



## **European Chlorinated Solvent Association**

Part of Euro Chlor, a Sector Group of CEFIC

### **WHITE PAPER**

#### *Methylene chloride*

#### **EXECUTIVE SUMMARY**

The chlorinated solvent, methylene chloride (also known as dichloromethane) has been used in industry for over 80 years. Its unique combination of properties - low boiling point, high solvency power, relative inertness, low toxicity and non flammability - has led to its wide variety of applications, such as paint and varnish removal, as an extraction medium/process solvent, and in aerosols, electronics and metal cleaning. It is the most widely-used of the chlorinated solvents, particularly for pharmaceutical production.

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.<sup>1</sup> When used with due care, methylene chloride poses no threat to human health, safety or the environment. With sound operating practices that ensure exposure levels at or below mandatory levels, methylene chloride does not present an unacceptable risk for human health 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.<sup>2</sup> As a result, good ventilation is essential in areas where the product is made or used. ECSA also strongly encourages use of state-of-the-art, contained systems to avoid the release of methylene chloride into the environment.

Methylene chloride does not deplete the ozone layer, and its contribution to global warming, acid rain and smog formation is negligible.<sup>3</sup> Chlorinated solvents are unlikely to accumulate in living organisms or the environment.

Methylene chloride use is regulated under the Solvent Emissions Directive (1999/13/EC).<sup>4,5</sup>

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<sup>1</sup> <http://www.eurochlor.org/facts>

