February 1989

HSIA Perchloroethylene White Paper

Executive Summary

Animal studies of perchloroethylene have shown an increased incidence of liver tumors in mice and marginal or equivocal results in rats. The relevance of these results to humans, however, has been questioned because of research indicating that the mechanism of liver tumor induction in mice does not apply to humans. Further, the results of an epidemiology study of 615 dry cleaner workers occupationally exposed only to perchloroethylene found no evidence of an increased overall cancer mortality rate.

On the basis of this available evidence, perchloroethylene does not appear to pose a health hazard to humans under normal conditions of occupational exposure, and when products are used in accordance with manufacturers instructions. It is nevertheless important that workplace activities and user operations should continue to be carried out in such a way as to keep exposure as low as is reasonably practicable.

Introduction

Perchloroethylene, also known as tetrachloroethylene, has been used safely in industry for almost 50 years, and is the primary solvent used in commercial and industrial dry cleaning. Since being introduced to the dry cleaning industry in the late 1930's, it has replaced carbon tetrachloride and most petroleum solvents because of its relatively low toxicity and nonflammability. Its other major uses are as a metal cleaning and degreasing solvent, and as a chemical intermediate in the production of several chlorofluorocarbons.

Perchloroethylene is a member of a family of aliphatic halogenated hydrocarbons. It is a colorless, volatile liquid that is essentially nonflammable and has no measurable flashpoint. In the United States, perchloroethylene is produced by Dow Chemical U.S.A., Occidental Chemical Corporation, PPG Industries, Inc., and Vulcan Materials Company. The 1987 production was about 473.1 million pounds (about 214,700 metric tons), of which 54.1 million pounds (24,500 metric tons) were exported. An additional 136.4 million pounds (61,900 metric tons) were imported.

Uses

For 1987 the uses of perchloroethylene can be broken down into the following categories:

dry cleaning/textile processing	50%
chemical intermediate	33%
metal cleaning/degreasing	11%
miscellaneous	6%

■DRY CLEANING

Perchloroethylene is used by approximately 75 percent of all dry cleaners, including industrial, commercial, and coin-operated establishments. It had replaced other synthetic solvents, such as carbon tetrachloride, by the late 1940's or early 1950's. A gradual shift from petroleum derivatives to perchloroethylene began in the late 1940's. This shift in solvents increased in the 1950's and early 1960's. However, in the period before 1960, petroleum derivatives were still the dominant solvents.

In addition to its nonflammability and relatively low toxicity, popularity of perchloroethylene in the dry cleaning industry can be attributed to the following properties:

- safe to use on all common textiles, fibers, and dyes;
- effective at removing fats, oils, and greases;
- free of residual odor;
- chemically stable under all common use conditions;
- non-corrosive to the metals and other materials used in dry cleaning machinery;
- easily removed from clothes by rapid, safe drying; and
- energy- and cost-efficient (can be easily distilled and reused).

The textile industry uses perchloroethylene as a spotting agent for the removal of spinning oils and lubricants. It also is used in wool scouring and as a solvent carrier in dyes and water repellants.

■CHEMICAL INTERMEDIATE

Perchloroethylene is used as a basic raw material in the manufacture of chlorofluorocarbons (CFC's), principally trichlorotrifluoroethane (CFC-113), which is used in the electronics industry, in metal cleaning, and in dry cleaning. The chemical also is used in the synthesis of hydrofluorocarbon 134a (HFC-134a), and can be used for the synthesis of hydrochlorofluorocarbon 142b and 141b (HCFC-142b and HCFC-141b).

■METAL CLEANING/DEGREASING

Many industries, including aerospace, appliance, and automotive manufacturers, use perchloroethylene for vapor degreasing metal parts during various production stages. Its high boiling point and resultant longer cleaning cycle are advantageous in removing "difficult" soils such as waxes with high melting points. The ability of the chemical to remove water during vapor degreasing is useful to jewelry manufacturers and other metal finishers.

Perchloroethylene's nonflammability and low vapor pressure make it an effective cold (room temperature) metal cleaner,

either alone or when blended with flammable solvents. Its low vapor pressure contributes to reduced emissions from cleaning operations where it is employed.

■MISCELLANEOUS

Perchloroethylene is used as an insulating fluid in some electrical transformers as a substitute for polychlorinated biphenyls (PCBs). Relatively small quantities of perchloroethylene are used in printing inks, aerosol specialty products, adhesive formulations, paper coatings, and silicones. In addition, perchloroethylene is used in chemical maskant formulations used to protect surfaces from chemical etchants.

Health Effects

■GENERAL

Overexposure to perchloroethylene can affect the central nervous system (CNS) and the liver. Prolonged exposure to concentrations of 200 parts per million (ppm) or more has been associated with dizziness, confusion, headache, nausea, and irritation of the eyes and mucous tissue. At higher level exposures (>600 ppm) these symptoms are intensified. Prolonged exposure to sufficiently high levels (>1500 ppm) may lead to unconsciousness due to anesthesia and, in extreme cases, death from respiratory depression.

