

IV. ENVIRONMENTAL DATA AND BIOLOGIC EVALUATION OF EXPOSURE

Environmental Concentrations

Concentrations of methylene chloride in a plant manufacturing plastic film were supplied by the Department of Labor and Industries, State of Massachusetts. (LD Pagnotto, written communication, December 1973) These data are discussed in detail below.

The solvent mixture used in the operation contained 75% methylene chloride, 22% chloroform, and the remaining 3% consisted of toluene, methyl glycol, and methanol. The plant operated 24 hours a day and used 240,000 pounds of methylene chloride a year. Four men were employed for each of 3 shifts. The employees spent most of their time in the room where the film was cast and most of the samples were taken in this environment. Besides the casting room, other general locations surveyed were the filter room, winding room, office, and laboratory.

For collection of samples, workroom air was drawn through a U-tube filled with 7 g of silica gel at a rate of 0.5 liters/min for 90-120 minutes. The collected vapors were desorbed from the silica gel by soaking in isopropyl alcohol for 2 hours. Aliquots of this solution were hydrolyzed by potassium hydroxide for 17 hours for chloroform estimates, and for 65 hours for methylene chloride estimates. The hydrolyzed solutions were neutralized with acetic acid and the chloride was titrated with silver nitrate, using potassium dichromate as the indicator.

To differentiate between the amounts of chloride recovered from methylene chloride and chloroform, it was necessary to use empirical chloride recovery factors determined from control samples analyzed in parallel. [59] During the first 17 hours of hydrolysis, averages of about

4% of the methylene chloride and about 80% of the chloroform were hydrolyzed. During 65 hours of hydrolysis, an average of about 20% of the methylene chloride, but virtually no additional chloroform, was hydrolyzed. Methylene chloride and chloroform controls were analyzed for each determination.

During 5 years of surveillance, 13 samples were taken near one of the desks in the casting room (Table XII-19). The concentrations varied from 55 to 310 ppm with an average of 169 ppm. At other locations in the casting room, 45 samples were collected with methylene chloride concentrations ranging from 70 to 495 ppm. The overall average methylene chloride concentration in the casting room was 203 ppm. Concentrations in the filter room varied from 155 to 590 ppm of methylene chloride, with an average of 294 ppm. In the winding room, office, and laboratory, the samples ranged from 35 to 215 ppm of methylene chloride. [59]

In 1973, another study (LD Pagnotto, written communication, December 1973) was conducted using charcoal as a collection medium with GC as the analytical method, in addition to the previously used method. In collecting the samples on charcoal, workroom air was drawn through a glass tube with an inside diameter of 6 mm. This tube was packed with 1 g of 6 x 16 mesh charcoal. The sample was collected at 1 liter/min for 10 minutes. Vapors adsorbed onto the charcoal were eluted with carbon disulfide by shaking on a mechanical shaker for 30 minutes. Aliquots of the resulting solution were injected into a GC in which the column consisted of a free fatty acid stationary phase on a solid support of coral shell treated with dimethyldichlorosilane. This method was modified from that of White et al. [105]

Two surveys were made on successive days. The data are presented in Table XII-12. During the first day, two 90- to 130-minute samples collected on silica gel near a desk in the casting room and analyzed by alkaline hydrolysis contained 210 and 250 ppm of methylene chloride. A 10-minute sample taken by the desk, collected on charcoal and analyzed by GC, indicated 471 ppm. The average concentration of these 3 samples was 282 ppm. The rest of the samples in the casting room varied between 30 and 594 ppm with an average of 457 ppm.

