NIOSH

Current Intelligence Bulletin 46

April 18, 1986

METHYLENE CHLORIDE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
National Institute for Occupational Safety and Health

DISCLAIMER

Mention of the name of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health.

DHHS (NIOSH) Publication No. 86-114

FOREWORD

Current Intelligence Bulletins (CIB's) are issued by the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control, Atlanta, Georgia, for the purpose of disseminating new scientific information about occupational hazards. A CIB may draw attention to a hazard previously unrecognized or may report new data suggesting that a known hazard is either more or less dangerous than was previously thought.

CIB's are prepared by the staff of the Division of Standards Development and Technology Transfer, NIOSH (Robert A. Taft Laboratories, 4676 Columbia Parkway, Cincinnati, Ohio 45226) and are distributed to representatives of organized labor, industry, public health agencies, academia, and public interest groups as well as to those federal agencies, such as the Department of Labor, which have responsibilities for protecting the health of workers. It is our intention that anyone with the need to know should have ready access to the information contained in these documents; we welcome suggestions concerning their content, style, and distribution.

NIOSH estimates that 1 million workers are potentially exposed to methylene chloride during its manufacture and use; as a solvent, aerosol propellant or fumigant, and as a blowing agent in flexible urethane foams. In 1976, NIOSH published a document entitled Criteria for a Recommended Standard....Occupational Exposure to Methylene Chloride. In that criteria document, NIOSH recommended a 10-hour time-weighted average (TWA) occupational exposure limit of 75 parts per million (ppm) in order to prevent interference by methylene chloride with delivery of oxygen to tissues, and impairment in functions of the central nervous system (CNS). Since 1976, the carcinogenicity of methylene chloride has been documented in several studies of chronic effects in animals. On the basis of carcinogenic and tumorigenic responses in rats and mice, and in accordance with the Cancer Policy of the Occupational Safety and Health Administration (OSHA) ("Identification, Classification, and Regulation of Potential Occupational Carcinogens," 29 CFR 1990), NIOSH recommends that methylene chloride be regarded as a "potential occupational carcinogen." Although the potential for methylene chloride-induced cancer in humans has not been determined, the probability of a population of exposed workers developing cancer could be decreased by reducing exposure. Therefore, NIOSH recommends that occupational exposure to methylene chloride be controlled to the lowest feasible limit.

It is also recommended that producers and users of methylene chloride disseminate this information to their workers and customers, that professional and trade associations and unions inform their members of the potential hazards of working with methylene chloride, and that appropriate engineering controls and work practices be used to reduce the exposure of workers to the lowest feasible extent.

J. Donald Millar, M.D., D.T.P.H. (Lond.)
Assistant Surgeon General
Director, National Institute for
Occupational Safety and Health
Centers for Disease Control

CURRENT INTELLIGENCE BULLETIN #46

METHYLENE CHLORIDE

APRIL 18, 1986

ABSTRACT

$B6C3F_1$ mice exposed to methylene chloride in air developed cancers (alveolar/bronchiolar carcinomas) and tumors (alveolar/bronchiolar adenomas) of the lung, and cancers (hepatocellular carcinomas) of the liver. Fischer 344/N rats exposed to methylene chloride in air developed tumors (fibromas and fibroadenomas) of the mammary gland. Sprague-Dawley rats exposed to methylene chloride in air developed cancers (sarcomas) of the salivary glands and tumors (fibromas and fibroadenomas) of the mammary glands. Though existing epidemiologic data derived from workers exposed to methylene chloride are inconclusive, the observation of cancers and tumors in both rats and mice treated with methylene chloride meets the criteria established in the Occupational Safety and Health Administration (OSHA) Cancer Policy for considering methylene chloride a "potential occupational carcinogen." Therefore, the National Institute for Occupational Safety and Health (NIOSH) recommends that worker exposure to methylene chloride be controlled to the lowest feasible limit.

BACKGROUND

Physical and Chemical Properties

Methylene chloride is a colorless, volatile, nonflammable liquid with a penetrating, ether-like odor that is detectable at about 200 parts per million (ppm) in air [1,2]. The chemical and physical properties of methylene chloride are listed in Table 1.

