Health Profile on Perchloroethylene
Executive Summary

The chlorinated solvent, perchloroethylene (also known as PER, PERC, tetrachloroethylene, and tetrachloroethene) has been widely used since the 1930s thanks to its aptitude for cleaning and its non-flammability properties. Perchloroethylene is mainly used as a chemical intermediate; in addition applications also exist in dry-cleaning, metal cleaning and degreasing. Use of perchloroethylene has fallen substantially since the mid-1980s due to more efficient dry-cleaning processes, greater recycling, use of enclosed systems, and other best practices.

When used appropriately, perchloroethylene poses no threat to human health, safety or the environment. Inhalation of solvent vapour is the most frequent and probable route of exposure. Fatalities and serious injuries have occurred only in instances where massive over-exposure occurred through a total disregard for good operating practices, or through deliberate misuse. Despite the fact that the international Agency on Cancer Research (IARC) concluded in 2012 that there is limited evidence in humans for the carcinogenicity (Category 2A) of perchloroethylene, the available human data does not allow a robust quantification of the cancer risk and does not suffice to identify a clear target organ for carcinogenicity. Based on extensive toxicological and epidemiological research, there is no reliable or consistent evidence that exposure to perchloroethylene under normal working conditions (<138 mg/m³, 8h TWA) increases the risk of cancer in humans.

Perchloroethylene does not deplete the ozone layer, and its contribution to global warming, acid rain and smog formation is negligible. Chlorinated solvents are unlikely to accumulate in living organisms or the environment. In sediment and soil, perchloroethylene is fairly mobile and can leach into groundwater. ECSA strongly encourages the use of state-of-the-art, contained systems to avoid the release of perchloroethylene into the environment.

Introduction

Perchloroethylene is a halogenated unsaturated aliphatic hydrocarbon. It is a colourless, volatile liquid, heavier than water, completely miscible with almost all other organic solvents, and slightly soluble in water. The substance has a boiling point of 121.4 °C and is non-flammable. Perchloroethylene vapours are heavier than air and can accumulate in confined or poorly ventilated areas. As a result, good ventilation is essential in areas where the product is made or used.

Chemical formula: $\text{C}_2\text{Cl}_4$
Molecular weight: 165.83 g/mol
CAS number: 127-18-4
EC number: 204-825-9

In Europe, perchloroethylene is manufactured by (in brackets: production location):

- Olin Corporation
- Inovyn
- Spolchemie

(Blue Cube Assets Germany)
(Blue Cube Assets Germany)
(Blue Cube Assets Germany)

Stabilizers are normally added to perchloroethylene to prevent its decomposition during storage and use. The total concentration of stabilisers is normally less than 0.05% in dry-cleaning grade, with highly stabilized grades for metal cleaning applications containing up to 0.5%. Due to its relatively high stability, PER requires less stabilizer to be added than other chlorinated solvents. To be effective during use, the stabilisers - which include epoxides (metal degreasing), alkylamines and phenols (inhibiting oxidation of PER by air), and secondary and tertiary alcohols - must vaporise at the same rate as perchloroethylene, so that both are present in the liquid and vapour phases.

During the production of chlorinated solvents, integrated manufacturing methods are employed so that waste from one process is used in another process. As a result, waste from the manufacturing plant is kept to a minimum; any toxic or potentially environmentally damaging wastes are recycled and converted to useful products, and final waste is disposed of by destruction/incineration.

Uses

Perchloroethylene’s main uses are:

**Intermediate:** the substance is used as raw material (chemical intermediate) for the industrial production of other (mainly fluorinated) substances.

**Dry cleaning:** perchloroethylene has a unique performance profile and is non-flammable. It is seen as the best choice for cleaning fine, delicate or sensitive garments.

**Metal cleaning:** for removing oils, grease and soils from metal parts in closed units, also referred to as metal or vapour degreasing.

**Other uses:** Use as heat transfer media or as a maskant in surface treatments.
Health Effects

Chlorinated solvents have been used extensively for many years. During this time, the only fatalities or serious injuries which have occurred have been due to massive over-exposure through a total disregard for good operating practices, or through deliberate misuse. When solvents are stored, used and disposed of properly, there is no risk to human health. Perchloroethylene is unlikely to accumulate in living organisms or the environment.

Inhalation of solvent vapour is the most frequent route of exposure: solvent vapours are heavier than air and can accumulate in confined or poorly ventilated areas. As a result, good ventilation is essential in areas where the product is made or used.