On the second sampling day, 3 samples were taken near the desk at intervals of 2 hours during the morning shift. The average methylene chloride concentration at this location, determined by GC, was 183 ppm. The overall average for all samples taken in the casting room on the second day was 312 ppm. The average of the 5 measured concentrations for the 2 days of sampling in the casting room was 391 ppm. [59]

The concentrations of methylene chloride found using the silica gel method appear to be lower than the ones collected with the charcoal and analyzed by gas chromatography (Table XII-20). The averages for the casting room differ by almost 100 ppm; the differences in the filter room and the office are even greater, while in the winding room the averages are essentially the same. Even though the samples for the 2 methods were not collected simultaneously, the possibility of error attributable to analytical method exists. The old method was not specific for methylene chloride, and the presence of chloroform could have interfered. Other sources of error, which may account for the lower methylene chloride concentrations in the old method than in the new one, are: (1) competition of water vapor with methylene chloride when silica gel is used as the

collecting medium; and (2) an elaborate hydrolysis procedure using empirical fractional chloride recovery factors derived from two hydrolyses. The problem of interference from water vapor in collection on charcoal is not as pronounced as with silica gel, [106] and with gas chromatography, methylene chloride and chloroform can be easily differentiated. [105]

During 1973 and 1974, 7 studies of methylene chloride exposure concentrations in a variety of jobs were reported. [107-113] The data are summarized in Table IV-1.

TABLE IV-1
METHYLENE CHLORIDE EXPOSURE CONCENTRATIONS

Type of Operation	Samples Type No.	CH ₂ Cl ₂ ppm	Reference
Servicing diesel engines	GA* 1	11	107
Spray painting booths	BZ** 8	1-74	108
Chemical plant	BZ 14	0-5,520	109
8 hr TWA exposure		875	109
Plastic tank construction	BZ 124	a few ppm	110
Ski manufacture	BZ 51	0-36	111
Cleaning foam heads	BZ 7	4-29	112
	GA 6	3-17	112
Cleaning nozzles in plastics manufacture	BZ 10	5-37	113
	GA 3	19-31	113

* General air

** Breathing zone

Another environmental study involving continuous use of methylene chloride was reported by Kuzelova and Vlasak. [55] The location was a plastic film factory in which cellulose triacetate was dissolved in organic solvents. Methylene chloride represented 78% of the mixture when charged. Trace impurities in methylene chloride were reported as 0.15% methyl chloride, 0.25% chloroform, and 1% methyl alcohol. A 3-year survey was

conducted in which environmental concentrations were reported within a range from 30 to 5,000 ppm. A total of 318 samples were taken in 13 working locations. The list of the sites and the concentrations found are presented in Table XII-11. The average concentration was 627 ppm. Unfortunately, the authors did not report the monitoring and analytical methods used to determine the reported environmental concentrations.

Environmental Sampling and Analytical Method

(a) Collection Methods

Most of the analytical methods are dependent on effective and reproducible uptake of methylene chloride by different collection media. Air samples are usually collected and transported to a laboratory, then desorbed or chemically treated, and finally analyzed quantitatively.

Silica gel has been used as a collection medium. [59,114] Silica gel is a polar adsorbent and shows pronounced selectivity in adsorbing polar molecules, particularly water. Hence, when sampling large volumes, atmospheric moisture may compete for the adsorption sites and displace methylene chloride. [106] When sampling more than 3 liters of air through 1-inch silica gel tubes, the silica gel could become saturated with water and this would impair its retentive properties. [106]

Activated charcoal has been used as a collection medium in conjunction with GC. [105] It is nonpolar and will generally adsorb organic vapors in preference to water vapor resulting in less interference from atmospheric moisture than silica gel. [106]

Williams and Umstead [115] reported the use of porous polymer beads as a collection medium. With this method, the same column was used for sample collection and GC analysis. The advantage of this method is that it consolidates collection and analysis into one operation. However, only one analysis can be performed on each sample. This method has not been developed for field use.

Liquids have been used to collect methylene chloride from contaminated atmospheres. Midget impingers containing m-xylene have been used for collection in conjunction with GC analysis, [116] and "bubble bottles" containing a pyridine solution have been used for collection in conjunction with the Fujiwara colorimetric analysis. [117] The successful use of impingers and bubble bottles for collection of breathing zone samples requires careful handling of glassware during collection and shipment of samples to the laboratory.

