European Chlorinated Solvent Association
Part of EURO CHLOR, a Sector Group of CEFIC

WHITE PAPER

Trichloroethylene

EXECUTIVE SUMMARY

The chlorinated solvent, trichloroethylene (also known as TRI, TCE, trichloroethene, acetylene trichloride, ethylene trichloride\(^1\), 1,1,2-trichloroethylene, ethinyl trichloride and 1,1,2-trichloroethene\(^2\)) is believed to have been discovered in 1864 and was first commercially produced in Germany in the early 1900s. It has been widely used for cleaning of metals and other parts since the introduction of the vapour degreasing process in the early 1930s, and continues to be the standard to which other cleaning processes are compared. Today, its primary uses are as an intermediate in the production of hydrofluorocarbon refrigerants and as a metal degreasing agent in industry.

Chlorinated solvents have been used extensively for many years. During this time, the 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.\(^3\) When used with due care, trichloroethylene poses no threat to human health, safety or the environment.

There is no evidence that exposure to normal levels of chlorinated solvents increases the risk of cancer in humans, based on extensive toxicological and epidemiological research.\(^4,5\)

The health effects of trichloroethylene have been studied extensively. The most significant findings to come from many long-term animal studies of this solvent are that it can cause liver and lung tumours in mice. The relevance of these findings to human health is unclear, however, because of research indicating that the mechanism of liver/lung tumor induction in mice does not apply to humans. This is supported by large epidemiological studies of workers exposed to trichloroethylene that generally indicate no overall increase in cancer risk. Recent studies of

\(^3\) [http://www.eurochlor.org/facts](http://www.eurochlor.org/facts)
\(^4\) [http://www.eurochlor.org/facts](http://www.eurochlor.org/facts)
\(^5\) Perchloroethylene - ECETOC Report No 37
small populations of heavily exposed workers in Germany and France appear to show an increase in kidney cancer. Although these studies suffer from major design flaws and are inconsistent with the results of larger, better conducted studies, they were used by the European Union to revise the cancer classification of trichloroethylene. In July 2002, trichloroethylene has been classified in the EU as a category 2 carcinogen (R45). All products containing this solvent must carry the R45 hazard-warning label: “may cause cancer.”

The three European trichloroethylene producers, Dow Europe, Ineos Chlor and Chimcomplex Borzesti (Romania), have signed a product stewardship charter aimed at ensuring safe use of this chlorinated solvent in all metal-cleaning applications. The charter commits signatories to selling trichloroethylene only to end-users with enclosed equipment, thus minimising workplace exposure.

INTRODUCTION

Trichloroethylene, a colourless, volatile liquid, is an unsaturated aliphatic halogenated hydrocarbon. This chlorinated solvent is used widely by industry as a metal degreaser. It is especially valuable because of its cleaning properties, low flammability and lack of a measurable flash point. Trichloroethylene also is used as a chemical process intermediate in fluorochemical and polyvinyl chloride (PVC) production. It has been used worldwide for more than 70 years.

In the European Union, this solvent is produced by Dow Europe, Ineos Chlor and Chimcomplex Borzesti (Romania). Sales in 2006 in the EU-25 plus Norway, Switzerland and Turkey totalled 25,000 tonnes, down by 16.7% on 2005 sales (28,000 tonnes) and less than half the figure recorded in 2002 (52,000 tonnes).  

The main uses of trichloroethylene in the EU in 2003 were as follows:

<table>
<thead>
<tr>
<th>Use</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feedstock (chemical intermediate)</td>
<td>67%</td>
</tr>
<tr>
<td>Metal degreasing in vapour degreasers</td>
<td>28%</td>
</tr>
<tr>
<td>Adhesives</td>
<td>3%</td>
</tr>
<tr>
<td>Others</td>
<td>2%</td>
</tr>
</tbody>
</table>

High-purity grades of trichloroethylene are used as a feedstock in the synthesis of the refrigerant, hydrofluorocarbon 134a. Trichloroethylene is also used in PVC manufacturing and in the production of chlorinated end-products such as polychlorinated aliphatics and flame retardants.

