



Chemical Emergency Medical Guideline

Information and recommendations for healthcare professionals

Chloroformiates

CAS No.: 79-22-1; 541-41-3; 24468-13-1; 108-23-6; 592-34-7

GHS symbols:



Acute toxicity



Corrosive

Signal word: Danger

Hazard statements:

For detailed information on the H statements for the individual substances within this group, it is recommended to consult the relevant safety data sheets of the distributor or official databases (e.g. <https://echa.europa.eu/de/search-for-chemicals>).

Overview

- Before paramedics/emergency doctors approach a patient, who has been or is exposed to chloroformates, they must ensure that there is no danger to themselves from chloroformates.
- There is no danger from contact with patients who have only been exposed to chloroformate gases. A patient who is wet with liquid chloroformates or solvents containing chloroformates, or whose clothing is wet with them, may endanger other people through direct contact or through chloroformates being released into the air.
- Chloroformiates cause severe irritation of the lungs. Due to slow hydrolysis in the alveoli, symptoms and severe lung damage may occur even 24 hours after exposure. Signs of toxic pulmonary oedema (shortness of breath, cyanosis, sputum, cough) usually only appear several hours after exposure, even in cases of severe exposure.
- There is no known specific antidote. Treatment depends on the extent of exposure and the symptoms.

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1. Information about the substance

Methyl chloroformate (CH₃-OCOCI), CAS 79-22-1

Synonyms: methyl chloroformate, methoxycarbonyl chloride

At room temperature, methyl chloroformate is a colorless to yellowish, clear liquid with a melting point of -61°C and a boiling point of 71°C.

Ethyl chloroformate (C₂H₅-OCOCI), CAS 541-41-3

Synonyms: Ethyl chloroformate, ethoxycarbonyl chloride

Ethyl chloroformate is a colorless-yellowish, clear liquid at room temperature with a melting point of -80°C and a boiling point of 93°C.

2-Ethylhexyl chloroformate (C₈H₁₇-OCOCI), CAS 24468-13-1

Synonyms: Ethyl hexyl chloroformate, ethoxyhexyl chloride

At room temperature, 2-ethylhexyl chloroformate is a colorless to yellowish, clear liquid with a melting point of -55°C and a boiling point of 100°C.

Isopropyl chloroformate (C₃H₇-OCOCI), CAS 108-23-6

Synonyms: Chlorformic acid isopropyl ester, isopropoxycarbonyl chloride

At room temperature, isopropyl chloroformate is a colorless to yellowish, clear liquid with a melting point of -70°C and a boiling point of 34°C.

Butyl chloroformate (C₄H₉-OCOCI), CAS 592-34-7

Synonyms: chloroformic acid butyl ester, butoxycarbonyl chloride

Butyl chloroformate is a colorless-yellowish, clear liquid at room temperature with a melting point of -70°C and a boiling point of 138°C.

Methyl chloroformate is the methyl ester of chloroformic acid, a phosgene derivative. Methyl chloroformate should not be confused with methyl chloroform (1,1,1-trichloroethane).

Chlorformates are used dissolved in solvents. They have a sharp, pungent and oppressive odor. They slowly decompose into hydrochloric acid when exposed to moisture.

Chlorformates are an important starting material in the production of many chemicals such as isocyanates, polyurethanes, polycarbonates, dyes, pesticides and medicines.

2. Exposition

2.1. Inhalation

Exposure to chloroformates occurs mainly through inhalation or skin/eye contact. The odor of chloroformates is not sufficient warning. Even low concentrations can pose a hazard. The irritant effect can be mild and delayed, so that chloroformates can have a long-lasting effect without being noticed. Chloroformates are heavier than air and spread along the ground.

2.2. Skin/eye contact

Chlorformiates can cause irritation and chemical burns to moist or wet skin or eyes. Absorption through the skin is possible.

2.3. Ingestion

Ingestion of chloroformates can cause irritation of the mouth, throat and stomach.

3. Acute health effects

Chlorformiates usually cause irritation to the eyes, nose, throat and stomach.

3.1. Dose-response relationship

| | | |
|--|---|--|
| <u>Methyl chloroformate concentration</u> | | <u>Effect/effects</u> |
| 0.2 ppm | - | Occupational exposure limit (AGS, Germany) |
| 4 ppm for 10 min | - | AEGL-2 (EPA, USA) |
| 12 ppm for 10 min | - | AEGL-3 (EPA, USA) |
| <u>Ethyl chloroformate concentration</u> | | <u>Effect/effects</u> |
| 1 ppm | - | Occupational exposure limit (United Kingdom) |
| 2.9 ppm for 10 min | - | AEGL-2 (EPA, USA) |
| 8.8 ppm for 10 min | - | AEGL-3 (EPA, USA) |
| <u>Ethylhexyl chloroformate concentration</u> | | <u>Effect/effects</u> |
| 1 ppm | - | Occupational exposure limit (United Kingdom) |
| 1.2 ppm for 10 min | - | AEGL-2 (EPA, USA) |
| 3.6 ppm for 10 min | - | AEGL-3 (EPA, USA) |
| <u>Isopropyl chloroformate concentration</u> | | <u>Effect/effects</u> |
| 1 ppm | - | Occupational exposure limit (United Kingdom) |
| 6 ppm for 10 min | - | AEGL-2 (EPA, USA) |
| 18 ppm for 10 min | - | AEGL-3 (EPA, USA) |
| <u>n-Butyl chloroformate concentration</u> | | <u>Effect/effects</u> |
| 0.2 ppm | - | Occupational exposure limit (AGS, Germany) |
| 4 ppm for 10 minutes | - | AEGL-2 (EPA, USA) |
| 12 ppm for 10 min | - | AEGL-3 (EPA, USA) |