Other investigators have collected grab samples of contaminated atmospheres in a variety of containers ranging from plastic bags to hypodermic syringes. [118]

(b) Desorption Methods

When solid collection media are used, it is necessary to desorb the methylene chloride from the medium. Isopropyl alcohol and heat were used by the Massachusetts Department of Labor and Industries to desorb methylene chloride from silica gel. Otterson and Guy [118] recommended the use of different desorbing agents for charcoal depending upon the comparative gas chromatograph retention times of the desorbent and the contaminant. They found that carbon disulfide was the best desorbent of those studied for methylene chloride.

(c) Analysis

Several methods have been used to quantify methylene chloride contained in air samples. The analytical methods can be divided into 2 broad categories: (1) methods based on chemical reactions, and (2) methods based on physicochemical characteristics.

(1) Chemical Methods

The 3 chemical methods that have been used extensively are: (1) dechlorination with strong alkali followed by titration of the chloride (alkaline hydrolysis); (2) colorimetric measurement of the reaction products of methylene chloride and pyridine heated in alkali solution (Fujiwara reaction) [117]; and (3) direct reading colorimetric indicators. [119]

For the alkaline hydrolysis method, methylene chloride collected with a suitable collection medium is hydrolyzed during about 20 hours by KOH in isopropyl alcohol. After neutralization and precipitation with silver nitrate, the liberated chloride is titrated with potassium cyanide. The hydrolyzed methylene chloride is determined by comparison between samples and known standards. Disadvantages of this method are that the amount of chloride liberated depends on the duration of the dechlorination step, and that, with a mixture of chlorinated hydrocarbons, it is difficult to differentiate the chloride liberated from the different components.

In the colorimetric analytical method based on the Fujiwara reaction, a stream of air containing methylene chloride is passed through a wash bottle containing pyridine. [117] After collection in pyridine, methyl-ethyl ketone (MEK) and NaOH are added to an aliquot of the sample, and this mixture together with an aliquot of the MEK and NaOH solution are heated in

a boiling water bath and cooled over a fixed time period. The absorption coefficients are then determined with a suitable spectrophotometer. This method requires less time than the dechlorination method, but the problem of specificity with mixtures of chlorinated hydrocarbons remains.

The third chemical method utilizes direct reading detector tubes. [119] These are glass tubes packed with solid chemicals that change color when a measured and controlled flow of air containing methylene chloride is passed through the packed material. The test vapor may be drawn directly through the tube followed by comparison with a calibration chart, or it may be drawn into a pyrolyzer, then through the packed tube. [119] Either way, the method is not specific for methylene chloride since the stain to be read is produced by the liberated halogen ion, and any halogen or halogenated compound will interfere. Colorimetric indicator tubes should be correct within $\pm 25\%$ of the values read, as specified in 42 CFR 84.20(e).

(2) Physicochemical Methods

The category of analytical methods based on the physicochemical properties of methylene chloride includes gas chromatography, [118] infrared spectrometry, [120] and photodetector analyzers. [121] Gas chromatography provides a specific quantitative analytical method when appropriate column conditions are specified. [105] However, the possibility exists that several compounds found in an occupational environment may have similar column retention times. Resolution of interferences can be overcome by altering the stationary phase of the GC column, or by changing the column temperature or other analytical parameters. Altering conditions will usually change the retention times and separate the components. Two

chromatographic columns with different stationary phases can also be used for more positive identification of compounds.

A mass spectrometer can be used with gas chromatography to identify the substances present more positively. A capillary charcoal tube can be employed to trap and transfer the material associated with a gas chromatogram peak to a mass spectrometer for qualitative identification as described by Cooper et al. [122]

Otterson and Guy [118] combined charcoal collection, carbon disulfide desorption, and gas chromatography and considered the combination to be the best available for industrial hygiene studies of substances for which it was applicable. Fraust and Hermann [123] determined optimal charcoal granule size, sampling rate, and total sample volume for charcoal sampling tubes. White et al [105] applied the findings of Fraust and Hermann [123] and, in addition, determined the optimal cross section of the charcoal tubes and the optimal number of charcoal sections. The tubes were further modified for use with personal air sampling pumps to determine exposure to chlorinated hydrocarbons. [124]

