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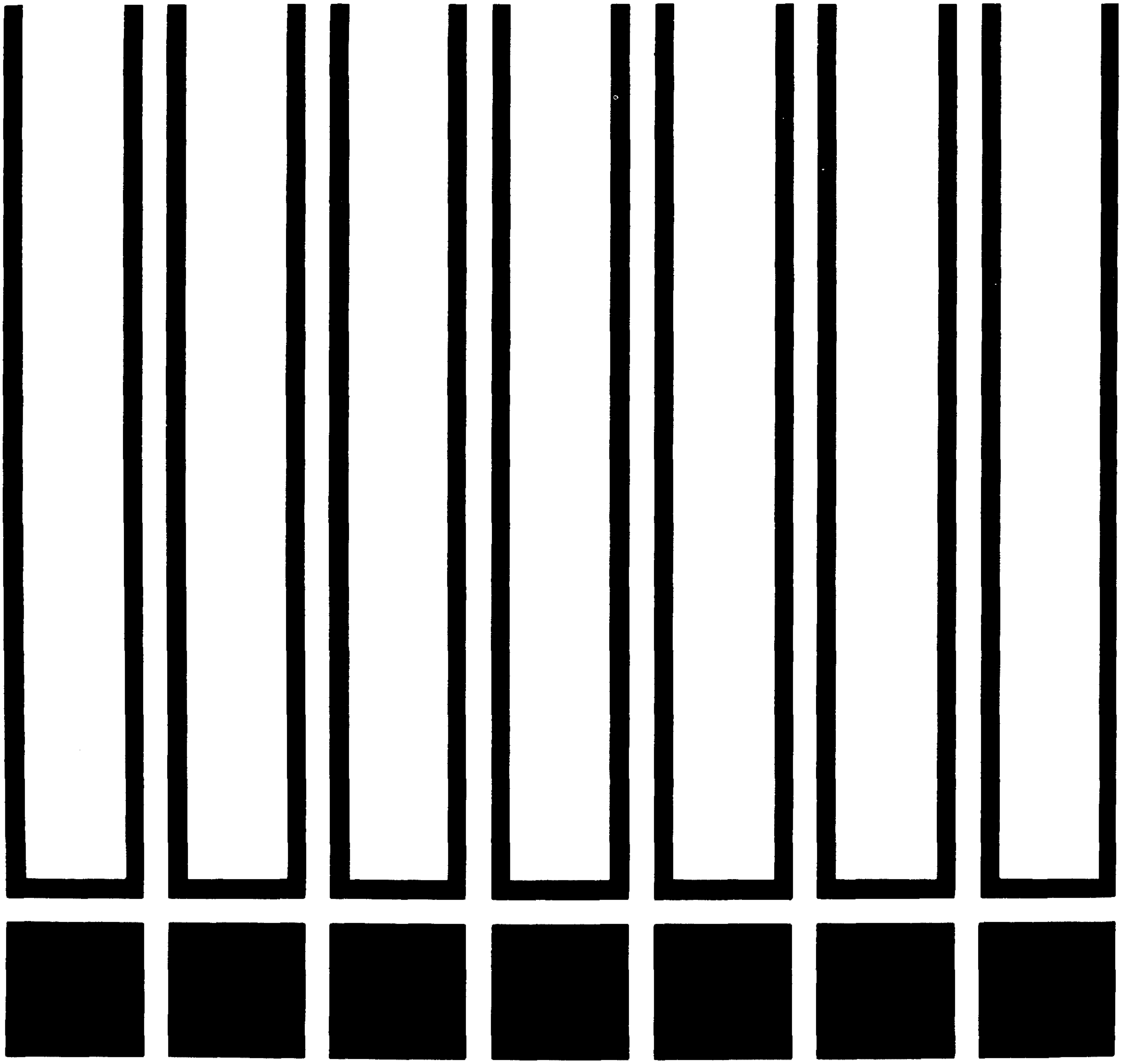
tetrachloroethylene
(PERCHLOROETHYLENE)



U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service Center for Disease Control
National Institute for Occupational Safety and Health

criteria for a recommended standard....