TABLE 1.--Chemical and physical properties of methylene chloride

Chemical identity	Methylene chloride
CAS[a] registry no.	75-09-2
RTECS[b] accession no.	PA8050000
Synonyms	DCM, dichloromethane, methane dichloride, methylene bichloride, methylene dichloride
Molecular weight	84.93
Empirical formula	CH_2Cl_2
Melting point	-96.7°C (-142°F)
Boiling point (at 760 mm Hg)	40.1°C (104.2°F)
Vapor density (air=1)	2.93
Concentration in saturated air (25°C)	550,000 ppm
Specific Gravity (20°C)	1.326
Solubility:	
Water	Slight
Ethyl alcohol	Soluble
Ethyl ether	Soluble
Acetone	Soluble
Carbon disulfide	Soluble

[a]Chemical Abstract Service
[b]Registry of Toxic Effects of Chemical Substances

Production, Use, and Potential for Occupational Exposure

In 1984, approximately 628 million pounds of methylene chloride [3] were produced and imported by the United States. Methylene chloride is widely used in paint removers, degreasing agents, and aerosol propellants; as a blowing agent in flexible urethane foams; as a process solvent in the manufacture of pharmaceuticals and food products, including the

decaffeination of coffee; and as a fumigant for grains and fruits [1,4]. An estimated 1 million workers are potentially exposed to methylene chloride or to products that contain this chemical [4].

EXPOSURE LIMITS

The current Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for methylene chloride (29 CFR 1910.1000 Table Z-2) is an 8-hour time-weighted average (TWA) concentration of 500 parts per million (ppm), with a ceiling concentration of 1000 ppm, and a maximum peak concentration of 2000 ppm for no more than 5 minutes within any 2 hours [5]. The PEL for methylene chloride was adopted in 1971, without rulemaking, under the authority of section 6(a) of the Occupational Safety and Health Act of 1970. The OSHA standard was derived from a standard recommended by the American National Standards Institute (ANSI).

In 1976, the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit (REL) for methylene chloride was 75 ppm, 261 milligrams per cubic meter (mg/m^3), as a TWA for up to a 10-hour workday, 40-hour workweek with a 500 ppm (1740 mg/m^3) peak exposure concentration as determined over any 15-minute sampling period during the workday. This REL was based on the need to prevent significant interference with the delivery of oxygen to the tissues of the body and abnormalities in functions of the central nervous system (CNS) as a result of the production of carboxyhemoglobin attendant to metabolism of methylene chloride. The toxicities of methylene chloride and carbon monoxide (CO) are additive [6]. Because of this additive effect, provisions for calculating a reduced REL for methylene chloride in the presence of CO were included in the NIOSH document entitled Criteria for a Recommended Standard....Occupational Exposure to Methylene Chloride [6]. When concentrations of CO exceed 9 ppm in the workplace, either the concentration of methylene chloride or the concentration of CO should be reduced. The 9 ppm value is that included in the air quality standard of the Environmental Protection Agency (EPA) and was derived from data which indicated that typical background concentrations of CO in environments, in the United States, were generally less than 10 ppm and frequently greater than 5 ppm [7].

The 8-hour TWA Threshold Limit Value (TLV®) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH) is 100 ppm (348 mg/m^3) with a 500 ppm Short Term Exposure Limit (STEL) [8]. This TLV is based on experimental data obtained from male, non-smoking subjects at rest. The ACGIH stated that the blood of workers who were exposed at 100 ppm of methylene chloride would have carboxyhemoglobin levels below 5% in their blood [9]. In addition, the TLV documentation indicates that the concentration of methylene chloride in air should be lowered in the presence of CO, according to the appropriate equation for mixtures. The ACGIH further cautioned that: "concurrent exposures to other sources of carbon monoxide or physical activity will require assessment of the overall exposure and adjustment for the combined effect" [9].

TOXICITY

Carcinogenic Effects

A study sponsored by the National Coffee Association (NCA) was designed to evaluate the oncogenic potential of methylene chloride administered to Fischer 344/N rats in their drinking water. There were 85 rats of each sex for each exposure group; 141 rats of each sex served as controls. Based on historical data for water consumption, the investigators designed the study so that the amount of methylene chloride ingested would be approximately 0, 5, 50, 125, or 250 milligrams of pure methylene chloride per kilogram of body weight per day (mg/kg/day) during the 2-year study [10]. In a second study, similarly treated $B6C3F_1$ mice consumed about 0, 60, 125, 185, or 250 mg/kg/day [11]. A total of 125 males and 100 females served as controls. The number of animals in the exposed groups varied. There were 200 males and 100 females at 60 mg/kg/day, 100 males and 50 females each at 125 mg/kg/day and 185 mg/kg/day, and 125 males and 50 females at 250 mg/kg/day. The actual delivered doses in each study were generally within 10% of the target doses. The data obtained from the rats indicated that methylene chloride-dosed females had an increased incidence of neoplastic nodules and/or hepatocellular carcinomas. The incidence of the neoplasms was significant with respect to matched controls; however, the incidence of tumors was stated, by the investigators, to be within the range of tumor incidence rates among control animals from previous studies that had been conducted in the investigators' laboratory. No carcinogenic response was indicated in any of the treated groups of mice. Under the conditions of their study, the investigators concluded that treatment with methylene chloride for up to 104 weeks did not induce a carcinogenic response.