Acute and short-term exposure

Toxicology studies yielded oral and dermal LD$_{50}$ values (3000 and 10000 mg/kg body weight respectively) and an inhalation LC$_{50}$ value (>3000 ppm) indicating that the acute toxicity of perchloroethylene is low. In animals, as in humans, the main signs of acute inhalation toxicity are indicative of depression of the central nervous system (CNS). Exposure to perchloroethylene at concentrations of 200 ppm or more has been linked to dizziness, confusion, headache, nausea, and irritation of the eyes and mucous membranes. These effects become more pronounced at higher exposure (>600 ppm). In addition to effects on the CNS, there may also be transient, minor alterations in liver or kidney function. Prolonged exposure to extremely high levels (>1,500 ppm) may lead to unconsciousness or even death from respiratory depression; indeed, perchloroethylene was used as a human anaesthetic agent in the past. Large accidental intakes (estimated at 1.6 - 4.8 g/kg) in children have led to effects such as vomiting, gastrointestinal bleeding, shock and, in one case, death.

A concentration of 40 ppm (275 mg/m$^3$) is concluded to be a concentration without the occurrence of these effects in humans.

Effects on skin and eyes

There is sufficient evidence both from human cases and toxicology studies showing that perchloroethylene is a weak skin irritant, but not corrosive. In one case report, extensive redness (erythema) and blistering were seen on a worker who had lain unconscious in a pool of solvents for about five hours. In a second case report, another worker who had been unconscious for half an hour while wearing clothes soaked in perchloroethylene showed similar symptoms. Considerable reduction of these symptoms was seen within five days, but some dryness, staining and irritation of the injured areas continued.

Slight, transient eye irritation developing within the first hours of exposure, and subsiding before the end of a work shift, has been reported at exposure levels around 100 ppm.
Repeated exposure

In laboratory animals, repeated inhalation exposure to high levels of perchloroethylene causes lung, kidney, and liver effects. High exposures to perchloroethylene cause increasing levels of trichloroacetic acid, a breakdown product of perchloroethylene, which can cause cellular damage. Relative to humans, laboratory animals (especially mice) have higher production rates of trichloroacetic acid. Liver damage seen in mice following either inhalation exposure or oral administration has been shown to involve peroxisomal proliferation, an effect considered not relevant to humans. No liver toxicity was observed in rats. For kidney damage, which was observed in both rats and mice following either inhalation or oral exposure, an inhalation lowest-observed-adverse-effect concentration (LOAEC) of 100 ppm (690 mg/m$^3$) and an oral lowest-observed-adverse-effect level (LOAEL) of 390 mg/kg bw/day have been identified. Evidence of hyaline droplet nephropathy was found in male rats following either inhalation or oral exposure, but the data indicate that this phenomenon, which is male rat-specific and hence not relevant to humans, only occurs at relatively high levels of exposure. Congestion of the lungs was seen in mice following inhalation exposure at 100 ppm (690 mg/m$^3$) for 2 years. One hundred ppm (690 mg/m$^3$) is therefore also the LOAEC for this effect in the lungs.

There are general worker health surveys and studies specifically investigating potential effects on the liver and kidney in workers likely exposed to perchloroethylene. Based on all available data, there is no clear or consistent evidence from studies in humans for repeated dose effects of perchloroethylene at exposure levels up to a level of 20 ppm (138 mg/m$^3$). This concentration can be regarded to be a no-observed-adverse-effect concentration NOAEC in humans as an 8-hour time-weighted-average (TWA) value.

It is strongly recommended that users maintain exposures within legislative or manufacturers' guidelines to keep human and environmental exposures to a minimum. Compliance with applicable regulations, use of engineering controls, best available work practices, and occupational health surveillance, will help ensure that perchloroethylene can continue to be used in a safe and environmentally sound manner.

Sensitization

Perchloroethylene tested positive in the local lymph node assay in mice. Therefore, classification according to Directive 67/548/EEC and the EU Classification, Labelling and Packaging of Substances and Mixtures (CLP) Regulation (EC) No. 1272/2008 for skin sensitisation is required. This experimental result contrasts with the rarity of case reports (n=3) associating skin or respiratory sensitisation with perchloroethylene exposure despite its widespread use.
**Genotoxicity**

A large number of studies have been conducted and overall no convincing evidence was found that perchloroethylene-induced effects result from mutations or damage to genetic material.

Convincing negative results have been obtained in *in vitro* genotoxicity tests. However, metabolites of perchloroethylene have been identified as genotoxic in bacterial test systems. Generally, the pattern of the *in vivo* results is negative. In humans, three studies have looked for evidence of genotoxicity in relation to occupational exposure to perchloroethylene. These studies proved negative, but limitations in the design of two of them (the older ones) mean that no firm conclusions can be drawn.

Overall, although positive results were obtained *in vitro* with metabolites of perchloroethylene, these were not expressed *in vivo* by relevant routes of exposure. Therefore perchloroethylene is considered non-genotoxic.