OCCUPATIONAL EXPOSURE
TO
TETRACHLOROETHYLENE
(Perchlorethylene)

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
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National Institute for Occupational Safety and Health
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PREFACE

The Occupational Safety and Health Act of 1970 emphasizes the need for standards to protect the health and safety of workers exposed to an ever-increasing number of potential hazards at their workplace. The National Institute for Occupational Safety and Health has projected a formal system of research, with priorities determined on the basis of specified indices, to provide relevant data from which valid criteria for effective standards can be derived. Recommended standards for occupational exposure, which are the result of this work, are based on the health effects of exposure. The Secretary of Labor will weigh these recommendations along with other considerations such as feasibility and means of implementation in developing regulatory standards.

It is intended to present successive reports as research and epidemiologic studies are completed and as sampling and analytical methods are developed. Criteria and standards will be reviewed periodically to ensure continuing protection of the worker.

I am pleased to acknowledge the contributions to this report on tetrachloroethylene by members of my staff and the valuable, constructive comments by the Review Consultants on tetrachloroethylene, by the ad hoc committees of the American Conference of Governmental Industrial Hygienists and the American Medical Association, and by Robert B. O'Connor, M.D., NIOSH consultant in occupational medicine. The NIOSH recommendations for standards are not necessarily a consensus of all the consultants and professional societies that reviewed this criteria document on tetrachloroethylene. Lists of the NIOSH Review Committee members and of the Review Consultants appear on the following pages.

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The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for development of the criteria and recommended standard for tetrachloroethylene. The Division Review staff for this document consisted of Keith H. Jacobson, Ph.D.; Richard A. Rhoden, Ph.D.; and Paul E. Caplan. Hervey B. Elkins, Ph.D., and Charles C. Hassett, Ph.D., served as special reviewers.

Agatha Corporation developed the basic information for consideration by NIOSH staff and consultants under contract No. HSM-99-73-20. Robert W. Mason, Ph.D., had NIOSH program responsibility and Paul A. Schulte served as criteria manager.

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CRITERIA DOCUMENT: RECOMMENDATIONS FOR AN OCCUPATIONAL EXPOSURE STANDARD FOR TETRACHLOROETHYLENE (PERCHLOROETHYLENE)

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I. RECOMMENDATIONS FOR A TETRACHLOROETHYLENE STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that worker exposure to tetrachloroethylene in the workplace be controlled by adherence to the following sections. Based on present information available to NIOSH, the standard is designed to protect the health and safety of workers for up to a 10-hour workday, 40-hour workweek over a working lifetime; compliance with the standard should prevent adverse effects of tetrachloroethylene on the health and safety of workers. The standard is measurable by techniques that are valid, reproducible, and available to industry and governmental agencies. Sufficient technology exists to permit compliance with the recommended standard. The standard will be subject to review and revision as necessary.

"Occupational exposure to tetrachloroethylene" is defined as exposure at a concentration greater than the action level (TWA) environmental limit. An "action level" is defined as half the time-weighted average (TWA) environmental limit. Occupational exposure to tetrachloroethyelene will require adherence to all the following sections. Exposure at lower environmental concentrations will not require adherence to the following Sections except for Sections 3(a), 4(a)(4), 4(b), 4(c), 5, 6, 7(a).

Section 1 - Environmental (Workplace Air)

(a) Concentration

Occupational exposure shall be controlled so that no workers are exposed to tetrachloroethylene in excess of 50 ppm (339 mg/cu m) determined as a time-weighted average (TWA) concentration for up to a 10-hour workday, 40-hour workweek, or at greater than a ceiling concentration of 100 ppm (678 mg/cu m) determined by 15-minute samples, twice daily.