In an inhalation study [12] sponsored by an industry group subsequently named the Halogenated Solvents Industry Alliance (HSIA), a total of 1,032 male and female Sprague-Dawley rats (129 of each sex at each exposure concentration) and a total of 866 male and female Golden Syrian hamsters (107 to 109 of each sex at each exposure concentration) were exposed at concentrations of 0, 500, 1500, or 3500 parts per million (ppm) of methylene chloride (99.5% pure) for 6 hours per day, 5 days per week for 2 years. The authors stated that "approximately" 95 rats and hamsters of each sex at each exposure concentration were used for studies of chronic toxicity and carcinogenicity. The remainder of the animals of each species, sex, and exposure group were used in hematologic and cytogenetic studies (rats at 6 months only) and killed after either 6, 12, 15, or 18 months of exposures. Groups of 4 rats and 4 hamsters of each sex, from each exposure group, were used to obtain blood for carboxyhemoglobin determinations after 6, 11, 18, 21, or 22 (hamsters only) months of exposures [12].

There were no unusual or statistically significant hematologic or cytogenetic effects observed among either rats or hamsters of either sex at any exposure concentration [12]. However, the mean percent of carboxyhemoglobin in the blood was increased and statistically significant

for each species and sex at each exposure concentration at each time examined (6, 11, 18, and 21 months) as compared to control animals. The increase did not appear to be dose- or time-related since the carboxyhemoglobin concentration did not vary with the concentration or duration of exposure to methylene chloride.

Although female rats, at all three exposure concentrations, had dose-related increases in the total number of benign mammary gland tumors (adenomas, fibromas, and fibroadenomas) per tumor-bearing rat, as compared to the tumor-bearing controls, the number of rats with tumors in each exposure group did not increase. An increased incidence of the mammary gland tumors was also reported for the male rats exposed at 3500 ppm, but the increase was less pronounced than that for the females. The male rats exposed to 3500 ppm of methylene chloride also had a statistically significant increase in the incidence of salivary gland cancer (sarcomas) compared with controls. A similar response, though not statistically significant, was reported among male rats exposed at 1500 ppm. The investigators suggested that a salivary gland viral disease (sialodacryoadenitis) in the rats, combined with the methylene chloride exposures, may have been associated with the development of this tumorigenic response; however, the sarcomas were not identified in the similarly infected female rats exposed to methylene chloride. Male and female hamsters exposed under similar experimental conditions as those used for studies on the Sprague-Dawley rats showed no evidence of a carcinogenic response [12].

A subsequent HSIA-sponsored inhalation study [13] was performed with male and female Sprague-Dawley rats at methylene chloride concentrations of 0, 50, 200, or 500 ppm, 6 hours per day, 5 days per week for 2 years. This study was designed to investigate further the responses observed at the higher exposure concentrations used in the previous study [12]. A slight increase, but not statistically significant, occurred for mammary fibromas and fibroadenomas per female rat exposed at 500 ppm of methylene chloride as compared to control rats. No increased incidence of salivary gland tumors (sarcomas) was observed in any exposure or control group.

As in the earlier study [12], the percent of carboxyhemoglobin in the blood was elevated in rats of each sex, at each exposure concentration, and at each time examined (6, 12, 15, 18, and 24 months). However, unlike the data obtained from the first study which used higher doses, the carboxyhemoglobin response obtained in this study [13], indicated to the investigators, that the metabolism of methylene chloride is dose-related and saturable.

Data from two additional studies of the animal carcinogenicity of methylene chloride are available from a 1985 National Toxicology Program (NTP) technical report [14]. Groups of Fischer 344/N rats and $B6C3F_1$ mice were exposed to methylene chloride (maximum purity, 99%) by inhalation for 2 years, 6 hours per day, 5 days per week at concentrations of 0, 1000, 2000, or 4000 ppm and 0, 2000, or 4000 ppm, respectively. There was a statistically significant increase in the number of benign mammary gland tumors (fibroadenomas) in male rats exposed at 4000 ppm and in the female

rats exposed at 1000, 2000, or 4000 ppm, when compared to controls. Based on these findings, the NTP stated that "...there was some evidence of carcinogenicity of dichloromethane for male F344/N rats as shown by an increased incidence of neoplasms of the mammary gland. There was clear evidence of carcinogenicity of dichloromethane for female F344/N rats as shown by increased incidences of neoplasms of the mammary gland."