<sup>2</sup> <http://www.eurochlor.org/facts>

<sup>3</sup> <http://www.eurochlor.org/facts>

<sup>4</sup> <http://www.eurochlor.org/solventsemissionsdirective>

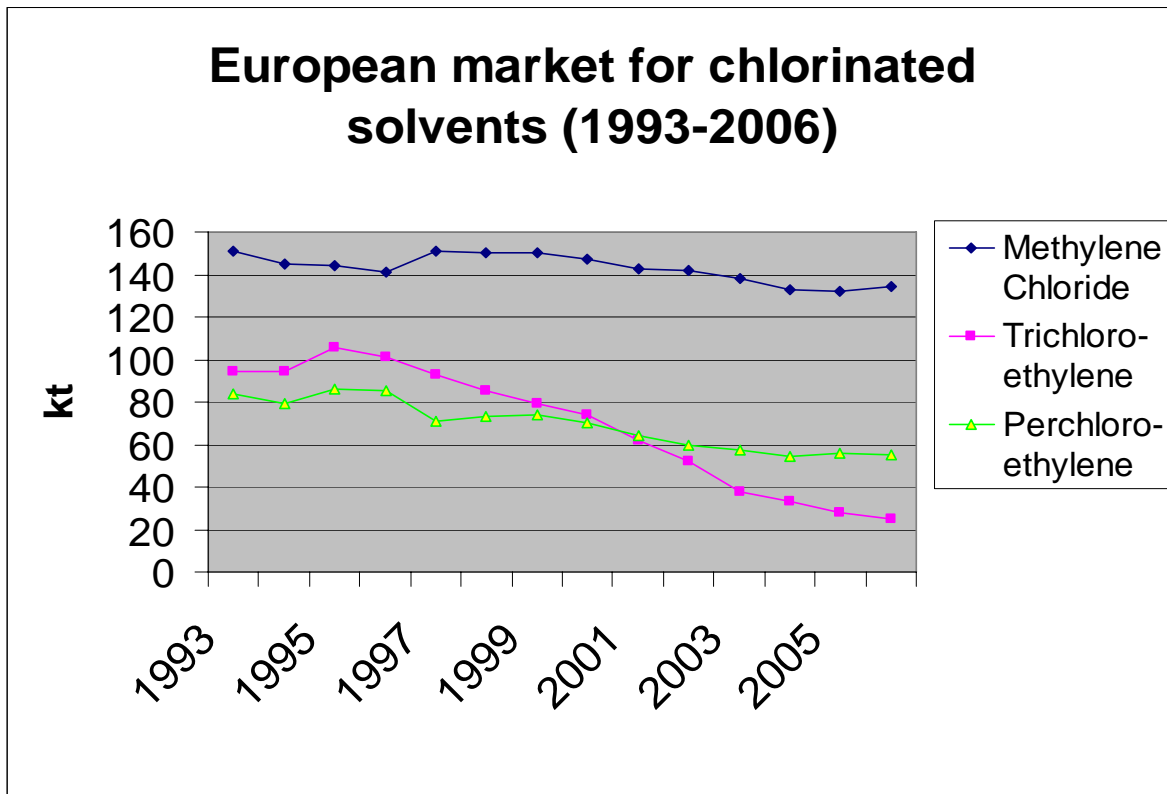
## INTRODUCTION

Methylene chloride is a widely used chlorinated solvent with diverse applications. It is commonly used in paint removers and industrial adhesives, and is also used in the production of flexible urethane foams, pharmaceutical products and plastics, as a cleaning agent for fabricated metal parts, and as an extraction solvent.

Methylene chloride is a saturated aliphatic halogenated compound. It is a colourless, volatile liquid, completely miscible with a variety of other solvents.

In Europe, methylene chloride is manufactured by Arkema, Dow Europe, Ercros, Ineos Chlor, LII Europe and Solvay.<sup>6</sup>

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



<sup>5</sup> [http://eur-lex.europa.eu/LexUriServ/site/en/oj/1999/l\\_085/l\\_08519990329en00010022.pdf](http://eur-lex.europa.eu/LexUriServ/site/en/oj/1999/l_085/l_08519990329en00010022.pdf)

<sup>6</sup> <http://www.eurochlor.org/solvents>

## USES

Methylene chloride's main uses are:

- **Chemical intermediate** : Methylene chloride is used as a chemical intermediate (for HFC 32)
- **Extraction medium** : Methylene chloride is used as an extraction medium in food and pharmaceutical processes because of its high solvency, high purity and the relative ease with which it can be distilled from the final product (used for tablet coating in pharmaceutical processes) These applications account for 52% of European “non feedstock” usage
- **Process solvent** : It is also used as process solvent for polycarbonate production, cellulose esters, triacetate production and triacetate esters which account for 10 % of European “non feedstock” usage. .
- **Paint and varnish remover**: Methylene chloride is the most commonly used solvent in paint stripping, which accounts for 11% of European usage of this compound. It is a quick acting solvent for both wash-off and scrape-off formulations.
- **Metal cleaning**: Vapour degreasing is an important method to remove oils, grease and soils from surface, accounting for 5% of European methylene chloride use. For sensitive metals, methylene chloride is ideal because of its low boiling temperature.
- **Aerosols**: Methylene chloride is an excellent solvent for most of the ingredients in aerosol formulations, an end-use that represents 4% of European usage of this product. When used in aerosols, it reduces flammability and also leads to less pressure inside the aerosol compared to other solvents.
- **Other uses**: Methylene chloride is also used in a variety of other applications, for example: adhesive formulations, plastic processing, secondary blowing agent in polyurethane foam, as a refrigerant, and as photoresistant stripper in the production of printed circuit boards. These end-uses account for the remaining 17% of European methylene chloride use.

## 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.<sup>7</sup> When solvents are stored, used and disposed of correctly, there is no risk to human health.

Individuals are usually exposed to methylene chloride by inhalation of its vapour. Splashes of the liquid can also come into contact with the skin and eyes and, occasionally, can be ingested, usually by accident.

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<sup>7</sup> <http://www.eurochlor.org/facts>

When inhaled, methylene chloride is rapidly absorbed through the lungs. It is also absorbed through the gastro-intestinal tract and to a lesser extent, the skin. Once in the body, it is quite rapidly excreted, mostly unchanged *via* the lungs. It can cross the blood-brain barrier, can be transferred to an unborn child across the placenta, and small amounts can be excreted in breast milk.

When high levels of methylene chloride are absorbed, most of it is exhaled unchanged. The remainder is metabolised to carbon monoxide, carbon dioxide and inorganic chloride. The metabolic pathway of carbon monoxide includes the formation of carboxyhemoglobin, which reduces the blood's ability to carry oxygen, and may exacerbate heart disease. However, the metabolic pathway becomes saturated in humans, thus limiting the production of carbon monoxide and preventing excessive build-up of carboxyhemoglobin.

#### ***Acute and short-term exposure***

The odour threshold of methylene chloride is 200 ppm. Its acute toxicity is low compared to many other chemicals.

Splashes of liquid methylene chloride entering the eyes can cause irritation that ceases when the eyes are rinsed. Repeated contact with the skin also causes irritation, mainly due to its de-fatting properties. Prolonged contact with undiluted product may cause blistering.