(b) Sampling and analysis

The procedures for sampling and analysis for workroom air shall be as provided in Appendices I and II or by any method shown to be at least equivalent.

Section 2 - Medical

Medical surveillance of workers occupationally exposed to tetrachloroethylene shall be made available as outlined below.

(a) Preplacement initial or interim medical and work history.

(b) Preplacement physical examinations giving attention to at least the neurological, cardiovascular, liver functions, and skin condition.

(c) A judgment should be made of the worker's ability to use positive or negative pressure respirators.

(d) Periodic examinations shall be made available on an annual basis or at some other frequency to be determined by the responsible physician.

(e) Proper medical management shall be made available to workers suffering from adverse effects of tetrachloroethylene.

(f) Initial medical examination shall be made available to all workers within 60 days of the promulgation of these standards.

(g) Workers shall be advised that available scientific Information from one experimental animal study has shown that the offspring of mice exposed at high levels of tetrachloroethylene were observed to have congenital abnormalities. The relevance of this study to male or female workers or their offspring has not yet been determined. It does, however, suggest that employers and workers attempt to minimize exposure to tetrachloroethylene whenever possible. If the physician becomes aware of any adverse reproductive effects including repeated spontaneous abortions in tetrachloroethylene exposed workers or congenital abnormalities in their children, this information should be forwarded to the Director, National Institute for Occupational Safety and Health.

(h) Medical records shall be maintained for all persons employed in work involving occupational exposure to tetrachloroethylene. All pertinent medical records with supporting documents shall be maintained for 20 years after the individual's employment is terminated. The designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employer, and of the employee or former employee shall have access to these records.

Section 3 - Labeling and Posting

(a) The following warning sign shall be affixed in a readily visible location on processing or other equipment, and on tetrachloroethylene storage tanks or containers:

TETRACHLOROETHYLENE
(PERCHLOROETHYLENE)

CAUTION

BREATHING VAPOR MAY BE
HAZARDOUS TO HEALTH.

Keep containers closed when not in use.
Use only with adequate ventilation.

AVOID CONTACT WITH SKIN.

May generate toxic gases on contact
with ultraviolet light, open flame, hot
surfaces, or other heat producing conditions.

This warning sign shall also be printed both in English and in the predominant language of non-English-speaking workers, if any. All employees shall be trained and informed of the hazardous areas with special instruction given to illiterate workers.

(b) This sign shall also be posted at or near entrances to areas in which there is occupational exposure to tetrachloroethylene.

Section 4 - Personal Protective Equipment and Clothing

(a) Respiratory Protection

(1) Engineering controls shall be used whenever necessary and feasible to maintain tetrachloroethylene concentrations at or below the recommended exposure limits. Compliance with the permissible exposure limits may be achieved by the use of respirators only:

(A) During the time period necessary to install or test the required engineering controls.

(B) For nonroutine operations such as brief exposure at concentrations in excess of the environmental limit for maintenance or repair activities.

(C) During emergencies when air concentrations of tetrachloroethylene may exceed the recommended limit.

(2) When respirators are permitted, a respirator program meeting the requirements of 29 CFR 1910.134 and 30 CFR 11.2-1 shall be established and enforced by the employer.

(3) Only appropriate respirators as described in Table I-1 shall be used pursuant to the following requirements:

(A) For the purpose of determining the class of respirator to be used, the employer shall measure the atmospheric concentration of tetrachloroethylene in the workplace initially and thereafter whenever process, worksite, climate, or control changes occur which are likely to increase the tetrachloroethylene concentration. This requirement shall not apply when only self-contained or combination supplied air and self-contained positive pressure respirators are used.

(B) The employer shall ensure that no worker is being exposed to tetrachloroethylene in excess of the exposure limit because of improper respirator selection, fit, use, or maintenance.

(C) When respirators are required the employer shall provide respirators in accordance with Table I-1 and shall ensure that the employee uses the respirator provided.