In the study of $B6C3F_1$ mice, a statistically significant increase in lung cancers (alveolar/bronchiolar carcinomas) and benign lung tumors (alveolar/bronchiolar adenomas) over controls was reported among males and females exposed at concentrations of 2000 or 4000 ppm. A statistically significant increase was also reported for cancers (hepatocellular carcinomas) of the liver in male mice exposed at 4000 ppm and in female mice exposed at 2000 or 4000 ppm. The NTP concluded "...that there was clear evidence of the carcinogenicity of dichloromethane for male and female $B6C3F_1$ mice as shown by increased incidences of alveolar/bronchiolar neoplasms and of hepatocellular neoplasms" [15].

The studies which indicate the potential of methylene chloride to induce cancers or tumors in experimental animals appear well conducted and without major shortcomings. A possible exception to this pattern is suggested by the report of sialodacryoadenitis among male rats exposed at 1500 ppm methylene chloride in the HSIA study. Otherwise, there were no indications of toxicity that would be expected to interfere with findings of carcinogenicity in these studies.

Epidemiologic Studies

The results of a proportionate mortality study of all deaths, occurring from 1956 through 1976, among active, disabled, or retired males who worked in areas of a plant which manufactured photographic products were published in 1978 [16]. Methylene chloride was used as a primary solvent in the plant studied. The environmental exposures varied from 0 to 350 ppm with a general decline in mean exposure concentrations from 118.8 ppm in 1966 to 40.3 ppm in 1975. The typical patterns of exposure encountered by these workers is unclear. Deaths of all other male workers at the plant were used as a comparison population. Although this proportionate mortality study did not demonstrate any significant excess mortality for any of the disease categories, the study design was limited by: (1) evaluation of only those who died while employed or who were disabled or retired workers, (2) the interrelated nature of the proportionate mortality categories, and (3) the necessary but unverified assumption of equal proportions of cause-specific mortality in the exposed and comparison populations except for the effects of exposure.

These same investigators [16] reported the results of a cohort mortality study of 751 hourly, male workers employed at this plant, in 1964, in the methylene chloride exposure areas, of which 252 had a minimum of 20-years work exposure. This cohort included a greater proportion of long-term

workers than was typical of cohort studies and did not include the mortality of exposed workers who terminated employment before 1964. Two comparison populations were used for this study; one included male hourly workers in the same plant, the other from the general male population of New York State, excluding New York City. Two updates of the original report have been published [17,18]. Each update covered an additional 4 years of mortality experience. The original report and subsequent updates cover a total of 20 years of follow-up (1964-1984). The hypertensive disease category (International Classification of Diseases, 8th Revision, 400-404) was reported as significant (4 observed vs. 1 expected on other Kodak Park workers) in the original report, but this category was not considered in the subsequent updates. No other excesses were reported as statistically significant in the three reports. A non-significant excess of cancer of the pancreas was observed in the total cohort (8 observed vs. 3.0 expected in the New York State and 2.6 expected in the in-plant comparison populations). However, it is noteworthy that this excess was associated with a significance level of less than 5% but greater than 1%, with the latter value being the statistical criteria used for non-hypothesized risk categories [19]. It is also noteworthy that this study had only a 35% statistical power to detect an association at this level of significance [20]. The conclusions from this study are limited by: (1) a narrow cohort definition, (2) limited documentation of exposure, (3) unclear standardization of coding between revisions of the International Classification of Diseases, (4) lack of follow-up on the small number of terminated, non-vested workers, and (5) low statistical power to detect modest increases in less common site-specific cancers.

A second study [21,22] described the mortality experience of two cohorts of workers involved in the manufacture of synthetic fibers: (1) 1,271 workers exposed to methylene chloride and acetone and (2) a reference group exposed only to acetone. Both groups were exposed to these substances for at least 3 months between 1954, when methylene chloride was first used, and 1977, when the study ended. Methylene chloride exposure concentrations ranged from 5 to 900 ppm [21]. Although exposure categories were defined as low, moderate, or high, the observed mortality was not analyzed according to these categories. The cause of death due to malignant neoplasms did not exceed the expected number of deaths based on the U.S. death rates. However, the small number of workers exposed and the relatively short latency period for most of the workers precludes the capability of definitively evaluating an occupational carcinogenic effect in the exposed cohort. When the methylene chloride-acetone exposed cohort mortality experience was compared using a summary statistical analysis to the acetone reference cohort mortality experience, statistically significant differences were observed for deaths from diseases of the circulatory system and from ischemic heart disease [22]. The interpretation of this study is limited by: (1) low statistical power to detect increases in overall malignant neoplasms and site-specific cancers, (2) absence of analysis for qualitative exposure categories, (3) loss to vital status follow-up for 18% of the cohort members, and (4) too brief of a follow-up to detect occupationally related cancer.

CONCLUSIONS

The research data presented in this Current Intelligence Bulletin (CIB) have focused on the carcinogenic effects observed in animals or workers exposed to methylene chloride. The lung, liver, and salivary and mammary glands are the primary sites of carcinogenic or tumorigenic responses in methylene chloride-treated mice and rats. One epidemiologic study, of a small worker population, provides limited evidence that methylene chloride exposure may be related to the increased risk of pancreatic cancer.