Occupational exposure limit: According to the Hazardous Substances Ordinance, the occupational exposure limit (OEL) is the limit value for the time-weighted average concentration of a substance in the air at the workplace in relation to a given reference period. It specifies the concentration of a substance at which acute or chronic adverse health effects are generally not to be expected.

AEGL-1 (acute exposure guideline levels): Guideline values for acute exposure. Concentration of a substance in the air above which the general population, including sensitive individuals, may experience noticeable discomfort, irritation or certain asymptomatic, non-sensory effects. However, the effects are not disabling and are temporary and reversible after exposure has ended.

AEGL-2: Concentration of a substance in the air above which the general population, including sensitive individuals, can be expected to suffer irreversible or other serious and long-lasting health effects or to be impaired in their ability to escape.

AEGL-3: Concentration of a substance in the air above which life-threatening health effects or death are expected to occur in the general population, including sensitive individuals.

EPA: Environmental Protection Agency

3.2. Respiratory tract

The symptoms immediately after exposure to chloroformates due to irritation of the upper respiratory tract may be mild (burning throat, coughing, feeling of pressure), but severe lung damage with fluid accumulation in the lungs (= pulmonary oedema) may occur up to 24 hours after exposure. Chloroformates can lead to respiratory and cardiovascular failure.

3.3. Skin contact

If the skin is wet or damp, contact with gaseous chloroformates may cause skin irritation or redness. High gas concentrations can cause redness and tear of the eyes, while eye contact with liquid chloroformates can result in clouding of the eye surface and later in permanent damage.

3.4. Possible consequences

If the patient survives the first 48 hours after exposure, further improvement in symptoms can be expected. Increased sensitivity to irritants may persist and cause bronchospasm or chronic bronchitis. Destruction of lung tissue or scarring can lead to chronic dilation of the bronchi and increased susceptibility to infection.

4. Measures

4.1. Self-protection of first aiders

If there is a suspicion that the area the helper must enter contains chloroformates, a self-contained breathing apparatus and a chemical protection suit must be worn. Do not use contaminated equipment. There is no danger from contact with patients who have only been exposed to chloroformate gases. A patient who is wet with liquid chloroformates or chloroformate-containing solvents, or whose clothing is wet with them, may endanger other people through direct contact or through chloroformate emissions.

4.2. Rescue

Patients should be removed from the danger zone immediately. If they are unable to walk unaided, they should be removed from the danger zone quickly using appropriate means, taking care to protect themselves. The "A, B, C procedure" has absolute priority in this case.

- A) Clear the airways** (check for blockages caused by the tongue or foreign objects)
- B) Ventilation** (check the patient's breathing; if necessary, begin ventilation with adequate self-protection, e.g. breathing mask)
- C) Circulation** (begin resuscitation for any person who does not respond to verbal commands and is not breathing normally)

CRASH decontamination

- Rescue patients who are unconscious or unable to move and contaminated with chloroformates (critically ill/injured patients according to the ABCDE scheme) from the immediate danger zone, taking personal precautions and using suitable personal protective equipment.
- If necessary, perform emergency measures (basic life support, e.g. bleeding control using a tourniquet, chest compressions, etc.).
- At a suitable location outside the danger zone, completely undress the contaminated patient using an emergency rescue knife, taking care to protect yourself.
(Duration: approx. 1 minute)
- Shower/rinse with plenty of water (duration: approx. 1 minute)
- Transfer to a clean stretcher. Ensure body heat is maintained. Transport/handover to the emergency services/emergency doctor (duration: approx. 1 minute)

4.3. Cleaning

Unlike all other patients, those who have only been exposed to chloroformate gases and show no signs of skin or eye irritation do not require any special cleaning measures.

If possible, patients should assist in their own cleaning. A patient who is wet with liquid chloroformates or chloroformate-containing solvents, or whose clothing is wet with these substances, may endanger other people through direct contact or through outgassing chloroformates. If liquid chloroformates or chloroformate-containing solvents have contaminated clothing and contaminated it, the clothing must be removed and securely wrapped.

Rinse affected skin and hair with water for at least 15 minutes. Protect eyes while rinsing. Continue other important first aid measures in the meantime.

In case of exposure to chloroformates, rinse eyes with water or neutral saline solution for at least 15 minutes. Remove any contact lenses, if possible, without additional risk to the eye. Continue other important first aid measures in the meantime.

4.4. Initial treatment (preclinical or clinical)

Empirical therapy; no specific antidote available.