TABLE I-1

RESPIRATOR SELECTION GUIDE FOR PROTECTION AGAINST TETRACHLOROETHYLENE

Concentrations of Tetrachloroethylene	Respirator Type
500 ppm or less	(1) A chemical cartridge respirator with a full facepiece and organic vapor cartridge(s)
	(2) A gas mask with chin-style or a front or back-mounted organic vapor canister.
	(3) A supplied-air respirator with a full facepiece, helmet or hood
	(4) A self-contained breathing apparatus with a full facepiece
>500 ppm or entry and escape from unknown concentrations	(1) Self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode
	(2) A combination respirator which includes a Type C supplied-air respirator with a full facepiece operated in pressure-demand or other positive pressure or continuous-flow mode and an auxiliary self-contained breathing apparatus operated in pressure-demand or other positive pressure mode
Firefighting	Self-contained breathing apparatus with a full facepiece operated in pressure-demand or other positive pressure mode
Escape	(1) A gas mask providing protection against organic vapors
	(2) An escape self-contained breathing apparatus

(D) Respiratory protective devices described in Table I-1 shall be those approved under provisions of 30 CFR 11.

(E) Respirators specified for use in higher concentrations of tetrachloroethylene are permitted in atmospheres of lower concentrations.

(F) The employer shall ensure that respirators are adequately cleaned, maintained, and stored, and that employees are instructed on the use of respirators and on testing for leakage.

(4) Where an emergency may develop that could result in employee injury from overexposure to tetrachloroethylene, the employer shall provide respiratory protection as listed in Table I-1.

(b) Protective Clothing

In any operation where the worker may come into direct contact with liquid tetrachloroethylene, protective clothing should be worn. The clothing should be resistant to tetrachloroethylene. In operations where repeated contact with tetrachloroethylene is necessary impervious gloves and other appropriate clothing should be worn. Gloves, boots, overshoes, and bib-type aprons that cover boot tops shall be provided when necessary. Impervious supplied-air hoods or suits shall be worn when entering confined spaces such as pits or tanks unless known to be safe. In situations where heat stress is likely to occur, air-supplied suits shall be used. All protective clothing shall be well-aired and inspected for defects prior to reuse.

(c) Eye Protection

Eye protection shall be provided for, and worn by, any employee engaged in an operation where tetrachloroethylene liquid or mist may enter the eye. Chemical-type goggles or safety glasses with splash shields made completely of tetrachloroethylene-resistant materials shall be used. Suitable eye protection shall be in accordance with 29 CFR 1910.133.

Section 5 - Informing Employees of Hazards from Tetrachloroethylene

All new and present employees in any tetrachloroethylene area shall be kept informed of the hazards, relevant symptoms, effects of overexposure to, and the precautions concerning safe use and handling of, tetrachloroethylene.

A continuing educational program shall be instituted to ensure that all workers have current knowledge of job hazards, proper maintenance procedures, and cleanup methods, and that they know how to correctly use respiratory protective equipment and protective clothing. It shall include a description of the general nature of the medical surveillance procedures and why it is advantageous to the worker to undergo these examinations.

The information explaining hazards of working with tetrachloroethylene shall be kept on file and readily accessible to the worker at all places of employment where tetrachloroethylene is manufactured, used, stored, or transported.

Information on file and readily accessible to workers shall include that specified in Appendix III, on US Department of Labor Form OSHA-20 "Material Safety Data Sheet," or similar form approved by the Occupational Safety and Health Administration, US Department of Labor.

Section 6 - Work Practices

(a) Materials Handling and Storage

(1) Containers delivered by closed truck or rail shall not be unloaded until the vehicle in which they arrived has been ventilated. The vehicle should not be entered if the odor of tetrachloroethylene is perceptible or if there is evidence of unsafe concentrations. Failure to perceive the odor of tetrachloroethylene does not ensure that concentrations in air are within a safe range. If there is liquid tetrachloroethylone on surfaces or if there is reason to believe there have been spills or leaks, respiratory protection shall be worn during unloading unless cleanup and ventilation is first accomplished. Protective clothing shall be worn to the extent needed to prevent skin contact with tetrachloroethylene.

