Annex 117
Halogenated derivates of the aliphatic or alicyclic hydrocarbons

In this class of hydrocarbons one hydrogen has been replaced by halogen fluorine (F), chlorine (Cl), bromine (Br), or iodine (I)]
[Examples: trichloroethylene, tetrachloroethylene, methylene chloride, carbon tetrachloride, chloroform,]
The following items are covered under this entry:

- methylene chloride
- trichloroethylene
- tetrachloroethylene
- vinylchloride monomer
- methylbromide

Methylene chloride

Definition of causal agent

Methylene chloride CH_2C1_2 (dichloromethane or methylene dichloride) is a colourless, volatile, water-soluble liquid. It has a sweetish odour detectable by most individuals above 200 to 300 ppm, although adaptation to the odour can occur. At 2300 ppm the odour is strong and intensely irritating.

Methylene chloride is metabolized in part to carbon monoxide. In presence of fire, methylene chloride may result in phosgene production.

The toxicity of methylene chloride is related to the toxicity of the other similar solvents and of carbon monoxide.

Main occupational uses and sources of exposure:
Degreasing agent used as paint and varnish remover; propellant for aerosol sprays; solvent for plastic and blowing agent for foams.

Toxic effects

1. Local effects

☐ Irritant effects

Methylene chloride is irritant to the skin, eyes and respiratory tract (pulmonary oedema, coma). See document on occupationally caused irritation of the skin and mucous membranes.

2. Systemic effects

Acute

☐ Narcotic syndrome

Headache, nausea, vertigo, drowsiness, weakness, confusion, loss of consciousness, sometimes coma.

Possibility of cardiovascular and neurological sequelae, the intensity of which depends on the severity of the exposure.

Exposure criteria:

Minimal intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and analysis of the working conditions showing significant exposure to methylene chloride,
— and, if available:
- biological monitoring:
  exposure confirmed by measurement of dichloromethane in blood and carboxyhaemoglobinaemia
  guide values:
  an increase of 4 % or more in carboxyhaemoglobin (in non-smokers) within an hour of exposure, or a similar increase of carbon monoxide in exhaled breath within two hours of exposure.
- workplace air monitoring: guide values:
  at exposures to 2 300 ppm over 5 minutes or for longer exposures above 300 ppm, dizziness results.

Minimum duration of exposure: A few minutes to a few hours depending on the intensity of the exposure.

Maximum latent period: The first symptoms should occur during the exposure and at the latest within 24 hours.

No evidence of adverse effects on workers' health has been found following exposures at concentrations of about 350 mg/m^3 (100 ppm) for several years.

Chronic

☐ Chronic toxic encephalopathy

Similarly to other organic solvents, methylene chloride can cause, in repeated, prolonged exposures, chronic toxic encephalopathy (See Annex I entry nr. 135 on ***Encephalopathies due to organic solvents which do not come under other headings***).

☐ Exacerbation of ischaemic heart disease

Prolonged exposure which gives rise to levels of carboxyhaemoglobinaemia in excess of 10% can exacerbate a pre-existing ischaemic heart disease.

Due to the multicausality of the occurrence of these pathologies, particularly tobacco smoking, the recognition of the occupational origin must be individually evaluated by experts.

To be attributable to the exposure to methylene chloride, the cardiovascular sequelae should occur not later than one month following the acute exposure.

☐ Cancer

Inhalation exposure to methylene chloride is associated with development of cancer in mice, but not in rats and hamsters. It is well known that the mouse model may not be adequate to point out a carcinogenic risk to humans, due to significant differences in methylene chloride metabolism. Therefore, the results of the studies conducted in mice are nor relevant to humans.

Trichloroethylene

Definition of causal agent

Trichloroethylene ($CHC1=CC1_2$) (synonyms: trichloroethene, chlorylene, TRI) is a non-inflammable fluid with a chloroform-like odour. It is not readily soluble in water but soluble in organic solvents. Vapour/air mixtures are explosive. Decomposition occurs on exposure to heat, with formation of dichloro-acetylene, hydrochloric acid fumes, carbon monoxide and phosgene (see the documents concerning these substances).
The principal metabolites of trichloroethylene are trichloroethanol and trichloroacetic acid.

Main occupational uses and sources of exposure:
Trichloroethylene is used as a solvent and extracting agent and as an insecticide. It is also a component of certain stain removers.

Toxic effects

1. Local effects

☐ Irritant effects

Trichloroethylene can cause irritation of the skin and mucous membranes.

See section on ***Occupationally caused irritation of the skin and mucous membranes*** in Annex I entry nr. 202.

2. Systemic effects

Acute

☐ Narcotic syndromes

Headache, dizziness, nausea, drowsiness, weakness, confusion, loss of consciousness, possibly leading to coma.

