical symptoms or histopathological changes in the nervous system. Changes in serum chloride concentrations were observed at the two highest doses, but the biological significance of this was considered minimal [17].

In a chronic study conducted at exposures of 0.42, 1.4 or 4.2 mg $m^{-3}$ (0.3, 1 or 3 ppm) phosphine for 6 h $day^{-1}$, 5 days $week^{-1}$, in which rats were treated for 52 weeks or 2 years, no clinical effects and no adverse affects on body weight, food consumption, urinalysis, haematology and organ morphology were noted that related to phosphine exposure [17].

### Ingestion

Data from two studies are reported here, although experimental data on chronic exposure to phosphine is generally lacking.

A rat study in which animals were fed 0, 50, 100, 200 or 500 mg $kg^{-1}$ zinc phosphide in the diet for 13 weeks reported reductions in both food intake and weight increase and dose-dependent depilation at all doses. At the two highest doses, 1/12 and 10/12 animals died, and the relative weights of liver, heart, brain and thyroid were increased. At 500 mg $kg^{-1}$ increased serum zinc and phosphatase levels were noted, and a dose-dependent reduction of haemoglobin, red blood cells and haematocrit was reported [5].

An oral study, in which rats were fed an unknown quantity of phosphine via aluminium phosphide-fumigated feed over a 2 year period, did not display any treatment-related differences in blood-glucose or urine chemistry in comparison to controls [12]. However, the study was considered of limited usefulness since toxic levels of phosphine were not achieved [10].

### Genotoxicity

Phosphine has been found to be consistently negative in the Ames test with *S. typhimurium* sp. TA98, TA100, TA1535, TA1537 and *E. coli* sp. WP2UVRA, at concentrations of 0.02 - 0.5% phosphine (in helium), with and without metabolic activation [14, 18]. However, *in-vitro* studies on mammalian cells suggest that phosphine may be mutagenic. For example, human lymphocyte cells exposed to phosphine exhibited dose-related chromosomal damage (deletions, gaps and strand breaks) similar to the genotoxic effects observed in some phosphine-exposed human pesticide workers [10]. Furthermore, Chinese hamster ovary cells exposed to 2500 or 5000 ppm phosphine without S9 activation, showed increased rates of chromosomal aberration [12].

Based on the available *in-vivo* data on rodents (overall negative results in bone marrow assays for clastogenicity and negative results in a liver UDS assay in rats and a dominant lethal assay in mice), the COM concluded that there was no convincing evidence that phosphine and metal phosphides are mutagenic *in vivo*, and concluded that there was 'sufficient reassurance regarding the *in-vivo* mutagenicity of phosphine'. The Committee suggested, based on other published data that the positive results observed *in-vitro* may be due to the formation of reactive oxides, rather than direct interaction of phosphine with DNA [14].

### Carcinogenicity

Rats exposed to 0.42, 1.4 or 4.2 mg $m^{-3}$ (0.3, 1 or 3 ppm) phosphine for 6 h $day^{-1}$, 5 days $week^{-1}$, for 52 weeks or 2 years did not exhibit any treatment-related increase in the incidence of any cancer [19]. Another study, in which rats were fed an aluminium phosphide-fumigated diet found that tumour incidences were similar between control and experimental

animals, although this study was judged as insufficient for assessing the carcinogenicity of phosphine since toxic levels of phosphine were not achieved [10].

## Reproductive and developmental toxicity

Only limited information is available on the reproductive and developmental toxicity of phosphine in experimental animals. This suggests that phosphine is unlikely to be a developmental toxin. Also no gross teratogenic effects from acute exposure to phosphine are known [4].

In a study on groups of pregnant Sprague-Dawley rats exposed to 0, 0.04, 0.4, 4, 7 or 10 mg $m^{-3}$ (0, 0.03, 0.3, 3, 5 and 7 ppm) phosphine for 6 h $day^{-1}$, on gestational days 6-15, high maternal mortality at the highest exposure concentration, and a significant increase in foetal resorptions at the lowest exposure, suggesting foetal toxicity, were noted in comparison to controls [9]. No other differences between exposed and control animals were reported.

In a study to evaluate the effect of inhaled phosphine on male germ cells, male mice were exposed to 7 mg $m^{-3}$ (5 ppm) phosphine for 6 h $day^{-1}$ for 10 days over a 12 day period, then mated to groups of untreated females. There was no effect on the percentage of females impregnated by exposed males or on percentage of resorptions or implants per female [10].

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