
Information and recommendations for doctors at hospitals/emergency departments

- Patients exposed only to chloroformates gas do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid chloroformates or solvents containing chloroformates can secondarily contaminate rescue and medical personnel by direct contact or through off-gassing chloroformates.
 - Chloroformates are severe pulmonary irritants. Because of its slow hydrolysis in the alveoli, serious pulmonary effects and, therefore, symptoms of toxicity may be delayed up to 24 hours. Signs of pulmonary edema (shortness of breath, cyanosis, expectoration, cough) do not usually appear for hours after even severely toxic exposures.
 - There is no antidote to be administered to counteract the effects of chloroformates. Treatment consists of supportive measures.
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1. Substance information

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

Synonyms: chloroformic acid methyl ester, methoxycarbonyl chloride
Methyl chloroformate is a colorless-yellow clear liquid at room temperature with a melting point of -61 °C and a boiling point of 71°C.

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

Synonyms : chloroformic acid ethyl ester, ethoxycarbonyl chloride
Ethyl chloroformate is a colorless-yellow 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: chloroformic acid ethylhexyl ester, 2-ethoxyhexylcarbonyl chloride

2-Ethylhexyl chloroformate is a colorless-yellow clear liquid at room temperature with a melting point of -55 °C and a boiling point of 100 °C.

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

Synonyms: chloroformic acid isopropyl ester, isopropoxycarbonyl chloride

Isopropyl chloroformate is a colorless-yellow clear liquid at room temperature 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-yellow 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).

Often chloroformates are used as a solution in organic solvents. Their odor is pungent and can be sharp and suffocating. Chloroformates are hydrolyzed slowly by moisture to form hydrochloric acid.

Chloroformates are used as an intermediate in the manufacture of many chemicals including isocyanates, polyurethane, polycarbonates, dyes, crop protection products, and pharmaceuticals.

2. Routes of exposure

Inhalation

Most exposures occur by inhalation or by skin/eye contact.

Chloroformates' odor may provide insufficient warning of hazardous exposure that can occur even at low concentrations. Its irritating quality can be mild and delayed, which may allow persons to be exposed for

prolonged intervals. Chloroformates are heavier than air and may travel along the ground.

Skin/eye contact

Chloroformates can cause irritation and burns of wet or moist skin and the eyes. Dermal absorption may occur.

Ingestion

Accidental ingestion of chloroformates may occur and may cause irritation of the mouth, throat and stomach.

3. Acute health effects

Chloroformates exposure usually causes eye, nose, throat, and pulmonary irritation. **Irritating effects immediately after exposure might be mild, but severe delayed pulmonary damage, primarily edema, can occur as late as 24 hours after exposure.** Chloroformates poisoning may cause respiratory and cardiovascular failure.

If the skin is wet or moist, contact with chloroformates gas can cause irritation and redness of the skin.

High gas concentrations may cause tearing and conjunctival erythema of the eye. Eye contact with liquid chloroformates may result in clouding of the eye surface and delayed perforation.

Dose-effect relationships

Dose-effect relationships are as follows:

<u>Methyl chloroformate concentration</u>	<u>Effect</u>
0.2 ppm	- occupational exposure limit
4 ppm for 10 min	- AEGL (acute exposure guidance level) II
12 ppm for 10	- AEGL (acute exposure guidance level) III
<u>Ethyl chloroformate concentration</u>	<u>Effect</u>
1 ppm	- occupational exposure limit
2.9 ppm for 10 min	- AEGL (acute exposure guidance level) II
8.8 ppm for 10 min	- AEGL (acute exposure guidance level) III
<u>Ethylhexyl chloroformate concentration</u>	<u>Effect</u>
1ppm	- occupational exposure limit
4 ppm for 10 min	- AEGL (acute exposure guidance level) II
12 ppm for 10 min	- AEGL (acute exposure guidance level) III
<u>Isopropy chloroformate concentration</u>	<u>Effect</u>
1ppm	- occupational exposure limit
6 ppm for 10 min	- AEGL (acute exposure guidance level) II
18 ppm for 10 min	- AEGL (acute exposure guidance level) III
<u>n-Butyl chloroformate concentration</u>	<u>Effect</u>
0.2 ppm	- occupational exposure limit
4 ppm for 10 min	- AEGL (acute exposure guidance level) II
12 ppm for 10 min	- AEGL (acute exposure guidance level) III
AEGL (acute exposure guidelines levels) II: airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious long-lasting adverse health effects, or an impaired ability to escape	
AEGL III: airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death	

Potential sequelae

If the patient survives the initial 48 hours after exposure, recovery is likely. Sensitivity to irritants may persist, causing bronchospasm and chronic inflammation of the bronchi. Pulmonary tissue destruction and scarring may lead to chronic dilation of the bronchi and increased susceptibility to infection.

4. Actions

Decontamination

Patients exposed only to chloroformates gas do not pose a significant risk of secondary contamination. Patients whose clothing or skin is contaminated with liquid chloroformates or solvents containing chloroformates can secondarily contaminate other people by direct contact or through off-gassing chloroformates.

Patients who are able and cooperative may assist with their own decontamination. If the exposure involved liquid chloroformates or solvents containing chloroformates and if clothing is contaminated, remove and double-bag the clothing.

Assure that exposed skin and hair have been flushed with plain water for at least 15 minutes. If not, continue flushing during other basic care. Protect eyes during flushing of skin and hair.

Assure that exposed or irritated eyes have been irrigated with plain water or saline for at least 15 minutes. If not, continue eye irrigation during other basic care.

Remove contact lenses if present and easily removable without additional trauma to the eye.

Initial treatment

Therapy will be empiric; there is no antidote to be administered to counteract the effects of chloroformates.