(2) Storage containers, piping, and valves shall be periodically checked for leakage.

(3) Storage facilities shall be designed to:

(A) Contain spills.

(B) Prevent contamination of workroom air.

(b) Contaminant Controls

(1) Suitable engineering controls shall be used if needed to limit exposure to tetrachloroethylene to workplace environmental limits. Ventilation systems, if used, shall be designed to prevent the accumulation or recirculation of tetrachloroethylene in the workroom and to effectively remove it from the breathing zones of workers. Adequate, uncontaminated make-up air shall be provided. Ventilation systems shall be subjected to regular preventive maintenance and cleaning to ensure maximum

effectiveness, which shall be verified by periodic airflow measurements.

(2) Portable exhaust ventilation or suitable general ventilation shall be provided for nonroutine operations using tetrachloroethylene if needed to limit exposure to safe limits. Welding should not be started without adequate ventilation near open sources of tetrachloroethylene because the tetrachloroethylene may be decomposed to phosgene and hydrochloric acid.

(c) Equipment Maintenance and Emergency Procedures

(1) Tetrachloroethylene hazard areas

A hazard area, ie, and space with physical characteristics and sources of tetrachloroethylene that could result in concentrations of tetrachloroethylene in excess of the environmental limit, shall have exits that are plainly marked. Emergency exit doors shall be conveniently located and shall open to areas which will remain free of contamination in an emergency. At least two separate means of exit shall be provided from each separate room or building in which tetrachloroethylene is stored or handled in quantities that could create a hazard.

(2) Confined spaces

(A) Entry into confined spaces or to other situations of limited egress shall be controlled by a permit system. Permits shall be signed by an authorized representative of the employer certifying that preparation of the confined space, precautionary measures, personal protective equipment, and procedures to be used are all adequate.

(B) Tanks, pits, tank cars, process vessels, tunnels, sewers, or other confined spaces which have contained tetrachloroethylene shall be thoroughly ventilated to assure an adequate supply of oxygen, as well as removing solvent vapor, and inspected prior to entry.

(C) Inadvertent infiltration of tetrachloroethylene into the confined space while work is in progress inside shall be prevented by disconnecting and blanking off tetrachloroethylene supply lines.

(D) Personnel entering confined spaces shall be furnished with appropriate personal protective equipment and protected by a lifeline tended by another worker outside the space, who shall also be equipped for entry with approved respiratory, eye, and skin protection, lifeline, and have contact with a third party.

(E) Written operating instructions and emergency medical procedures shall be formulated and posted in conspicuous locations where accidental exposure at concentrations of tetrachloroethylene in excess of the recommended limits may occur. These instructions and procedures shall be printed both in English and in the predominant language of non-English-speaking workers, if any. Special instructions shall be given to illiterate workers.

(d) Showers and Eye Wash Fountains

Showers and eye wash fountains shall be provided and so located as to be readily accessible in all areas where skin or eye splash with tetrachloroethylene is likely. If tetrachloroethylene is splashed on the worker, contaminated clothing shall be promptly removed and the skin washed with soap and water. If liquid tetrachloroethylene contacts the eyes, they shall be irrigated for a minimum of 15 minutes with a directed flow of clean water. Medical assistance shall be promptly provided in cases of eye or skin splash. Such incidents shall be reported to the immediate supervisor by the affected employee or by a fellow worker.