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Key properties that contribute to trichloroethylene’s suitability for use as a metal cleaner and degreaser are:

- high solvency
- low flammability
- non-corrosiveness
- high stability
- low specific heat
- low boiling point
- low latent heat of vaporization

Trichloroethylene’s advantages for metal cleaning include the ability to degrease more thoroughly and several times faster than alkaline cleaners, and its compatibility with smaller equipment that consumes less energy. This product is an important solvent for degreasing aluminium and for cleaning sheet and strip steel prior to galvanizing. It is also used for cleaning liquid oxygen and hydrogen tanks. Commercial trichloroethylene formulations include a stabilizer system to help prevent solvent breakdown caused by contaminants such as acids, metal chips and fines, and exposure to oxygen, light and heat.

Trichloroethylene is also used as a solvent in some non-flammable adhesive and aerosol formulations, and as a low temperature heat-transfer medium.

Figure 1: European “non feedstock” market for chlorinated solvents
HEALTH EFFECTS

Chlorinated solvents have been used extensively for many years. During this time, the 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.\(^8\) When solvents are stored, used and disposed of correctly, there is no risk to human health.

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.\(^9\) As a result, good ventilation is essential in areas where the product is made or used.

**General**

Acute (short-term) overexposure to trichloroethylene vapour can cause central nervous system effects - such as light-headedness, drowsiness, headache, giddiness - which may lead to unconsciousness or prove fatal in extreme circumstances. Also, at very high exposure levels, trichloroethylene can sensitise the heart to the effects of adrenaline and similar agents, which may lead to sudden cardiac arrest. In addition, trichloroethylene may irritate the respiratory tract at high vapour concentrations. Repeated or lengthy contact with the chemical in liquid form can cause irritation of the skin and eyes. Chronic (repeated) overexposure, well in excess of recommended occupational limits, has been associated with damage to the liver and kidneys, although this is less well-documented in humans than in animals.

**Mutagenicity**

Trichloroethylene has been tested for its mutagenicity (genotoxicity) in a number of assays in bacterial and mammalian systems, both *in vivo* (laboratory animal experiments) and *in vitro* (test tube experiments). Several of these assays have been complicated by the presence of stabilizers that are known to cause positive responses. Overall, these studies indicate that pure trichloroethylene or low-stabilised trichloroethylene either has no mutagenic activity or only weak activity under certain conditions. Binding of trichloroethylene or its metabolites to protein, RNA, and DNA has been shown *in vitro*. Extremely low or no binding to DNA has been reported *in vivo*. Hence, trichloroethylene does not show significant evidence of genotoxicity in these test systems.

In the EU, trichloroethylene is classified as a category 3 mutagen, and must carry the R68 hazard-warning label: “Possible risk of irreversible effects.”

**Carcinogenicity**

*Laboratory animal studies*

The potential of trichloroethylene to cause cancer in laboratory animals has been well studied. Several studies have examined its carcinogenicity to mice, rats, and hamsters, providing both positive and negative results. Trichloroethylene has been shown to cause an increased incidence of liver and lung tumours in certain laboratory mice, and small increases in kidney tumours in male rats in some studies. Interpretation of these conflicting results requires careful examination of several factors, including variations in the purity of the test substances and difficulties in

\(^8\) [http://www.eurochlor.org/facts](http://www.eurochlor.org/facts)

\(^9\) [http://www.eurochlor.org/facts](http://www.eurochlor.org/facts)
establishing the maximum tolerated dose. Due to species differences in the metabolism of trichloroethylene, the relevance of these results to humans is uncertain.

**Significance of animal data**

Extensive research into the induction of mouse liver tumours has shown that the presence of one or more metabolites of trichloroethylene increases the number of certain intracellular organelles (peroxisomes) in the mouse liver, with an associated increase in cell division. This suggests that trichloroethylene promotes the growth of existing tumours rather than causing their initial formation.

In rats, the liver does not show peroxisome proliferation or other evidence of promotional activity following trichloroethylene exposure. This observation is consistent with the absence of liver tumour induction in long-term toxicity tests in rats. Human liver cells, similarly, do not show increases in peroxisomes in response to treatment with trichloroethylene or its metabolites. Consequently, it appears that the mechanism leading to an increase in mouse liver tumours is unlikely to occur in humans.

Laboratory research indicates that the probable mechanism underlying the increase in mouse lung tumours observed in some inhalation studies may also not be relevant to humans. A specific cell type, the Clara cell, in the mouse lung shows a dramatic cytotoxic response to the substance, chloral, which is formed in these cells by the metabolism of trichloroethylene by the cytochrome P450 pathway. The formation of mouse lung tumours is believed to result from the repeated cycle of damage and repair in the Clara cell, which occurs during the dosing regimen of the cancer study. Human lungs, in contrast, have far fewer Clara cells and exhibit little or no P450 activity. Thus, chloral is not expected to accumulate in human Clara cells.