An IR spectrophotometer in conjunction with a suitable recorder can be used to indicate instantaneous concentrations. With this method, concentrations are measured directly and it is not necessary to collect individual samples and transport them to a laboratory for analysis. IR has been used for continuous monitoring of industrial operations for chlorinated hydrocarbons. [120] However, complicated instrumentation is necessary to draw samples and to continuously record the data. There is also the need to assure that the atmosphere of relevant working stations is sampled, and that such samples correspond to the breathing zone of the workers at the

working stations. [120] IR analysis is subject to interferences from other air contaminants and these interferences are not easily detected or resolved without substantial knowledge of IR spectrophotometry.

Halide meters are based on the detection of the increased brightness of an a-c arc (metal electrode) when enveloped by an atmosphere contaminated with halogenated hydrocarbons. [121] These instruments are sensitive to all halogens and halogenated compounds and consequently are not specific for methylene chloride. Halide meters seem suitable for continuous monitoring if there is only methylene chloride present as the air contaminant.

(d) Conclusions and Recommendations

(1) Compliance Method

On the basis of the review of analytical methods, it is recommended that GC be chosen as the method of sample analysis with sample collection in tubes containing activated charcoal. Carbon disulfide is the preferred desorbent.

The selection of this sampling and analytical method is based on the following attributes:

- (A) Charcoal tubes are easy to ship and store.
- (B) Estimation of exposure with personal samplers is easy.
- (C) Desorption with carbon disulfide is efficient and reproducible.

(D) Methylene chloride can be identified in combination with many other compounds.

(E) At the sample volumes recommended, interference by moisture is minimal.

(F) The sampling tubes and personal pumps are commercially available.

A disadvantage of the method is the indirect system of measurement requiring collection and desorption prior to analysis.

(2) Monitoring Methods

It is also recommended that direct reading colorimetric tubes (gas detection tubes) be used as an inexpensive way to estimate methylene chloride concentrations. The tubes must be used as instructed by the manufacturer. The indicators must be accurate to $\pm 25\%$.

For situations in which there is a continuous and constant methylene chloride use, it is recommended that a continuous system of monitoring the working location be established. The workroom air should be monitored by a multiprobe continuous air sampler/analyzer in different locations representative of the exposures of workers. An appropriate time-location study of the workmen at the different probe locations can be used to estimate the TWA exposures.

The analytical apparatus for continuous monitoring should be a calibrated IR spectrophotometer or, if the only halogenated hydrocarbon present is methylene chloride, a halide meter may be used. If various other hydrocarbons are present, a GC or IR should be used. [120] The continuous monitoring findings should be corroborated with the recommended personal sampling method (Appendix I).

Biologic Evaluation of Exposure

Methylene chloride exposure may be monitored by its determination in blood, breath, or urine of exposed persons. [39,44,45,47,48,52]

Methylene chloride and formic acid were found in measurable amounts in the urine of persons exposed to methylene chloride. [48,55] The amount of methylene chloride found during a 24-hour period after 24-hour exposure at 100 and 200 ppm was proportional to the exposure concentrations. [48] Formic acid was found in the urine of most persons exposed to methylene chloride in a particular occupational study, but no correlation between the intensity of exposure and the concentration of formic acid could be determined. [55]

Methylene chloride has also been measured in the blood and breath of persons exposed to it. [44,47,48] The concentrations of methylene chloride in the blood and breath have been representative of the exposure. In one study, a model was developed for the determination of exposure concentrations from breath data. [47]

Measurements of COHb in persons exposed to methylene chloride at rest are related to the exposure concentrations and exposure times, as well as CO exposure. [39,41,42] However these relationships are disrupted by work, and where work is involved, maximum COHb values may not be attained until 3-4 hours after the end of the exposure. [45,44] COHb can and should be monitored in workers exposed to methylene chloride, but the time that the measurements should be made in relation to the end of exposure is not well established; consequently, a series of measurements is suggested. Until relationships between alveolar CO and COHb have been established for methylene chloride workers, it is not recommended that breath analysis for CO be used to estimate COHb.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