#### ***Genotoxicity***

Methylene chloride consistently gives positive results in only one of the wide variety of tests for genotoxicity, the Ames bacterial mutagenicity test. These have been reported from a range of independent laboratories. In other *in vitro* test systems, the product gives negative or equivocal results. In the majority of *in vivo* studies that have been reported, it has no effect. Based on currently available information, there is no conclusive evidence that methylene chloride is mutagenic in living organisms.

#### ***Neurotoxicity***

Several toxicological studies have been performed to investigate the effects of long-term exposure to methylene chloride on the Central Nervous System (CNS). The results indicate no significant neurotoxic effects after exposure to concentrations of up to 2,000 ppm for 90 days. There is, therefore, no evidence that long-term exposure to methylene chloride causes irreversible CNS effects. No neurotoxic effects have been seen in people at typical occupational exposures.

However, over-exposure by inhalation (to concentrations in air >300 ppm) can cause reversible CNS effects and may initially result in light-headedness and headache. Continued exposure to high levels may result in loss of consciousness and can suddenly prove fatal. Since methylene chloride is metabolised to carbon monoxide, an increase in carboxyhaemoglobin levels occurs in the blood, reducing its ability to carry oxygen and adding to the reversible CNS effects.

#### ***Reproductive and developmental toxicity***

Several studies of potential reproductive and developmental effects of methylene chloride have been carried out on mice and rats. Results indicate that there are no adverse effects at concentrations of up to 5,000 ppm for one hour. In three animal studies, no effects were reported on the incidence of skeletal malformations or other developmental parameters. In a two-generation inhalation study in

rats exposed to methylene chloride at up to 1,500 ppm, no adverse effect on any reproductive parameter was found in either generation.

Based on these data there is no evidence that exposure to methylene chloride causes adverse effects on reproduction or development.

### ***Carcinogenicity***

#### *Laboratory animal studies*

Following lifetime exposure to high concentrations (2,000 and 4,000 ppm), methylene chloride is carcinogenic to mice, causing both lung and liver tumours. These tumours are not seen in rats or hamsters.

In inhalation studies conducted on rats, an increase in the number of benign mammary tumours was found on exposure to concentrations of 500 to 3,500 ppm methylene chloride. At lower concentrations (50 to 200 ppm), no significant increase in these tumours was observed.

Importantly, no progression toward malignancy was observed in these studies. A small increase in sarcomas in the region of the salivary gland has been reported, but this was not seen in subsequent studies with rats at the same exposure. Furthermore, it was reported that the rats in the first study had been infected with a common viral disease that affects primarily the salivary gland.

The mammary tumours in rats are probably due to an indirect mechanism operating *via* increased prolactin levels in blood. The absence of mammary tumours in mice and hamsters, together with a difference in prolactin response (absent in mice and hamster) suggests that the findings are of little relevance for human risk assessment.

#### *Significance of animal data*

Following the observation that methylene chloride produces tumours in mice but not in rats or hamsters, research was initiated to investigate the reason for these differences and to determine their significance for human health.

The first phase of the research established that methylene chloride is metabolised by two pathways. At low doses in mice, rats and humans, it is metabolised primarily by the cytochrome P450 oxidative pathway. The second pathway involves metabolism by a specific member of the theta glutathione-S-transferase (GST) class of enzymes. The oxidative pathway is used in all rodents studied and in humans, and seems to be the predominant metabolic route at lower concentrations (<500 ppm). The GST pathway is a major metabolic pathway only in mice and then only at high dose levels after saturation of the P450 pathway.

The research showed that the tumours in mice were associated with the metabolism of methylene chloride *via* GST, a pathway that is species specific. It was shown that this pathway is used to a far greater extent by mice than by rats, which in turn use it more than hamsters or humans.

Sophisticated studies of enzyme distributions in mouse, rat, and human liver and lung provide strong biochemical support for the conclusion that the increase in lung and liver tumours seen in mice exposed to high levels of methylene chloride is unique to that species. The enzyme kinetic data,

along with other relevant physiological data, have been used to create toxicokinetic models of methylene chloride metabolism in humans. These models have shown that the carcinogenic risk for humans following exposure to methylene chloride is negligible, a conclusion that is supported by the findings of epidemiological studies.