**Neurotoxicity**

It is generally agreed that (acute) high-level exposures cause a depression of the central nervous system. More controversy exists on the associations that have been identified linking chronic low-level exposures to subtle effects on the nervous system function, such as reaction time measures, cognitive changes, and visual function changes. The putative neurotoxic potential of PER at low concentrations is still under debate and a common view on the matter has not yet been reached. However, the “low-dose neurotoxicity” of perchloroethylene has determined the setting of the Reference Concentration by the US EPA.

**Reproductive and developmental toxicity**

Epidemiological studies of workers in the dry-cleaning sector have found very limited and inconsistent evidence for effects on fertility (quality of semen) and foetal development (spontaneous abortions). It is unclear whether any such effects may be related to perchloroethylene alone, or to a mixture of solvents. Experimental studies with laboratory animals indicated that developmental effects only occurred at exposure levels at which the parental animals showed clear signs of toxicity.

This confirms the need for all users of perchloroethylene to comply with regulations and to implement best practices at all times.
Carcinogenicity

Laboratory animal studies

Five studies of the potential of perchloroethylene to cause cancer in laboratory animals have been conducted. Three of these showed a significant increase in formation of liver tumours in mice exposed to the solvent. A small increase in incidence of certain kidney cancers and leukaemia has been reported in rats. However, the ways these cancers form have been identified and the mechanisms are considered specific to rodents and not relevant to humans.

Epidemiology studies

In humans, there is no evidence of a link with kidney cancer, liver cancer, or leukaemia. Some studies indicate a higher risk of oesophageal cancer among people exposed to perchloroethylene, which may not be entirely attributable to lifestyle factors such as smoking and drinking alcohol. Two recent studies found no association between dry-cleaning work and cancers (including those of the oesophagus and cervix). The International Agency for Research on Cancer (IARC) concluded recently (2012) on a consistent pattern associating perchloroethylene exposure in dry cleaning workers to (only) bladder cancer as being limited evidence. However, the available human data overall does not allow a robust quantification of the cancer risk and does not suffice to identify a clear target organ for carcinogenicity. Based on extensive toxicological and epidemiological research, there is no reliable or consistent evidence that exposure to normal levels of perchloroethylene under normal working conditions increases the risk of cancer in humans.
Environmental Effects

Air

Direct photolysis is not expected to be an important removal process for perchloroethylene, but it undergoes reactions with hydroxyl radicals in the atmosphere, resulting in a half-life in the atmosphere of around 50 days. Perchloroethylene does not deplete the ozone layer, and its contribution to global warming, acid rain and smog formation is negligible.

Water

Hydrolysis in water is not an important removal process for perchloroethylene; it does not undergo photolysis in water. The most likely elimination route is evaporation to the air compartment. Generally, discharge of the substance and formulations to waste water should be prevented and recovered as much as possible. Waste waters containing perchloroethylene above certain levels need to be treated by industrial or municipal sewage treatment plants, to keep emissions to natural waters below the limits set by legislation.

Soil

In sediment and soil, perchloroethylene is fairly mobile and can leach into groundwater. Under these conditions no physico-chemical breakdown (hydrolysis) has been reported. The solvent is not biodegradable under standard test conditions, and may be resistant to breakdown in the presence of oxygen (aerobic conditions). However, in anaerobic conditions, some breakdown has been measured.

Predicted No Effect Concentrations (PNECs) derived under REACH

<table>
<thead>
<tr>
<th>Compartment</th>
<th>PNEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freshwater</td>
<td>0.051 mg/L</td>
</tr>
<tr>
<td>Marine water</td>
<td>0.0051 mg/L</td>
</tr>
<tr>
<td>Intermittent releases to water</td>
<td>0.0364 mg/L</td>
</tr>
<tr>
<td>Sediments (freshwater)</td>
<td>0.903 mg/kg sediment dry weight</td>
</tr>
<tr>
<td>Sediments (marine water)</td>
<td>0.0903 mg/kg sediment dry weight</td>
</tr>
<tr>
<td>Sewage treatment plant</td>
<td>11.2 mg/L</td>
</tr>
<tr>
<td>Soil</td>
<td>0.01 mg/kg soil dry weight</td>
</tr>
<tr>
<td>Air</td>
<td>n.a.</td>
</tr>
<tr>
<td>Secondary poisoning</td>
<td>n.a.</td>
</tr>
</tbody>
</table>
Occupational Exposure Limits

In Europe, the Scientific Committee on Occupational Exposure Limits (SCOEL) published the following recommendation in 2009:

8 hour OEL (TWA): 20 ppm (138 mg/m³)
15 min STEL (TWA): 40 ppm (275 mg/m³)

Biological Limit Values:
- 0.4 mg perchloroethylene per litre blood [sampling time: prior to the last shift of a work-week]
- 3 ppm [0.435 mg/m³] perchloroethylene in end-exhaled air [sampling time: prior to the last shift of a work-week]

