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.

1. Substance information

Methyl chloroformate (CH3-OCOCl), CAS 79-22-1
Synonyms: carbonochloridic acid methyl ester, 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-OCOCl), CAS 541-41-3
Synonyms: carbonochloridic acid ethyl ester, 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-OCOCl), CAS 24468-13-1
Synonyms: carbonochloridic acid ethyl hexylester, 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-OCOCl), CAS 108-23-6
Synonyms: carbonochloridic acid isopropyl ester, 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-OCOCl), CAS 592-34-7
Synonyms: carbonochloridic acid butyl ester, 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 as well as irritation of the eyes and pulmonary system may provide warning of hazardous exposure even at low concentrations. However, its irritating quality can be mild and delayed pulmonary symptoms may occur. 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:

<table>
<thead>
<tr>
<th></th>
<th><strong>Effect</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methyl chloroformate concentration</strong></td>
<td></td>
</tr>
<tr>
<td>0.2 ppm</td>
<td>occupational exposure limit</td>
</tr>
<tr>
<td>4 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) II</td>
</tr>
<tr>
<td>12 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) III</td>
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<tr>
<td><strong>Ethyl chloroformate concentration</strong></td>
<td></td>
</tr>
<tr>
<td>1 ppm</td>
<td>occupational exposure limit</td>
</tr>
<tr>
<td>2.9 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) II</td>
</tr>
<tr>
<td>8.8 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) III</td>
</tr>
<tr>
<td><strong>Ethylhexyl chloroformate concentration</strong></td>
<td></td>
</tr>
<tr>
<td>1 ppm</td>
<td>occupational exposure limit</td>
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<tr>
<td>4 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) II</td>
</tr>
<tr>
<td>12 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) III</td>
</tr>
<tr>
<td><strong>Isopropyl chloroformate concentration</strong></td>
<td></td>
</tr>
<tr>
<td>1 ppm</td>
<td>occupational exposure limit</td>
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<tr>
<td>6 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) II</td>
</tr>
<tr>
<td>18 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) III</td>
</tr>
<tr>
<td><strong>n-Butyl chloroformate concentration</strong></td>
<td></td>
</tr>
<tr>
<td>0.2 ppm</td>
<td>occupational exposure limit</td>
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<tr>
<td>4 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) II</td>
</tr>
<tr>
<td>12 ppm for 10 min</td>
<td>AEGL (acute exposure guidance level) III</td>
</tr>
</tbody>
</table>

**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.
- **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:

**If not already done, initially, administration of 8 puffs of beclomethasone (800 µg beclomethasone dipropionate) from a metered dose inhaler.**

**Thereafter, administration of 4 puffs every 2 hours for 24 hours.**

If not already done, establishment of intravenous access and intravenous administration of 1.0 g methylprednisolone (or an equivalent steroid dose).

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

If inhalation exposure has occurred, humidified air or oxygen should be provided. If signs of hypoxemia are present, humidified supplemental oxygen should be administered.

Intubation of the trachea should be considered in cases of respiratory compromise. When the patient’s condition precludes endotracheal intubation, perform cricothyotomy if equipped and trained to do so.
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. Should it become clear that pulmonary edema is worsening, positive end-expiratory pressure (PEEP) therapy should be started within the first 24 hours after exposure even if oxygenation can be maintained by mask.

**Early indication for PEEP therapy is tachypnea (>30/min) with a simultaneous decrease of the partial pressure of carbon dioxide.**

An inadequate increase or a relative decrease of the partial pressure of oxygen despite hyperventilation indicates the development of 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 1 g methylprednisolone (or an equivalent steroid dose) should be continued in intervals of 8-12 hours.

Patients with bronchospasms should be treated as follows:

a) Aerolized β2-selective adrenergic agonist, e.g. 4 puffs of terbutaline, or salbutamol, or fenoterol from a metered dose inhaler (1 puff usually contains 0.25 mg terbutaline sulfate, or 0.1 mg salbutamol, or 0.2 mg fenoterol, respectively); may be repeated once after 10 min.

If inhalation is not possible, terbutaline sulfate (0.25-0.5 mg) subcutaneously or salbutamol (0.2-0.4 mg over 15 min) intravenously.

b) If a) is not effective or insufficient: theophylline (5 mg/kg body weight intravenously over 20-30 min).

c) If a) and b) are not effective or insufficient: 2 puffs of epinephrine (0.4 mg per puff) from a metered dose inhaler; may be repeated after 5 min.

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**

Patients with an exposure of **less than AEGL II and no signs or symptoms of toxicity** may be discharged from the emergency department in less than 24 hours 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.

d) 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 examination and no signs or symptoms of toxicity after observation for 24 hours may be discharged from the emergency department 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

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