### ***Epidemiology studies***

Several epidemiological studies have investigated the mortality and cancer incidence patterns in large populations exposed to methylene chloride during its manufacture or use. These studies, where cohorts of industrial workers are compared with corresponding non-exposed populations, show no association between increased cancer risk and exposure to relatively high concentrations of methylene chloride. The exposure concentrations in the facilities under investigation regularly exceeded 100 ppm as daily time weighted averages and occasionally exceeded 500 ppm. The typical follow-up periods of these studies were between 20 and 50 years of observation. Considered as a whole, the available epidemiological evidence does not indicate a carcinogenic risk associated with occupational exposure to methylene chloride.

### ***Carcinogenicity classification***

In the EU, methylene chloride is classified as a category 3 carcinogen, described as “Substances which cause concern for man owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment. There is some evidence from appropriate animal studies, but this is insufficient to place the substance in category 2”. The chemical has to be labelled as Harmful (Xn), with the risk phrase R40 (“Limited evidence of a carcinogenic effect”).<sup>8</sup>

## **REGULATION**

Methylene chloride use is regulated under the Solvent Emissions Directive (1999/13/EC).<sup>9,10</sup> 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.

Methylene Chloride will be controlled under the EU Water Framework Directive (2000/60 EC) which is setting objectives to keep rivers, lakes, groundwater and coastal beaches clean.

### ***Environmental exposure***

#### ***Air***

The atmospheric lifetime of methylene chloride is several months. Due to its high volatility, this substance will mainly be transferred from the aquatic environment to air. In the troposphere, methylene chloride is then broken down in carbon dioxide and hydrogen chloride.

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<sup>8</sup> [http://ec.europa.eu/enterprise/chemicals/docs/studies/tno-methylene\\_chloride.pdf](http://ec.europa.eu/enterprise/chemicals/docs/studies/tno-methylene_chloride.pdf), page 38

<sup>9</sup> <http://www.eurochlor.org/solventemissionsdirective>

<sup>10</sup> [http://eur-lex.europa.eu/LexUriServ/site/en/oj/1999/l\\_085/l\\_08519990329en00010022.pdf](http://eur-lex.europa.eu/LexUriServ/site/en/oj/1999/l_085/l_08519990329en00010022.pdf)

*Methylene Chloride White Paper ( 2007) -*

Methylene chloride does not have ozone depletion potential. In addition, it does not significantly contribute to smog formation nor to global warming.

*Water*

In the aquatic environment as well as in soil, methylene chloride is completely degraded *via* natural processes.

Methylene chloride is not expected to bioaccumulate in aquatic organisms.

***Occupational exposure***

Occupational Exposure Limits (8-hour TWA)

Netherlands (MAC) : 100 ppm

United Kingdom (OEL) : 100 ppm (MEL)

Germany (MAK) : 100 ppm (IIIB suspected carcinogen)

Sweden (TLV) : 35 ppm (skin notation)

France (VME) : 50 ppm

Switzerland (MAK) : 100 ppm

USA (ACGIH): 50 ppm (A2, suspected human carcinogen)

***Beyond Compliance***

ECSA strongly recommends that methylene chloride 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 methylene chloride and methylene chloride-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.

***Regulatory and Other Information for Methylene Chloride***

Chemical formula : CH<sub>2</sub>Cl<sub>2</sub>

Molecular weight : 84.93

CAS number : 75-09-2

Odour threshold : 250 to 300 ppm

EU number : 602-004-00-3

Labelling EU (67/548/EEC) : Xn. R40, Harmful : Limited Evidence of a Carcinogenic Effect

Cosmetic EEC 76/768 dichloromethane allowed up to 35% amended by 2003/15/EC prohibition of CMRs 1, 2 and 3, in cosmetics although cat 3 substances can be used if found acceptable by SCCNFP

Food extraction EEC 88/334 amended by 92/115/EC: allowed:

coffee : max residue 2 mg/kg

tea : max residue 5 mg/kg

Maximum residue limits in the foodstuff due to the use of extraction solvents in the preparation of flavourings from natural flavouring materials 0.02 mg/kg.<sup>11</sup>

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<sup>11</sup> Exception: 1 mg /kg in confectionery and pastry products containing flavourings which are characteristic of the foodstuff and are obtained from extracts of alcoholic beverages of an alcoholic strength of over 35.