Derived No Effect Levels (DNELs) for Workers and General Population derived under REACH

Workers

- DNEL inhalation long term, systemic effects: 20 ppm (138 mg/m³)
- DNEL inhalation short term, systemic effects: 40 ppm (275 mg/m³)
- DNEL dermal long term, systemic effects: 39.4 mg/kg bw/day

General Population

- DNEL inhalation long term, systemic effects: 5 ppm (34.5 mg/m³)
- DNEL inhalation short term, systemic effects: 20 ppm (138 mg/m³)
- DNEL dermal long term, systemic effects: 23 mg/kg bw/day
- DNEL oral long term, systemic effects: 1.3 mg/kg bw/day

Classification & Labelling

The below information is meant as a summary. Full information on Classification & Labelling (including precautionary statements) of the substance is to be found on the ECHA webpage of registered substances.

a) Regulation EC 1272/2008:
- Classification:
  - Carcinogenicity Cat 2: H351 Suspected of causing cancer.
  - Aquatic Chronic Cat 2: H411: Toxic to aquatic life with long lasting effects.
- **Labelling:**
  
  o Signal word: Warning

  o Pictogram: GHS08 (health hazard)  
    GHS09: environment

  o Hazard Phrase  
    H351 Suspected of causing cancer.  
    H411: Toxic to aquatic life with long lasting effects.

**b) Self-classification by the REACH consortium after GHS criteria (Regulation EC 1272/2008):**

- **Classification**

  o Skin corrosion / irritation Cat 2: H315 Causes skin irritation

  o Serious eye damage/eye irritation Cat 2: H319 Causes serious eye irritation

  o Skin Sens. 1B: H317: May cause an allergic skin reaction.

  o Carcinogenicity Cat 2: H351 Suspected of causing cancer.  
    Route of exposure: Inhalation

  o Specific target organ toxicity - single exposure Cat 3:  
    H336 May cause drowsiness or dizziness  
    Affected organs: central nervous system  
    Route of exposure: Inhalation

  o Aquatic Chronic 2 H411: Toxic to aquatic life with long lasting effects.

- **Labelling:**

  o Signal word: Warning

  o Pictograms: GHS07 (exclamation mark)  
    GHS08 (health hazard)

  o Hazard Phrase  
    H315: Causes skin irritation  
    H317: May cause an allergic skin reaction.  
    H319: Causes serious eye irritation  
    H336: May cause drowsiness or dizziness.  
    Affected organs: central nervous system.  
    Route of exposure: Inhalation

    H351: Suspected of causing cancer.  
    Route of exposure: Inhalation

    H411: Toxic to aquatic life with long lasting effects
Regulation & Voluntary Industry Action

As a highly volatile organic compound (VOC), emissions of perchloroethylene from industrial installations are regulated in the EU under the Industrial Emissions Directive (2010/75/EU) (formerly by the Solvent Emissions Directive (1999/13/EC)), and other directives. ECSA welcomes the implementation of this directive, with its goals of reducing workplace exposures and emissions from industrial installations. Modern equipment allows more efficient use of chlorinated solvents, and will continue to contribute to the sustainability of this class of products.

In 2010 ECSA members registered perchloroethylene under REACH (Regulation EC 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals). An excerpt of the registration dossier can be consulted via the ECHA website on registered substances.

In 2013 the REACH dossier was reviewed as part of the Substance Evaluation process under REACH. The resulting Evaluation Report for perchloroethylene, published by ECHA, concludes that, based on the REACH registration dossier, “no regulatory action [is] needed at EU level based on this evaluation”

ECSA released in 2011 an online toolbox, freely accessible via the ECSA website, to provide users of chlorinated solvents with information about the safe and sustainable use of these products. The recommendations do take into account REACH as well as other European legislation or voluntary industry commitments. The content of the toolbox is based on the REACH Chemical Safety Assessment (CSA) of the substances; however, it also includes recommendations based on experience of ECSA members that go beyond the given legal framework of the CSA.

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ECSA - The European Chlorinated Solvent Association

ECSA represents the interests of the producers of chlorinated solvents in the EU that are organised under Euro Chlor.

Euro Chlor is the Brussels based business association representing chlor-alkali producers in the EU and EFTA regions, employing 39,000 people at nearly 70 manufacturing sites. Almost 2,000,000 jobs in Europe are related to chlorine and its co-product caustic soda. These two key chemical building blocks underpin 55% of the European chemical industry turnover. More than 90% of the European drinking water is made safe with chlorine and about 85% of all medicines are synthesized using chlorine chemistry.

Euro Chlor is an affiliate of Cefic - the European Chemical Industry Council.

ECSA
Avenue E Van Nieuwenhuyse 4 - Box 2
B-1160 Brussels
Belgium
Web: www.chlorinated-solvents.eu
E-mail: ecsa@cefic.be