A list of maximum allowable concentrations (MAC) of atmospheric contaminants compiled by Cook, [125] in 1945, included one state standard for methylene chloride (California, 200 ppm), one unofficial state guide (New York State Department of Labor, Division of Industrial Hygiene, 500 ppm), and his own recommendation of 500 ppm based on the report of Heppel et al. [69] The concentrations tabulated by Cook [125] were accepted as MAC for prolonged exposures, ie, a 40-hour week.

The recommendation of Cook [125] was adopted by the American Conference of Governmental Industrial Hygienists (ACGIH) in 1946. [126]

The methylene chloride TWA occupational exposure limit of 500 ppm for an 8-hour day, 40-hour week was supported in edition 2 (1966) of Documentation of Threshold Limit Values [127] by 2 published reports. [35,69]

The American Industrial Hygiene Association in a hygienic guide for dichloromethane published in 1965 suggested a TWA of 500 ppm and a short exposure tolerance of "approximately 1,000 ppm" for 30 minutes. [128] This recommendation was based in part on the report by Nuckolls, [34] the monograph by von Oettingen et al, [64] and unpublished data.

In 1969, the American National Standards Institute Inc (ANSI) recommended, for methylene chloride, an 8-hour day TWA of 500 ppm. It also established an acceptable ceiling concentration of 1,000 ppm and an acceptable maximum peak above the acceptable ceiling concentration of 2000 ppm for no more than 5 minutes in any 2 hours. [5] These recommendations

were based on the review by Irish, [129] the animal experiments of Heppel et al, [69] and the experiments of Stewart et al. [39]

The 1971 Documentation of Threshold Limit Values for Substances in Workroom Air [130] recommended 500 ppm for methylene chloride and cited references 35,50,55,58,63,64,69, and 131. In 1972, the Committee on Threshold Limit Values of the ACGIH included methylene chloride in the list of intended changes [132] and proposed a TLV of 250 ppm. The basis for this recommendation included the studies of Stewart et al [39] in addition to the information used in the 1971 documentation. [126]

In 1970 the International Labour Office in Geneva published tables of permissible levels of toxic substances for many countries. [57] The methylene chloride standards for 8 countries are given in Table V-1.

TABLE V-1
PERMISSIBLE LEVELS OF TOXIC SUBSTANCES FOR 8 COUNTRIES

Country	Standard, ppm	Type
Czechoslovakia	141	MAC normal
Czechoslovakia	707	MAC peak exposure
Finland	500	MAC 8-hour
Germany (Federal Republic)	500	MAC
Japan	500	Not specified
Poland *	141**	Not specified
Poland *	14**	Not specified
Rumania	57	MAC
USSR	14**	MAC
Yugoslavia	500	MAC

** Original tabulation in mg/cu m

* Dichloromethane and methylene chloride were both listed
Derived from reference 57

The Czechoslovak Committee of MAC listed standards for Hungary (6 ppm), Great Britain (500 ppm) and GDR (141 ppm). [133] The Czechoslovak Committee considered that contamination of methylene chloride with methyl chloride was the reason for the low USSR standard.

The 1969 ANSI Z-37 standard [5] was adopted as the federal standard, 29 CFR 1910.1000, Table G2. This standard is a TWA of 500 ppm for an 8 hour/day, a ceiling concentration of 1,000 ppm, and a maximum peak of 2,000 ppm for no more than 5 minutes in any 2 hours.