Although marginal increases in kidney tumour incidence have only been seen in rats in certain experiments, this finding has been considered by some to be biologically significant. Hypotheses concerning the response of the rat kidney to trichloroethylene are being tested experimentally, and it is generally believed that the mechanism involved has no relevance to humans. In any case, it appears that risk to humans is negligible at current levels of exposure. This conclusion is supported by the findings of large, well-conducted epidemiological studies.

**Epidemiological studies**

Studies of US workers exposed to trichloroethylene have consistently indicated no overall increase in cancer risk. A retrospective study of over 7,000 U.S. aircraft maintenance workers followed for an average of 25 years failed to demonstrate any significant association between exposure to trichloroethylene and an excess rate of cancer. Two similar studies of 4,700 and 2,300 exposed workers found no significant increase in cancer mortality despite additional potential exposure through contaminated groundwater in one of the studies. These and other epidemiological studies on trichloroethylene provide support for the conclusion that this substance does not pose a risk of cancer, including kidney cancer, under normal conditions of occupational exposure and when products are used in accordance with manufacturers’ instructions.

A study of a small number of employees at a German cardboard factory reported a substantial increase in the risk of kidney cancer, which appeared to be associated with trichloroethylene exposure. Reviewers of this study have criticised its conclusions because the existence of a cluster of cases was recognisable before the study began. As a result, they note that the study
cannot be used as an independent test of an association. Two small case-control studies conducted in Germany by the same group also appeared to support a link between trichloroethylene exposure and kidney cancer. However, the design of these studies has also been criticised, particularly the selection of control subjects. The results of these studies are not consistent with other larger, well-conducted epidemiological studies, none of which has associated trichloroethylene exposure with an increased risk of kidney cancer. More recently a case-control study on kidney cancer and occupational exposure to trichloroethylene has been conducted in France (Charbotel et al 2006). The study consisted of 86 cases of kidney cancer and 316 controls. In the highest exposure group with over 335 ppm-years of trichloroethylene exposure a statistically significant association with kidney cancer was reported.

Impairment of the function of the von Hippel-Lindau (VHL) tumour suppressor gene is known to be involved in most cases of human kidney cell cancer. Recently, a German group of researchers reported a possible association between trichloroethylene exposure and multiple mutations of the VHL gene among kidney cancer patients, including a high proportion of subjects showing a specific "hot spot" mutation. Induction of multiple mutations in a single gene, however, is believed by experts to be highly unlikely to lead to development of a tumour. While experts in the VHL research field believe that a specific “hot spot” mutation could be highly significant, further testing has failed to confirm the original observation. Additional research on the VHL gene on cases of human kidney cell cancer of a trichloroethylene exposed group was conducted recently. An association between VHL gene mutations and exposure to trichloroethylene was not confirmed.

Cancer classification
The International Agency for Research on Cancer (IARC) currently classifies trichloroethylene in Group 2A, as a substance considered "probably carcinogenic" to humans. IARC, following its own restrictive classification scheme, concluded that the combination of the results from some of the epidemiology studies provided “limited” evidence of carcinogenicity in humans.

In the EU, trichloroethylene is classified as a category 2 carcinogen (R45), and must carry the R45 hazard-warning label: “may cause cancer.”

Reproductive and developmental toxicity
There have been a number of inconclusive reports of developmental toxicity in populations exposed to trichloroethylene and other chemicals in their drinking water. In an attempt to understand trichloroethylene’s developmental toxicity more fully, the US industry recently sponsored a new study following Environmental Protection Agency guidelines. Pregnant rats were exposed to up to 600 ppm trichloroethylene for 6 hours per day, 7 days per week during gestation. The top dose of 600 ppm was chosen because it is known to result in some toxicity in pregnant rats. No maternal toxicity was observed in the lower doses (50 and 150 ppm) and no evidence of developmental toxicity was observed in the foetuses at any dose.