The following measures are recommended if the AEGL II value has been reached or exceeded, symptoms are present, or if exposure cannot be estimated but is likely to have occurred:

- Oxygen administration
- Administration of 8 puffs of beclomethasone (800µg beclomethasone dipropionate) from a metered dose inhaler.

If there are signs of airway constriction (e.g. bronchospasm or stridor)

- Nebulization of adrenalin (epinephrine): mix 2mg adrenalin (2ml) with 3ml NaCl 0.9% and administer via a nebulizer mask
- Administration of a β 2-selective adrenoceptor agonist, e.g. four puffs of terbutaline or salbutamol or fenoterol (one puff usually contains 0.25mg terbutaline sulphate; or 0.1mg salbutamol; or 0.2mg fenoterol); this can be repeated once after 10 minutes.

Alternatively, 2.5mg salbutamol and 0.5mg ipratropium bromide can be administered via a nebulizer mask.

If inhalation is not possible, administer terbutaline sulphate (0.25mg to 0.5mg) subcutaneously or salbutamol (0.2mg to 0.4mg over 15 minutes) intravenously.

Intravenous administration of 250mg methylprednisolone (or an equivalent steroid dose).

If there are signs of toxic pulmonary oedema (e.g. frothy sputum, moist rales)

- CPAP therapy
- Intravenous administration of 1000mg methylprednisolone (or an equivalent steroid dose)
In case of (increasing) respiratory insufficiency, advanced airway management, e.g. endotracheal intubation or coniotomy if necessary.

Note: The efficacy of corticosteroid administration has not yet been proven in controlled clinical trials.

Skin contact with chloroformates can result in severe damage; this should be treated as burns: adequate fluid administration, analgesic therapy, maintenance of body temperature, covering the affected skin area with a sterile dressing.

Serious damage may also result from exposure of the eyes; this should also be treated as a burn. Consult an ophthalmologist immediately.

Note: Any exposure to liquid chloroformates in the facial area should be taken seriously.

4.5. Further action and treatment

In addition to taking medical history, performing a physical examination and checking vital signs, pulse oximetry, a chest X-ray and spirometry should be performed. Clear radiological signs of pulmonary oedema – enlargement of the hili, typical, centrally emphasized, patchy shadows on the chest X-ray – are late signs that only become apparent 6 to 8 hours or even later after exposure. The X-ray is typically normal on initial presentation at the hospital, even after inhalation of a larger dose.

Patients with possible exposure should be monitored for an appropriate period and re-examined repeatedly before any damage to health can be ruled out.

If oxygen saturation falls below 90%, arterial blood gas concentrations should be checked immediately and the chest X-ray repeated.

If blood gas concentrations deteriorate and/or the chest X-ray shows signs of toxic pulmonary oedema, oxygen should be administered via a mask. If deterioration manifests (especially in the case of tachypnoea (>30/min) and a simultaneous decrease in carbon dioxide partial pressure), CPAP therapy should be started within the first 24 hours after exposure.

In the event of pulmonary oedema developing, fluid intake and excretion as well as electrolytes should be closely monitored. A positive balance should be avoided. To optimize fluid management, the insertion of a central venous catheter should be considered.

If signs of pulmonary oedema persist, intravenous administration of methylprednisolone (or an equivalent steroid) should be continued at intervals of 8 to 12 hours.

4.6. Discharge of the patient / instructions for further rules of conduct

Patients with exposure below the AEGL-2 value and clinically asymptomatic patients who show normal examination findings and no signs of toxic effects after an appropriate follow-up period may be discharged under the following circumstances:

- Even if the patient's clinical condition has not deteriorated, a further chest X-ray should be performed before discharge. The patient should not be discharged if this shows even the slightest indication of pulmonary oedema.
- Information and recommendations for patients with instructions for further action were provided verbally and in writing.
- The patient is aware of and understands the toxic effects of chloroformates.
- The local doctor has been informed that regular contact between the patient and the doctor is possible in the following 24 hours.
- Heavy physical work should not be done in the following 24 hours.
- Do not smoke and avoid cigarette smoke for at least 72 hours; smoke can impair lung function.
- Patients with eye injuries should be re-examined after 24 hours.
- Spirometry should be repeated at regular intervals after discharge until the values have returned to the patient's baseline values.

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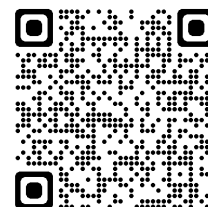
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Administrative Information

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| Document Type | Chemical Emergency Medical Guideline |
| Number of Version | DE.1.0.0 |
| Initial Publication | 01.01.2026 |
| Next Revision | 2029 |
| Responsible Unit (Author) | ESG/CH ESG/AS |
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BASF has taken every possible care to ensure that the information presented in this document is accurate and up to date but does not claim that this document comprehensively covers all possible situations in this regard. This document is intended as an additional source of information for doctors in hospitals and is designed to assist in the assessment of the condition and treatment of patients exposed to chloroformates. However, it does not replace the professional assessment of the respective situation by physicians in hospitals and must be interpreted in accordance with legal regulations and provisions as well as specific information available about the respective patients.