As stated earlier, the studies which indicate the potential for methylene chloride to induce cancers or tumors in experimental animals are without major shortcomings. The strains of animals used and the route and doses selected for administration of methylene chloride impose no limitations on the interpretation of the results. Therefore, NIOSH believes that the collective carcinogenicity data provide sufficient evidence to warrant concern about the potential consequences of occupational exposure to methylene chloride.

It is of interest that the studies funded by the Halogenated Solvents Industry Alliance (HSIA) [12,13] found that the concentration of carboxyhemoglobin in the blood of experimental animals was dose related over the exposure range of 0 to 500 ppm and was elevated, but not dose related over the range of 500 to 3500 ppm, indicating to the investigators that metabolic saturation had occurred. These results may explain, in part, why neoplasms were found only among those animals exposed at concentrations in excess of 500 ppm in the HSIA studies. However, these data provide no insight concerning the potential for tumor development among animals that may have been exposed at the lower doses for periods greater than 2 years. This cannot be supported by results from the National Toxicology Program (NTP) study [14] because the animals were exposed at concentrations of 1000 ppm and higher, and because carboxyhemoglobin concentrations were not determined. Some data on the dose-related increase of carboxyhemoglobin were previously described in the 1976 NIOSH criteria document on methylene chloride [6]; in that document, carboxyhemoglobin concentrations were reported to increase with exposure concentration and time over a range of concentrations of 50 to 1000 ppm following exposures of 1 to 7.5 hours per day, 5 days per week. These latter data indicate that the pathway to produce carboxyhemoglobin had not been saturated at methylene chloride exposure concentrations as high as 1000 ppm.

RECOMMENDATIONS

Several methods for identifying a substance as a carcinogen have been proposed. Such classifications have been developed by the National Toxicology Program (NTP) [15], the International Agency for Research on Cancer (IARC) [23], and the Occupational Safety and Health Administration (OSHA) in its "Identification, Classification, and Regulation of Potential Occupational Carcinogens" (29 CFR 1990) [24], also known as "The OSHA Cancer

Policy." Since the OSHA Cancer Policy specifically addresses occupational exposures, NIOSH considers that policy to be the most appropriate for use in identifying a substance as a potential occupational carcinogen.

In its Cancer Policy, OSHA provides criteria that must be applied in order to identify, classify, and regulate a substance as a potential occupational carcinogen. In 29 CFR 1990.112(b), the Policy states: "A substance shall be identified and regulated as a Category II Potential Carcinogen if, upon scientific evaluation, the Secretary determines that; (ii) the substance meets the criteria set forth in 1990.112(a) in a single mammalian species without evidence of concordance." In 1990.112(a) concordance is defined as: "Positive results from independent testing in the same or other species, positive results in short-term tests, or induction of tumors at implantation sites."

Provisions for the use of human and animal data are provided in 1990.143 of the OSHA Cancer Policy. In 1990.143(f), the Policy accepts data obtained following oral, respiratory, or dermal exposure; in 1990.143(g) the Policy allows the use of "high" dose exposures; and in 1990.143(i), the Policy allows the use of either benign or malignant tumors to establish a qualitative inference of carcinogenicity.

The data obtained by the NTP from studies with methylene chloride using rats [14] demonstrate exposure and dose-related increases in benign mammary tumors in males and females, respectively, and exposure-related malignant tumors of the lung and liver in male and female mice. These data in conjunction with the data obtained by the HSIA [12] are sufficient to classify methylene chloride as an OSHA Category I potential carcinogen as described in 1990.112(a).

Although additional support for this classification is not provided by the epidemiologic studies conducted to date [16-18,21,22], such concordance is not required by the OSHA Cancer Policy.

Because methylene chloride has been shown to induce increased numbers of benign and malignant neoplasms in rats and mice, it meets the criteria provided in the OSHA Cancer Policy for classifying a substance as a potential occupational carcinogen; therefore, NIOSH recommends that methylene chloride be considered a potential human carcinogen in the workplace.

The finding of an excess of pancreatic cancers (non-statistically significant) in a small cohort of methylene chloride-exposed workers is also of concern.

The excess risk of cancer to workers exposed to specific airborne concentrations of methylene chloride has not yet been determined, but the

probability of developing such an adverse effect would be decreased by reducing exposure. As prudent public health policy, employers should voluntarily assess the conditions under which workers may be exposed to methylene chloride and take all reasonable precautions to reduce exposures to the lowest feasible limit.