Basis for Recommended Environmental Standard

From the review of the literature in Chapter III on the biologic effects of methylene chloride, the most salient parts of which are summarized below, the basis for the recommended standard is prevention of significant interferences with delivery of oxygen to tissues and terminal oxidation phenomena, and abnormalities in CNS function. Complaints commonly reported by workers using methylene chloride indicative of these effects include chest pains, heart palpitations, rapid pulse, shortness of breath, dyspnea, tingling in the hands and feet, muscular pains in the arms and legs, headache, and increased fatigue. [35,51,54,55,58]

Methylene chloride has been shown through studies with labeled carbon to be metabolized to CO, [82,100,102] and CO and COHb have been studied extensively in animals and man in connection with methylene chloride exposures. [39,41,43-45, 59,67,68,70,82,100,102] These studies have shown that COHb concentrations are a function of the methylene chloride absorbed and depend on methylene chloride exposure concentration and time and amount of air inhaled.

Human male subjects (nonsmokers) exposed experimentally to methylene chloride for 7.5 hours daily on 5 consecutive days attained average peak COHb percentages of 2.9% at 50 ppm methylene chloride, 5.7% at 100 ppm methylene chloride, and 9.6% at 250 ppm methylene chloride. In each case, the peaks were attained on the 5th day of exposure. [41] Higher values would be expected if subjects exercised during exposure.

Undesirable COHb values ranging up to 12% at the end of the workday were reported in workers exposed daily to methylene chloride (see Tables XII-12 and XII-13). [59] These data need to be evaluated cautiously because of the high values observed at the beginning of the workdays (Table XII-13) and the uncertainty of the total exposure. However, the limited experimental data on subjects exposed to methylene chloride during exercise indicate that the COHb values observed in these workers might be consistent with the reported exposure concentrations.

In subjects experimentally exposed at rest to methylene chloride at 50 ppm COHb percentages returned to baseline values by the following morning after each 7.5-hour day of exposure. The maximum COHb (2.9%) observed with 50 ppm methylene chloride together with the ability to recover normal values overnight suggests that it is not necessary to restrict occupational exposures to this level to prevent undesirable COHb concentrations. [41] However further research is needed with subjects exposed during exercise to substantiate this suggestion.

With 7.5-hour daily experimental exposures during rest to methylene chloride at 100 or 250 ppm, baseline values were not recovered the following mornings. [41,42] However, baseline values were recovered by the following Monday morning after daily exposures for 7.5 hours on Monday

through Friday at either 100 or 250 ppm methylene chloride. [41] COHb percentages in nonsmokers exposed at rest at 100 ppm reached 5.7% on Friday, the 5th consecutive day of 7.5-hour exposures. If the subjects had exercised during the exposure, this level may have been reached earlier in the week. COHb concentrations of workers engaged in light work and exposed at this level of methylene chloride would probably not be acceptable.

In addition to forming CO, methylene chloride has been shown to combine with the respiratory pigments ferrihemoglobin, cytochrome P-450, cytochrome B5, and metmyoglobin. [91,92,95-97] Since CO is an inhibitor of cytochrome P-450 reactions, when formed in the tissues from methylene chloride, the same degree of CO inhibition could occur with less COHb than when the CO source is environmental air. [68] It has been suggested from comparative biochemical studies that methylene chloride may increase the affinity of hemoglobin for CO. [97] This has not been confirmed by studying the relationship between COHb and alveolar CO in humans during and after experimental or occupational exposures to methylene chloride and CO. However, the additive effects on COHb concentrations in rats simultaneously exposed to methylene chloride and CO (see Table V-2) tend to confirm that the affinity of hemoglobin for CO is increased. [67]

Some information exists that if these effects occur in man they would not be of significant magnitude with TWA daily exposures at 50-100 ppm. [43] The affinity of Hb for oxygen was slightly increased in experimental subjects by 7.5-hour/day exposures at 100 ppm methylene chloride, but not at 50 ppm, [43] In the subject's exposure at 100 ppm, arterial blood lactate levels attained during exercise were not increased over their control values, indicating that occupational exposures of this magnitude

would not cause significant interference with oxygen transport or cellular oxidation. [43]