NB: In patients undergoing treatment, trichloroethylene can also cause cardiac arrhythmia as a result of depression of the threshold of sensitivity to catecholamines.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of acute exposure to trichloroethylene,
— and, if available:
  • Biological monitoring

trichloroethanol in blood > 5 mg/L (end of shift sample)
trichloroacetic acid in urine > 100 mg/L

- Workplace air monitoring

108 mg/m^3 (20 ppm): perceptible odour,

594 mg/m^3 (110 ppm): increase in reaction time may occur,

6,9 g/m^3 (1 280 ppm): state of prenarcosis after six minutes,

13,5 g/m^3 (2 500 ppm): rapid full narcosis.

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 24 hours.

Chronic

☐ Chronic toxic encephalopathy

Similarly to other organic solvents, trichloroethylene can cause, in repeated, prolonged exposures, chronic toxic encephalopathy (See Annex I entry nr. 135 on ***Encephalopathies due to organic solvents which do not come under other headings***).

☐ Damage to cranial nerves

Hypoaesthesia, paraesthesia of the trigeminal nerve.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure to trichloroethylene (taking account of the possibility of cutaneous absorption),

— and, if available:

- biological monitoring:
  guide values:
  trichloroethanol in blood: > 5 mg/L
  trichloroacetic acid in urine: > 100 mg/L
- workplace air monitoring:
  guide value:
  atmospheric concentration well above 270 mg/m^3 (50 ppm).

Minimum duration of exposure:

Chronic toxic encephalopathy:	10 years.
Damage to trigeminal nerve:	Several years.

Maximum latent period:

Chronic toxic encephalopathy:	The first signs of nervous system disturbance should occur in the year following cessation of exposure.
Damage to the trigeminal nerve:	Immediate.

☐ Cancer

A wide debate is at present running in the scientific community, with a wide range of opinions about classification, but available data support the characterization of trichloroethylene as a human carcinogen (renal cancer). Nevertheless, the onset of this neoplasm is confined to few cases characterized by very high exposures in the past, especially peak exposures.

A practical threshold was found in rats at 250 ppm.

It is not possible, at the current status of knowledge, to define criteria for diagnosis of occupational cancer due to trichloroethylene. Cases of renal cancer occurring in very heavily exposed workers should be considered as possible occupational diseases.

Tetrachloroethylene

Definition of causal agent

Tetrachloroethylene (CC12=CC12) (synonyms: tetrachlorethene, perchloroethylene) is a colourless, volatile, flammable solvent with a smell similar to the ether's one. When heated, it breaks down with the production of carbon monoxide, phosgene and hydrochloric acid fumes. 80 to 90% of the absorbed dose is excreted unchanged with exhaled air. A small amount (< 3%) is biotransformed in trichloroacetic acid.
Tetrachloroethylene has a prolonged biological half life because of accumulation in body fat.

Main occupational uses and sources of exposure:
This compound is widely used for dry cleaning, textile treatments and metal degreasing.

Toxic effects

1. Local effects

☐ Irritant effects

Tetrachloroethylene can cause irritation of the skin and mucous membranes.
See section on ***Occupationally caused irritation of the skin and mucous membranes*** in Annex I entry nr. 202.

2. Systemic effects

Acute

☐ Narcotic syndromes

Headache, dizziness, nausea, drowsiness, weakness, confusion, loss of consciousness, possibly leading to coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of working conditions providing evidence of acute exposure to tetrachloroethylene, f
— and, if available:
- biological monitoring
  Tetrachloroethylene in blood > 1 mg/L (prior to the next shift sample)
- workplace air monitoring

Guide values:

680 mg/m^3 (100 ppm): slight smell; dizziness; headache after several hours of exposure.
34 g/m^3 (5000 ppm): strong smell; symptoms after few minutes of exposure.

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 24 hours.

Chronic

☐ Chronic toxic encephalopathy

Similarly to other organic solvents, trichloroethylene can cause, in repeated, prolonged exposures, chronic toxic encephalopathy (See Annex I entry nr. 135 on ***Encephalopathies due to organic solvents which do not come under other headings***).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of working conditions providing evidence of prolonged or repeated exposure (taking account of the possibility of cutaneous absorption),
— and, if available:
- biological monitoring: blood tetrachloroethylene concentration.

- workplace air monitoring:
  guide value:
  atmospheric concentration well above 345 mg/m^3 (50 ppm).

Minimum duration of exposure: 10 years.

Maximum latent period: Chronic toxic encephalopathy: The first signs of nervous system disorder should appear no later than one year after the end of the exposure.

☐ Cancer

Tetrachloroethylene has induced liver cancer in mice and renal tubular tumours in male rats. Some studies suggest that it might cause cancer in humans, but the evidence is inconclusive. Interpretation is hampered by concomitant exposure to other solvents and limited by lack of control for lifetime related factors.

Vinyl chloride monomer

Definition of causal agent

At normal temperature and pressure, vinyl chloride is a gaseous monomer.