Indications of the carcinogenicity of methylene chloride are not the only concern NIOSH has regarding worker exposure to this widely used solvent. NIOSH's original recommendation concerning exposure to methylene chloride was based, in part, on findings of impaired delivery of oxygen to tissues. At that time, NIOSH described methylene chloride-exposed workers who experienced chest pains, heart palpitations, and rapid pulse. The report of excess mortality from ischemic heart disease in one methylene chloride-exposed cohort [22] appears to be consistent with earlier findings reported by NIOSH. Those findings are not conclusive and require additional verification. Nevertheless, by controlling methylene chloride exposures to the lowest feasible limit, employers can ensure that the concentration of carboxyhemoglobin in the blood does not exceed acceptable levels as described in the 1976 NIOSH criteria document [6].

REFERENCES

1. Methylene chloride. In: Kirk-Othmer encyclopedia of chemical technology. 3rd ed. New York: John Wiley & Sons, Inc., 1979;5:691-692.

2. Leonardos G, Kendall D, Barnard N. Odor threshold determinations of 53 odorant chemicals. J Air Pollut Control Assoc 1969;19(2):91-107.

3. Analysis of the applicability of TSCA section 4(f) to methylene chloride. [Report prepared by U.S. Environmental Protection Agency, 1985. Public docket no. OPTS 48503, ECAD, 45-8503024].

4. Occupational exposure and environmental release assessment of methylene chloride. [Report prepared for Office of Pesticides and Toxic Substances, U.S. Environmental Protection Agency, contract no. 68-02-3935, by PEI Associates, Inc., Cincinnati, 1985. Public docket no. OPTS 48503, 45-8503010].

5. Code of Federal Regulations. U.S. Department of Labor. Occupational Safety and Health Administration. 29 CFR 1910.1000, Table Z-2, rev. July 1, 1985.

6. Criteria for a recommended standard....occupational exposure to methylene chloride. Cincinnati: U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, 1976;DHEW (NIOSH) publication no. 76-138.

7. Code of Federal Regulations. U.S. Environmental Protection Agency. 40 CFR 50.8, rev. July 1, 1985.

8. American Conference of Governmental Industrial Hygienists. TLVs® Threshold limit values and biological exposure indices for 1985-86. Cincinnati: ACGIH, 1985.

9. American Conference of Governmental Industrial Hygienists, Inc. Documentation of the Threshold Limit Values. 4th Ed. Cincinnati: ACGIH, 1980:275-276.

10. Twenty-four month chronic toxicity and oncogenicity study of methylene chloride in rats: Vol. 1 [Unpublished final report prepared for the National Coffee Association by the Hazleton Laboratories America, Inc., Vienna, Virginia, 1982].

11. Twenty-four month chronic toxicity and oncogenicity study of methylene chloride in mice: Vol. 1 [Unpublished final report prepared for the National Coffee Association by the Hazleton Laboratories America, Inc., Vienna, Virginia, 1983].

12. Burek JD, Nitschke KD, Bell TJ, et al. Methylene chloride: a two-year inhalation toxicity and oncogenicity study in rats and hamsters. Fund Appl Toxicol 1984;4:30-47.

13. Nitschke KD, Burek JD, Bell TJ, Rampy LW, McKenna MJ. Methylene chloride--a two-year inhalation toxicity and oncogenicity study in rats. [Unpublished final report prepared by the Toxicology Research Laboratory, Health and Environmental Sciences, Dow Chemical, Midland, Michigan, 1982].

14. National Toxicology Program--technical report series no. 306. Toxicology and carcinogenesis studies of dichloromethane (methylene chloride) (CAS No. 75-09-2) in F344/N rats and B6C3F$_1$ mice (Inhalation Studies). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Feb 1985; NTP publication no. 85-024.

15. National Toxicology Program--technical report series no. 288. Toxicology and carcinogenesis studies of 1,3-butadiene (CAS No. 106-99-0) in B6C3F$_1$ mice (Inhalation Studies). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, 1984; NIH publication no. 84-2544.

16. Friedlander BR, Hearne FT, Hall S. Epidemiologic investigation of employees chronically exposed to methylene chloride--mortality analysis. J Occup Med 1978;20(10):657-666.

17. Hearne FT, Friedlander BR. Follow-up of methylene chloride study [Letters]. J Occup Med 1981;23:660.

18. Friedlander BR, Pifer JW, Hearne FT. 1964 Methylene chloride cohort mortality study--update through 1984. Epidemiology Section, Health and Environment Laboratories, Eastman Kodak Company, Rochester, New York, 1985.

19. Confidence limits for the expectation of a Poisson variable. In: Biometrika tables for statisticians, vol. I. Cambridge: University Press, 1956:203.

20. Beaumont J, Bressler N. Power considerations in epidemiologic studies of vinyl chloride workers. Amer J Epidemiol 1981;114(5):725-734.