Reversible changes in the liver and kidney of laboratory animals have been reported following prolonged exposure to concentrations of 200 ppm or more. In humans, reversible alterations in liver function also have been noted in persons exposed to high levels of perchloroethylene vapor for extended periods of time. No cause-effect relationship has been established between kidney effects and exposure to perchloroethylene in humans.

■GENOTOXICITY

The ability of perchloroethylene to cause genetic mutations has been tested in bacteria, laboratory animals, and human tissue. The preponderance of these data indicate that the chemical is not mutagenic. Commercial formulations of the chemical have elicited weakly positive responses in some yeast and bacterial assays, but only when toxic concentrations of perchloroethylene were used. Moreover, no dose-response relationships were established. In a study conducted using highly purified perchloroethylene, no evidence of mutagenic effect was observed in the bacteria tested.

■CARCINOGENCITY

Laboratory Animal Studies

Three studies of the carcinogenic potential of perchloroethylene in laboratory animals have been conducted. Two of the studies showed a significant increase in liver tumors in mice. The strain of mice used in these studies (B6C3F1), however, has a high and variable spontaneous incidence of liver tumors.

A study, reported by the National Cancer Institute (NCI) in 1977, exposed (by gavage) Osborne-Mendel rats and B6C3F1 mice to up to 949 milligrams of perchloroethylene per kilogram (mg/kg) body weight and up to 1072 mg/kg body weight, respectively, each day, 5 days a week, for 78 weeks. The study showed a significant increase in liver tumors in both sexes of mice. Low survival in the rats tested, believed to result from exposure to doses higher than the maximum tolerated dose (MTD), compromised the study's ability to detect a carcinogenic effect in this species. Because of several significant limitations in its design and conduct, the results of this study should be interpreted with caution.

The Dow Chemical Company conducted an inhalation study of the carcinogenic effect of perchloroethylene on Sprague-Dawley rats. The Dow study exposed male and female rats to 0, 300, and 600 ppm of the chemical for 6 hours per day, 5 days per week, for 52 weeks (and observed them for another 52 weeks), and showed no significant differences between the exposed and control animals.

In 1986 the National Toxicology Program (NTP) reported the results of a 2-year inhalation study that found a significant increase in liver tumors in male and female B6C3F1 mice. The study exposed the mice and Fischer 344 rats to perchloroethylene concentrations of 0, 100, and 200 ppm and 0, 200, and 400 ppm, respectively, for 6 hours per day, 5 days a week, for the length of the study. NTP also reported an increased incidence in mononuclear cell leukemia in male and female rats and a marginal increase in kidney tumors in male rats. NTP concluded that these data demonstrated "clear evidence" of carcinogenicity in mice and male rats and "some evidence" of carcinogenicity in female rats.

Science Advisory Board Review of the NTP Study

After reviewing the results of the NTP study, the Science Advisory Board of the Environmental Protection Agency (EPA) concluded that the study does not provide a basis for associating either the leukemias or the kidney tumors observed in the rats with exposure to perchloroethylene. The Board's conclusion was based on the high spontaneous background rate of leukemia in concurrent and historical controls in this particular rat strain and the low incidence of rat kidney tumors in the NTP study. In addition, the Board stated that the mechanism responsible for the marginal increase in kidney tumors appears to be unique to male rats and is probably not operative in humans. The Board also indicated that the increase in the mouse liver tumors may have been due to the operation of a mechanism such as peroxisome proliferation (see below).

Significance of the Mouse Liver Data

Following the observation that perchloroethylene produces liver tumors in mice, but not in rats, studies were initiated to investigate the reasons for this species difference and to determine the significance of the mice data to humans. This research indicates that perchloroethylene is not the proximal (actual) carcinogen in the mouse bioassays, but that a metabolite of perchloroethylene, trichloroacetic acid (TCA), is the likely cause of the mouse liver tumor response. Tumor induction in rodent liver cells has been associated with TCA and the TCA-induced proliferation of enzyme-containing organelles (called peroxisomes) in the cells. Production of TCA occurs at a much higher rate in mice than in rats, which are genetically similar organisms, and at an even lower rate in humans than in mice or rats. Moreover, in vitro exposure of human liver cells to TCA did not result in peroxisome proliferation.

This research explains why liver tumors were seen in mice, but not rats, and strongly suggests that perchloroethylene is unlikely to cause liver cancer in humans.

Epidemiology Studies

A number of epidemiology studies have investigated the incidence of cancer mortality among dry cleaning workers. These studies, for the most part, cover dry cleaning workers who were exposed to a variety of cleaning agents, including petroleum solvents. Results have recently become available, however, from an exhaustive epidemiology study of the dry cleaning industry sponsored by the National Institute for Occupational Safety and Health (NIOSH), which has the potential to show a cause-effect relationship to perchloroethylene exposure. Significantly, this study shows no increased risk of cancer in a subgroup of dry cleaning workers exposed only to perchloroethylene.