TABLE V-2
CARBOXYHEMOGLOBIN CONCENTRATIONS IN RATS
EXPOSED TO CO AND METHYLENE CHLORIDE

Exposure Concentrations, ppm		
CH ₂ Cl ₂	CO	COHb
100	0.5-2	6.2
1000	0.5-2	12.5
0	100	10.9
100	100	16.4
1000	100	19.0

Derived from Fodor et al [67]

On the basis of COHb values attained by repeated 7.5 hour exposures at rest at 50 ppm methylene chloride, [41] it appears that daily TWA exposures of workers at 75 ppm methylene chloride would be a safe level of exposure for most work situations and it is concluded that the environmental exposure limit to recommend, in the absence of occupational exposure to CO, is 75 ppm as a time-weighted average.

There are several reasons for not recommending higher daily TWA exposures to methylene chloride. The experimental basis for determining the safe level was data obtained from nonsmoking males exposed at rest. [41] Exposure during rest to methylene chloride at 100 ppm for 7.5 hours [41,42] has resulted in COHb values that are similar to those resulting from exposure to CO at the recommended occupational exposure limit of 35

ppm as a workday TWA. [134] Subjects who exercised during exposure absorbed greater amounts of methylene chloride than when they were exposed at rest. [44] Other subjects who exercised during exposure developed higher COHb levels than their companions who did not exercise. [45] The maximum COHb levels in subjects exposed during exercise were attained 3-4 hours after removal from exposure. [45,44] In an experimental exposure of females at 250 ppm, somewhat higher COHb values were obtained than in males similarly exposed. [42] During exposures of males at 500 ppm, blood lactate during exercise became slightly more elevated during exercise than in the same subjects when not exposed to methylene chloride. [43] COHb values in excess of 9% were obtained by exposures at 250 ppm for 7.5 hours. [41,42] Finally, the affinity of Hb for oxygen was increased in proportion to methylene chloride exposure concentrations in the 50-500 ppm range. [43]

Experimental studies of humans exposed to combinations of methylene chloride and CO have not been reported. However, with 3-hour exposures of rats to combinations of methylene chloride and CO, Foder et al [67] found that the effects of COHb concentrations were additive as shown by their data presented in Table V-2. Therefore, if there is exposure to both methylene chloride and CO in the work environment, it is recommended that the exposure limits of both compounds be reduced. This indicates the need for monitoring CO where there is work with methylene chloride. Procedures for monitoring CO are included in the Criteria for a Recommended Standard...Occupational Exposure to Carbon Monoxide. [134]

For substances with an additive effect, the limits of exposure to combinations of these two substances can be determined from equation

(a) (29 CFR 1910.1000):

$$\frac{C(\text{CO})}{L(\text{CO})} + \frac{C(\text{CH}_2\text{Cl}_2)}{L(\text{CH}_2\text{Cl}_2)} \leq 1$$

where:

C(CO) = the TWA exposure concentration of CO

L(CO) = the recommended TWA exposure

limit of CO = 35 ppm [135]

C(CH₂Cl₂) = the TWA exposure concentration of
methylene chloride

L(CH₂Cl₂) = the recommended TWA exposure

limit of methylene chloride = 75 ppm

Concentrations of CO in the air of US cities are usually less than 10 ppm but frequently greater than 5 ppm. [135] The federal air quality standard for CO is 9 ppm for an 8-hour average not to be exceeded more than once a year (40 CFR 50.8). It is recommended that no adjustment in the recommended environmental limit for methylene chloride be made unless TWA CO exposure concentrations in the workplace are more than 9 ppm. When CO exposures are more than this, it is recommended that either CO or methylene chloride exposures or both be reduced in accordance with equation (a). The solution of equation (a) for CO concentrations of 10-35 ppm is shown graphically in Figure XII-1. Examples of TWA exposure limits derived from equation (a) and selected from Figure XII-1 are shown in Table V-3.

Restrictions on the magnitude of exposure to methylene chloride for shorter time periods are necessary to prevent undesirable CNS effects. Stupor, headache, irritability, giddiness, drowsiness, and forgetfulness have all been experienced with occupational exposures to methylene chloride. [35,50,51]

Table V-3

TWA EXPOSURE LIMITS FOR METHYLENE CHLORIDE WHEN CO IS JOINTLY PRESENT IN THE OCCUPATIONAL ENVIRONMENT.