21. Ott MG, Skory LK, Holder BB, Bronson JM, Williams PR. Health evaluation of employees occupationally exposed to methylene chloride--general study design and environmental considerations. Scand J Work Environ Health 1983;9(Suppl 1):1-7.

22. Ott MG, Skory LK, Holder BB, Bronson JM, Williams PR. Health evaluation of employees occupationally exposed to methylene chloride--mortality. Scand J Work Environ Health 1983;9(Suppl 1):8-16.

23. World Health Organization. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Lyon, France: IARC, 1979; (Suppl 1).

24. Code of Federal Regulations. U.S. Department of Labor. Occupational Safety and Health Administration. 29 CFR 1990, rev. July 1, 1985.

APPENDIX

GUIDELINES FOR MINIMIZING WORKER EXPOSURE TO METHYLENE CHLORIDE

Based on the conclusions described in this Current Intelligence Bulletin (CIB), NIOSH recommends that employers, workers, and health care professionals take the following actions to reduce the long-term risk of cancer and the possible risk of adverse effects on the cardiovascular system as a result of methylene chloride exposure.

1. Employers should:

   A. Control worker exposure to the lowest feasible limit through effective engineering controls, good work practices, and proper maintenance procedures.

   B. Provide appropriate exhaust ventilation or control exposure by enclosed processes.

   C. Provide isolation of workers by the use of remote control rooms and utilization of automated equipment.

   D. Provide appropriate personal protective clothing and equipment to minimize contact with the skin and eyes, and require workers to change clothing that has become contaminated with methylene chloride.

   E. Provide clothing change rooms, showers, and eating areas free from methylene chloride or other chemical exposure. Eating and smoking should not be permitted in areas where methylene chloride is manufactured, stored, or used.

   F. Provide suitable and effective respiratory protective equipment (Table 2); provide fit testing and training on the proper use of respirators and provide for regular maintenance, inspection, and cleaning of respirators.

   G. Provide routine personal air monitoring for workers potentially exposed to methylene chloride and inform them of the results of analysis. Monitoring for carbon monoxide (CO) should also be conducted.

   H. Provide a medical monitoring program that will detect methylene chloride-induced health effects (Table 3). Provide physicians or other health care personnel with all toxicologic information, industrial hygiene sampling data, and a listing of protective devices or equipment the worker may be required to use when a potential for exposure to methylene chloride exists. Conduct medical evaluations to determine the worker's physical fitness for using respiratory protective equipment.

TABLE 2.--Respirator selection for methylene chloride

Conditions of use	Recommended respirator
For any condition requiring the use of respirators except as noted below	Self-contained breathing apparatus equipped with a full facepiece and operated in a pressure-demand or other positive pressure mode or Supplied-air respirator equipped with a full facepiece and operated in a pressure-demand or other positive pressure mode in combination with an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode
Firefighting situation	Self-contained breathing apparatus with a full facepiece and operated in a pressure-demand or other positive pressure mode
Escape situations	Any air-purifying respirator equipped with a full facepiece (gas mask) and an organic vapor canister; or any appropriate escape-type self-contained breathing apparatus

TABLE 3.--Signs and symptoms of methylene chloride exposure

Eye or skin irritation

Dizziness

Incoordination

Nausea

Tingling or numbness of extremities

Irritability

Lethargy

Stupor

I. When possible, replace methylene chloride with a chemical that has been shown not to cause cancer or other adverse health effects in animals or in humans.

J. Provide a worker education program which is designed to inform the worker about the potential health risks from exposure to methylene chloride, the proper use of personal protective equipment or clothing, smoking cessation programs, and proper work practice procedures.

K. Provide all workers who are or who may be exposed to methylene chloride with a copy of this CIB pointing out the list of adverse symptoms and health effects associated with exposure to methylene chloride (Table 3).

II. Workers should:

A. Make appropriate use of personal protective equipment and respirators provided by the employer.

B. Avoid contact with methylene chloride and immediately change clothing that has become contaminated with the chemical.

C. Immediately and thoroughly wash with soap and water all areas of the body that come into contact with methylene chloride.

D. Report any health signs and symptoms of exposure to methylene chloride to the responsible health professional. If a private physician is used, see that the physician receives a copy of this CIB.

III. Physicians and other health care professionals should:

A. Be familiar with the signs and symptoms that are suggestive of exposure of workers to methylene chloride (Table 3).

B. Maintain complete medical, chemical exposure, and occupational history information for each worker.

C. Perform periodic medical examinations, giving particular attention to the respiratory, cardiovascular, and nervous systems and to the liver, pancreas, blood, and skin, as these are the primary targets of exposure to methylene chloride.