Several earlier studies evaluated the ability of trichloroethylene to affect the reproductive or developmental process in animals. Inhalation studies in rats, mice, and rabbits at concentrations ranging from 300 ppm to 1,800 ppm showed no significant developmental effects. At 300 ppm, no significant maternal toxicity, embryotoxicity or foetotoxicity was seen in Sprague-Dawley rats or Swiss-Webster mice. No significant effects were observed in Sprague-Dawley rats
exposed to 500 ppm. A non-significant increased incidence of hydrocephalus (brain swelling) was seen in New Zealand rabbits exposed to 500 ppm. This effect is now recognized as an artefact of the techniques employed, however, and unrelated to solvent exposure. Slight foetotoxicity and growth depression were seen in Long-Evans rat offspring at 1,800 ppm. A dominant lethal study in mice suggests the absence of any adverse effect on the male reproductive system.

This spectrum of animal data indicates that trichloroethylene is unlikely to have an adverse effect on human reproduction or development when handled in accordance with manufacturers' instructions.

**ENVIRONMENTAL EFFECTS**

Trichloroethylene does not deplete the ozone layer, and its contribution to global warming, acid rain and smog formation is negligible.\(^9\)

**REGULATION**

Trichloroethylene use is regulated under the Solvent Emissions Directive (1999/13/EC).\(^11,12\) ECSA welcomes the implementation of this directive, with its goals of reducing workplace exposures and environmental emissions. Modern equipment allows more efficient use of chlorinated solvents, and will continue to contribute to the sustainability of this class of product.

For any solvent classified as a carcinogenic, mutagenic or reprotoxic (CMR) substance, it is important to strictly control human exposure. In metal cleaning, this is best achieved by ensuring that solvents are only used in closed systems. Such control measures are important not only for trichloroethylene but also for some solvents marketed as alternatives.

**Occupational exposure**

The exposure limits for trichloroethylene are as follows\(^13\):

**Occupational Exposure Limits (8-hour TWA)**

<table>
<thead>
<tr>
<th>Country</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>50 ppm</td>
</tr>
<tr>
<td>Belgium</td>
<td>50 ppm</td>
</tr>
<tr>
<td>Denmark</td>
<td>10 ppm</td>
</tr>
<tr>
<td>France</td>
<td>75 ppm</td>
</tr>
</tbody>
</table>

\(^9\) [http://www.eurochlor.org/facts](http://www.eurochlor.org/facts)
\(^10\) [http://www.eurochlor.org/solventemissionsdirective](http://www.eurochlor.org/solventemissionsdirective)
\(^12\) [http://www.eurochlor.org/qandatrienglish](http://www.eurochlor.org/qandatrienglish)
Beyond Compliance

ECSA strongly recommends that trichloroethylene only be used in applications where all relevant workplace, disposal and other environmental regulatory requirements are met. In addition, many prudent operators have chosen to adopt practices and standards that go beyond the strict legal requirements for use, management and disposal of trichloroethylene and trichloroethylene-containing wastes. In addition to taking full responsibility for environmental protection, these operators help to avoid potential liability for any environmental contamination that can be traced to their solvent wastes - whether at their own plant or elsewhere - regardless of whether they have complied with the letter of the law. Such additional measures that go “beyond compliance” make good business sense because they minimise risks of liability.

The three European trichloroethylene producers, Dow Europe, Ineos Chlor and Chimcomplex Borzesti (Romania), have signed a product stewardship charter aimed at ensuring safe use of this chlorinated solvent in metal-cleaning applications. The charter commits signatories to selling trichloroethylene only to end-users with enclosed equipment, thus minimising workplace exposure. This will ensure adequate control of the risks in this application identified in the EU Risk Assessment.

In line with the Responsible Care® initiative, signatories agree to phase out sales of trichloroethylene for open metal-cleaning systems no later than 31 December 2010. This is intended to safeguard the long-term sustainable use of TRI in closed systems for metal cleaning.

This charter – developed by ECSA – continues the European chlorinated solvent sector’s commitment to best product stewardship practices along the entire supply chain. It will be presented to the European Commission as a follow-up to an action plan put forward on 12 December 2006. ECSA is now working to identify all companies who plan to import trichloroethylene into the EU via the REACH registration process. All such firms will be strongly encouraged to sign the charter.

Regulatory and technical information for trichloroethylene

Chemical formula: C$_2$HCl$_3$
Molecular weight: 131.4
CAS-number: 79-01-6
EINECS-number: 201-167-4
Classification: Carc.Cat.2; R45 – Muta.Cat. 3; R68 – R67 – Xi; R36/38 – R52-53
Risk phrases: R45, R36/38, R67, R52/53
Safety phrases: S53, S45, S61