The following measures are recommended if the exposure dose is AEGL II or greater, if symptoms have developed, or if no exposure dose can be estimated but exposure has possibly occurred:

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

Patients with severe clinical respiratory symptoms (e.g. bronchospasms, stridor) should be treated as follows:

a) Nebulization of adrenaline (epinephrine): 2 mg adrenaline (2 ml) with 3 ml NaCl 0.9% and inhale through a nebulizer mask.

b) Administration of a β 2-selective adrenoceptor agonist, e.g., four strokes of terbutaline or salbutamol or fenoterol (one stroke usually contains 0.25 mg of terbutaline sulfate; or 0.1 mg of salbutamol; or 0.2 mg of fenoterol); this may be repeated once after 10 minutes. Alternatively, 2.5 mg salbutamol and 0.5 mg atrovent may be administered by nebulizer mask.

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

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

Patients with clinical signs of a toxic lung edema (e.g. foamy sputum, wet crackles) should be treated as follows:

a) Start CPAP-therapy (Continuous Positive Airway Pressure Ventilation).

b) Intravenous administration of 1000 mg methylprednisolone (or an equivalent steroid dose) is recommended.

Intubation of the trachea or an alternative airway management should be considered in cases of respiratory compromise. When the patient's condition precludes this, consider cricothyrotomy if equipped and trained to do so.

Note: Efficacy of corticosteroid administration has not yet been proven in controlled clinical studies.

If chloroformates were in contact with the skin or eyes chemical burns may result; treat as thermal burns: adequate fluid resuscitation and administration of analgesics, maintenance of the body temperature, covering of the burn with a sterile pad or clean sheet.

After eye exposure immediately consult an ophthalmologist.

Note: Any facial exposure to liquid chloroformates should be considered as a serious exposure.

Further evaluation and treatment

To the standard intake history, physical examination, and vital signs add pulse oximetry monitoring and a PA chest X-ray.

Spirometry should be performed. Routine laboratory studies should include a complete blood count, blood glucose and electrolyte determinations.

Evidence of pulmonary edema - hilar enlargement and ill-defined, central-patch infiltrates on chest radiography - **is a late finding that may occur 6 to 8 hours or later after exposure. The chest X-ray is typically normal on first presentation to the emergency department even with severe exposures.**

Patients who have possible exposure should be observed for a minimum of 24 hours and reexamined frequently before confirming the absence of toxic effects.

If oxygen saturation is less than 90 % or if it appears to drop, immediately check arterial blood gasses and repeat the chest X-ray.

If blood gasses begin to show deterioration and/or if the chest X-ray begins to show pulmonary edema start oxygen supplementation.

In case of worsening clinical signs (especially tachypnea >30/min with a simultaneous decrease of the partial pressure of carbon dioxide) CPAP-therapy (Continuous Positive Airway Pressure Ventilation) should be started within the first 24 hours after exposure.

In case of a pulmonary edema fluid intake/output and electrolytes should be monitored closely. Avoid net positive fluid balance. Central line or Swan-Ganz catheterization might be considered, to optimize fluid management.

As long as signs of pulmonary edema are present, intravenous administration of methylprednisolone (or an equivalent steroid) should be continued in intervals of 8-12 hours.

Prophylactic antibiotics are not routinely recommended but may be used based on the results of sputum cultures. Pneumonia can complicate severe pulmonary edema.

Patient release/ follow-up instructions

Clinically asymptomatic patients exposed to a concentration of **less than AEGL-II** (depending on the period of time exposed) **as well as patients who have no signs or symptoms of toxicity may be discharged after an appropriate observation period in the following circumstances:**

- a) The evaluating physician is experienced in the evaluation of individuals with chloroformates exposure.
- b) Information and recommendations for patients with follow-up instructions are provided verbally and in writing.
- c) The physician is comfortable that the patient understands the health effects of chloroformates.
- a) Site medical is notified, so that the patient may be contacted at regular intervals in the 24-hour period following release from the emergency department.
- e) Heavy physical work should be precluded for 24 hours.
- f) Exposure to cigarette smoke should be avoided for 72 hours; the smoke may worsen the condition of the lungs.

Patients with an exposure of **AEGL II or above** who have a normal clinical examination and no signs or symptoms of toxicity may be discharged after an appropriate observation period in the following circumstances:

- a) The evaluating physician is experienced in the evaluation of individuals with chloroformates exposure.
- b) Even if there has not been clinical deterioration, the patient's chest X-ray should be repeated prior to release. The patient should not be released if any degree of pulmonary edema is demonstrated.**
- c) Information and recommendations for patients with follow-up instructions are provided verbally and in writing.
- d) The physician is comfortable that the patient understands the health effects of chloroformates and the provided follow-up instructions.
- e) Site medical is notified, so that the patient may be contacted at regular intervals in the 24-hour period following release from the emergency department.
- f) Heavy physical work should be precluded for 24 hours.
- g) Exposure to cigarette smoke should be avoided for 72 hours; the smoke may worsen the condition of the lungs.

Patients who have eye injuries should be reexamined in 24 hours. Post-discharge spirometry should be repeated until values return to the patient's baseline values.

In this document BASF has made a diligent effort to ensure the accuracy and currency of the information presented but makes no claim that the document comprehensively addresses all possible situations related to this topic. This document is intended as an additional resource for doctors in assessing the condition and managing the treatment of patients exposed to Chloroformate. It is not, however, a substitute for the professional judgement of a doctor and must be interpreted in the light of specific information regarding the patient available to such a doctor and in conjunction with other sources of authority.

BASF SE
Corporate Health Management
Carl-Bosch-Straße 38
67056 Ludwigshafen
Germany

BASF Corporation
Medical Department
100 Campus Drive, M/S F 221
Florham Park, NJ 07932
USA