The NIOSH study found the overall cancer mortality rate in dry cleaning workers to be higher than, but not significantly different from, that predicted using U.S. mortality rates. The relative number of cancer deaths among the workers studied was reduced when compared to the higher cancer mortality rates in the metropolitan areas investigated. Among the site-specific cancer mortalities, urinary tract cancer (particularly in the bladder) was the only one found to have a significant increase. Within the subgroup of workers exposed only to perchloroethylene, the incidence of mortality from urinary tract cancer (and from cancer, in general) was lower than that expected from overall U.S. mortality rates.

Carcinogenicity Classification
The International Agency for Research on Cancer (IARC) has classified perchloroethylene in Group 2B, as a substance considered "possibly carcinogenic to humans." The American Conference of Governmental Industrial Hygienists (ACGIH) has not classified perchloroethylene as a carcinogen. A final decision has not been made by EPA as to the classification of perchloroethylene under its Guidelines for Carcinogen Risk Assessment.

■REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Several studies of the effects of perchloroethylene on mammalian reproduction have been performed on mice, rats, and rabbits. The results of these animal tests do not indicate any significant reproductive effects.

In studies of female Sprague-Dawley rats and Swiss-Webster mice exposed by inhalation to a perchloroethylene concentration of 300 ppm during gestation, no reproductive effects were observed. A similar result was observed in CD rats and New Zealand rabbits after females were exposed to 500 ppm of the chemical before and during gestation. An inhalation study of Long-Evans hooded female rats exposed to 1000 ppm of perchloroethylene prior to and during gestation found a significant reduction in body weight and excess variation in skeletal and soft tissue development. However, weight gain and survival of offspring followed up to 18 months of age were not influenced by exposure to perchloroethylene. Some changes in maternal body weight and liver and kidney weight were noted in these studies.

On the basis of these laboratory data, EPA concluded that there is no evidence suggesting that the fetus is uniquely susceptible to the effects of perchloroethylene.

Regulation

Perchloroethylene is regulated as a volatile organic compound (VOC) under most state regulations implementing the national ambient air quality standards for ozone. Although EPA has recognized that perchloroethylene does not contribute appreciably to smog formation, it has not taken final action to allow the exemption of perchloroethylene from state VOC regulations.

In 1985 EPA published a notice of intent to list perchloroethylene as a hazardous air pollutant under the Clean Air Act. Perchloroethylene may be regulated as a toxic air pollutant in some states.

For various industries EPA has established effluent limitation guidelines, which may contain effluent limitations for perchloroethylene. EPA also has published water quality criteria for perchloroethylene for use by states in developing water quality standards. Various states also may have drinking water regulations that may apply to perchloroethylene. Perchloroethylene waste is considered hazardous waste under the Resource Conservation and Recovery Act (RCRA).

The reportable quantity for release of perchloroethylene under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA, or Superfund) is 1 pound. EPA has proposed raising this level to 100 pounds. Perchloroethylene is one of several hundred chemicals subject to material safety data sheet (MSDS), inventory, and release reporting under Sections 311, 312, and 313 of the Emergency Planning and Community Right-to-Know Act (Title III of Superfund Amendments and Reauthorization Act of 1986.)

The Occupational Safety and Health Administration (OSHA) recently lowered the permissible exposure limit (PEL) for perchloroethylene from 100 ppm to 25 ppm for an 8-hour time-weighted average (TWA), based on potential carcinogencity. ACGIH currently recommends threshold limit values (TLV's) of 50 ppm (TWA) and 200 ppm (15-minute short-term exposure limit, or STEL) for workplace exposure.

REGULATORY (FEDERAL) AND OTHER INFORMATION FOR PERCHLOROETHYLENE

Chemical Formula	$CCl_2=CCl_2$
Molecular Weight	165.9
CAS Number	127-18-4
OSHA PEL	
8-hr TWA	25 ppm
ACGIH TLV	
8-hr TWA	50 ppm
15-min STEL	200 ppm
IARC Classification	2B[1]
CERCLA Reportable Quantity	1 lb[2]
Maximum Contaminant Level (Drinking Water)	—
RCRA Hazardous Waste Number	U 210
DOT Hazard Class	ORM-A
DOT ID Number	UN 1897
SARA Title III Reporting	YES

1 - A chemical in IARC Group 2B is considered "possibly carcinogenic to humans." This classification for perchloroethylene is based on IARC's finding of "sufficient" evidence for carcinogenicity in animals, and "inadequate" evidence of carcinogenicity in humans.

2 - EPA proposed raising the reportable quantity for perchloroethylene from 1 pound to 100 pounds in March 1987, but has not yet taken final action on this proposal.

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