CO TWA	CH ₂ Cl ₂ , ppm	
	TWA	Action
0-9	75	37.5
10	54	27
15	43	21.5
20	32	16
25	21	10.5
30	11	5.5
35	0	0

Responses of the central nervous system to acute methylene chloride exposure also have been studied experimentally in humans. [37,38,39,40] Stewart et al [39] found that some subjects exposed at either 868 or 986 ppm for 1 hour became light-headed. A response of this nature was not reported by subjects exposed at concentrations of 750 ppm or less for up to 5 hours. [37] Some objective measurements have shown that central nervous system function was depressed by exposure at concentrations of 317-986 ppm. [37,38,39] Other measurements of psychomotor function were not affected by 2 hours of exposure at concentrations of 250, 500, 750, and 1,000 ppm during consecutive 30-minute periods. [40]

After 1 hour of exposure at either 514 or 986 ppm methylene chloride, Stewart et al [39] found alterations in the VER resembling those of the initial phases of CNS depression. Motor speed, speed of reaction, and control precision (especially left-hand control precision) were impaired during exposures at 750 ppm, in an experiment reported by Winneke. [38]

These functions were not studied at lower concentrations.

Another visual function, CFF, was impaired by exposure to methylene chloride at 317 ppm or more. The decrease in CFF attained similar magnitudes at 317 and 470 ppm, but developed more rapidly at 470 ppm. The magnitude of the decrease attained at 750 ppm was double that found at the lower concentrations. [38] More than 77 minutes of exposure were required to significantly reduce CFF at the lower concentrations whereas, at 750 ppm, the decrease was significant at this time. CFF was not studied in exposures at less than 317 ppm methylene chloride.

In auditory vigilance tests, the subjects exposed to methylene chloride at 317 ppm began to miss more signals after about 1 hour of exposure than they did in a similar experiment when they were not being exposed to methylene chloride. When the same subjects were exposed at 750 ppm in a similar experiment they began to miss signals sooner and missed more as the exposure progressed than they did at 317 ppm. [38]

The data indicate that neither undesirable CNS responses nor COHb values are likely to occur with exposures to methylene chloride at 300 ppm for up to 1 hour. [38-42] It was reported [39] that a CNS response was obtained within 15 minutes of exposure at about 900 ppm methylene chloride following exposure at 500 ppm for 1 hour, indicating that exposures of this magnitude should not be allowed. Exposures at 750 ppm have affected CNS function in less than 1 hour indicating that this concentration is also excessive. [38] Exposures at 500 ppm for less than 1 hour have been without CNS effect. However at this level, exposure for 1 hour would likely produce excessive COHb levels. In addition, it seems unsound industrial hygiene practice to allow excursions up to nearly 7

times TWA limit for as long as an hour. Therefore, a ceiling of 500 ppm, as determined by a sampling time of 15 minutes, is recommended.

It is recognized that many workers handle small amounts of methylene chloride or work in situations where, regardless of the amounts used, there is only negligible contact with the substance. Under these conditions, it should not be necessary to comply with all of the provisions of this recommended standard. However, concern for worker health requires that protective measures be instituted below the enforceable limit to ensure that exposures stay below that limit. For these reasons, "occupational exposure to methylene chloride" has been defined as exposure above half the environmental limit that is appropriate for the concomitant CO exposure level. This action level delineates those work situations that do not require the expenditure of health resources for environmental and medical monitoring and associated recordkeeping. One-half the environmental limit has been chosen on the basis of professional judgment rather than on quantitative data that delineate nonhazardous areas from areas in which a hazard definitely exists.

Regardless of environmental concentrations, many work practices are necessary for protection of the worker. These are discussed in Chapter VI and it is recommended that all sections of the standard not specifically exempted apply to all work with methylene chloride.