Main occupational uses and sources of exposure:
Mainly used in the production of polyvinyl chloride.

Toxic effects

☐ Irritant effects

Vinyl chloride monomer may be irritant to the skin (irritant dermatitis), the eyes (keratoconjunctivitis) and the upper respiratory tract.

See section on ***Occupationally caused irritation of the skin and mucous membranes*** in Annex I entry nr. 202.

☐ Narcotic syndrome

Headache, dizziness, nausea, somnolence, weakness, confusion, unconsciousness, may lead to coma.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of working conditions showing evidence of intense exposure to vinyl chloride monomer at atmospheric concentration > 2.08 g/m^3 (800 ppm)
— and, if available:
  • workplace air monitoring:
  guide value: atmospheric concentration > 2.08 g/m^3 (800 ppm).

Minimum duration of exposure: From a few minutes to a few hours, depending on intensity of exposure.

Maximum latent period: 24 hours.

☐ Raynaud's phenomenon in the hands and feet

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;

— and, if available:
  • workplace air monitoring:
  guide value: atmospheric concentration > 130 mg/m^3 (50 ppm).

Minimum duration of exposure: One year.

Maximum latency period: Three years.

☐ Acro-osteolysis in the terminal phalanges of the hands and feet

May accompany angioneurotic disorders. Confirmed by X-ray (loss of structure from bones)

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;

— and, if available:
- workplace air monitoring:
  guide value: atmospheric concentration > 130 mg/m^3 (50 ppm).

Minimum duration of exposure: One year.

Maximum latent period: Three years.

☐ Distal skin disorders

Scleroderma-like syndrome with smooth, shiny skin, possibly accompanied by general symptoms (arthralgia, myalgia).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
— and, if available:
- workplace air monitoring:
  guide value: atmospheric concentration > 130 mg/m^3 (50 ppm).

Minimum duration of exposure: One year.

Maximum latent period: Three years.

☐ Liver fíbrosis with portal hypertension

Portal hypertension syndrome.
Fibrosis confirmed by histology or indirectly by echography.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
— and, if available:
- workplace air monitoring:

guide value: atmospheric concentration > 130 mg/m^3 (50 ppm).

Minimum duration of exposure: Two years.

Maximum latent period: 30 years.

Minimum induction period: Five years.

☐ Liver Tumours

Angiosarcoma and hepatocellular carcinoma of the liver.

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:

— anamnesis and study of exposure conditions showing evidence of prolonged/repeated exposure to vinyl chloride monomer;
— and, if available:
  • workplace air monitoring:

SCOEL assessed the risk of hepatic angiosarcoma upon exposure for working life time and concluded for 3 x 10^{-4} for 1 ppm and 9 x 10^{-4} for 3 ppm.

Minimum duration of exposure: 10 years.

Minimum induction period: 10 years.

See also section on ***Occupational cancers*** in the **Preface.**

Methyl bromide

Definition of causal agent

At ambient temperature and pressure, methyl bromide is a colourless and normally odourless gas which is heavier than air. At high concentrations its smell resembles that of chlorine.

Main occupational uses and sources of exposure:
Used as insecticide and nematocide via fumigation (greenhouse, grain silos etc.), rodenticide, refrigerant, methylation agent in the chemical industry.

Toxic effects

1. Local effects

☐ Irritant effects

Methyl bromide is highly irritating to the ocular and respiratory mucous membranes (pulmonary oedema may develop after a latency period of 6 to 24 or even 48 hours). It causes erythema, blisters and swellings.
As a liquid, methyl bromide is also highly irritant to the mucous membranes and causes severe skin burns.
See section on ***Occupationally caused irritation of the skin and mucous membranes*** in Annex I entry nr. 202.

2. Systemic effects

☐ Acute neurological syndrome

Signs and symptoms:

Headache, vertigo, sleepiness, blurred vision, nausea, vomiting, anorexia.

Dysarthria, ataxia, muscular incoordination, twitching, fasciculations, myoclonia, trembling, convulsions.

Healing may be very slow and there may be sequelae (motor impairment, cortical deafness, optic neuritis).

Exposure criteria:

Minimum intensity of exposure: Occupational exposure confirmed, if possible assessed, by:
— anamnesis and study of exposure conditions showing acute poisoning by methyl bromide via inhalation or skin contact;
— and, if available:
  • biological monitoring:
    blood: bromide (qualitative dose);
  • workplace air monitoring

Minimum duration of exposure: From some minutes to some hours, depending on the intensity of exposure.

Maximum latent period: 24 hours.

☐ Chronic toxic encephalopathy

Some studies are available suggesting the capacity of this compound to cause chronic toxic encephalopathy in repeated, prolonged exposures (See Annex I entry nr. 135 on ***Encephalopathies due to organic solvents which do not come under other headings***).

Due to its toxic acute properties, long term exposures are very unlikely.