CUMULATIVE LIST OF NIOSH CURRENT INTELLIGENCE BULLETINS

1.	Chloroprene	- January 20, 1975
2.	Trichloroethylene	- June 6, 1975
3.	Ethylene Dibromide	- July 7, 1975
4.	Chrome Pigment	- June 24, 1975 - October 7, 1975 - October 8, 1976
5.	Asbestos - Asbestos Exposure during Servicing of Motor Vehicle Brake and Clutch Assemblies	- August 8, 1975
6.	Hexamethylphosphoric Triamide (HMPA)	- October 24, 1975
7.	Polychlorinated Biphenyls	- November 3, 1975
8.	4,4'-Diaminodiphenylmethane (DDM)	- January 30, 1976
9.	Chloroform	- March 15, 1976
10.	Radon Daughters	- May 11, 1976
11.	Dimethylcarbamoyl Chloride (DMCC) Revised	- July 7, 1976
12.	Diethylcarbamoyl Chloride (DECC)	- July 7, 1976
13.	Explosive Azide Hazard	- August 16, 1976
14.	Inorganic Arsenic - Respiratory Protection	- September 27, 1976
15.	Nitrosamines in Cutting Fluids	- October 6, 1976
16.	Metabolic Precursors of a Known Human Carcinogen, Beta-Naphthylamine	- December 17, 1976
17.	2-Nitropropane	- April 25, 1977
18.	Acrylonitrile	- July 1, 1977
19.	2,4-Diaminoanisole in Hair and Fur Dyes	- January 13, 1978
20.	Tetrachloroethylene (Perchloroethylene)	- January 20, 1978
21.	Trimellitic Anhydride (TMA)	- February 3, 1978
22.	Ethylene Thiourea (ETU)	- April 11, 1978
23.	Ethylene Dibromide and Disulfiram Toxic Interaction	- April 11, 1978
24.	Direct Black 38, Direct Blue 6, and Direct Brown 95 Benzidine Derived Dyes	- April 17, 1978
25.	Ethylene Dichloride (1,2-Dichloroethane)	- April 19, 1978
26.	NIAX® Catalyst ESN	- May 22, 1978
27.	Chloroethanes - Review of Toxicity	- August 21, 1978
28.	Vinyl Halides - Carcinogenicity Vinyl Bromide, Vinyl Chloride, and Vinylidene Chloride	- September 21, 1978
29.	Glycidyl Ethers	- October 12, 1978
30.	Epichlorohydrin	- October 12, 1978
31.	Adverse Health Effects of Smoking and the Occupational Environment	- February 5, 1979
32.	Arsine (Arsenic Hydride) Poisoning in the Workplace	- August 3, 1979
33.	Radiofrequency (RF) Sealers and Heaters: Potential Health Hazards and Their Prevention	- December 4, 1979
34.	Formaldehyde: Evidence of Carcinogenicity	- April 15, 1981
35.	Ethylene Oxide (EtO): Evidence of Carcinogenicity	- May 22, 1981
36.	Silica Flour: Silicosis	- June 30, 1981
37.	Ethylene Dibromide (EDB) Revised	- October 26, 1981

CUMULATIVE LIST OF NIOSH CURRENT INTELLIGENCE BULLETINS (CONTINUED)

38.	Vibration Syndrome	- March 29, 1983
39.	The Glycol Ethers, with Particular Reference to 2-Methoxyethanol and 2-Ethoxyethanol: Evidence of Adverse Reproductive Effects	- May 2, 1983
40.	2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD, "Dioxin")	- January 23, 1984
41.	1,3-Butadiene	- February 9, 1984
42.	Cadmium	- September 27, 1984
43.	Monohalomethanes: Methyl Chloride, Methyl Bromide, and Methyl Iodide	- September 27, 1984
44.	Dinitrotoluene	- July 4, 1985
45.	Polychlorinated Biphenyls (PCB's): Potential Health Hazards from Electrical Equipment Fires or Failures	- February 24, 1986
46.	Methylene Chloride	- April 18, 1986

NOTE: For the convenience of those who desire a complete series of Current Intelligence Bulletins, #1 through #18 and #19 through #30 have been reprinted as NIOSH publications #78-127 and #79-146, respectively. These publications and single copies of Bulletins #31 and higher are available from Information Dissemination, DSDTT; National Institute for Occupational Safety and Health; 4676 Columbia Parkway, Cincinnati, Ohio 45226 (513) 841-4287

☆U. S. GOVERNMENT PRINTING OFFICE:1986/646-117/20933

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
ROBERT A. TAFT LABORATORIES
4676 COLUMBIA PARKWAY, CINCINNATI, OHIO 45226

OFFICIAL BUSINESS
PENALTY FOR PRIVATE USE. $300

Third Class Mail

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF HHS
HHS 396

DHHS (NIOSH) Publication No. 86-114