Section 7 - Monitoring and Recordkeeping

(a) General

Workers are not considered to be occupationally exposed to tetrachloroethylene if environmental concentrations, as determined on the basis of an industrial hygiene survey, do not exceed the action level, ie, half the recommended TWA environmental limit, or if there is no operation, storage, or handling of tetrachloroethylene in any form or contamination of workplace air by tetrachloroethylene from other sources. These industrial hygiene surveys shall begin within 6 months after this standard is promulgated, and be repeated at least every 3 years and within 30 days after any process or operating change likely to result in increases of airborne concentrations of tetrachloroethylene. Records of these surveys, including the basis for concluding that airborne concentrations of tetrachloroethylene are at or below, the action level, shall be maintained until the next survey has been completed.

The following requirements apply to occupational exposure to tetrachloroethylene, ie, to workplaces where the action level is exceeded.

(b) Personal Monitoring

A program of breathing zone or personal monitoring shall be instituted to identify and measure the exposure of all employees occupationally exposed to tetrachloroethylene. This sampling and analysis shall be conducted every 3 months on at least 25% of the workers so that each worker's exposure is measured at least every year: this frequency and percentage of employees sampled may be different if so directed by a professional industrial hygienist. Sufficient samples shall be taken and analyzed to permit construction of valid estimates of the TWA and ceiling concentration exposures. If monitoring of any worker shows exposure in excess of either recommended environmental limit, additional monitoring shall be promptly initiated. If confirmed, control procedures shall be instituted as soon as possible; these may precede and obviate confirmatory monitoring if the employer desires. Affected employees shall be advised that exposures have been excessive and be notified of the control procedures being implemented. Monitoring of these employees shall be conducted at least as often as every 30 days and shall continue until 2 successive samplings at least a week apart confirm that exposure no longer exceeds recommended limits. Normal monitoring may then be resumed.

For each TWA concentration determination, a sufficient number of samples to characterize each worker's exposure during each workshift shall be taken and analyzed. The number of TWA and ceiling concentration determinations for an operation shall be based on such factors as the variations in location and job functions of workers in that operation.

(c) Recordkeeping

Environmental monitoring records shall be maintained for at least 20 years. These records shall include methods of sampling and analysis used, types of respiratory protection used, and TWA and ceiling concentrations found. Each employee shall be able to obtain information on his own environmental exposures.

Pertinent medical records shall be retained for 20 years after the last occupational exposure to tetrachloroethylene if the employee dies sooner. Records of environmental exposures applicable to an employee should be included in that employee's medical records. These medical records shall be made available to the designated medical representatives of the Secretary of Labor, of the Secretary of Health, Education, and Welfare, of the employer, and of the employee or former employee.

II. INTRODUCTION

This report presents the criteria and the recommended standard based thereon which were prepared to meet the need for preventing occupational diseases arising from exposure to tetrachloroethylene. The criteria document fulfills the responsibility of the Secretary of Health, Education, and Welfare, under Section 20(a)(3) of the Occupational Safety and Health Act of 1970 to "...develop criteria dealing with toxic materials and harmful physical agents and substances which will describe...exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience."

The National Institute for Occupational Safety and Health, after a review of data and consultations with others, formalized a system for the development of criteria upon which standards can be established to protect the health of workers from exposure to hazardous chemical and physical agents. The criteria and recommended standard should enable management and labor to develop better engineering controls resulting in more healthful work environments and should not be the final goal.

These criteria for a standard for tetrachloroethylene are part of a continuing series of criteria developed by NIOSH. The proposed standard applies only to the processing, manufacture, and use of tetrachloroethylene as applicable under the Occupational Safety and Health Act of 1970. The standard was not designed for the population-at-large, and any extrapolation beyond occupational exposures is not warranted. It is intended to (1) protect workers against development of systemic effects, and against local effects on the skin and eyes, (2) be measurable by techniques that are valid, reproducible, and available to industry and governmental agencies, and (3) be attainable with existing technology.

The development of the recommended standard for occupational exposure to tetrachloroethylene revealed a lack of information in certain areas of concern. These areas included: the neurologic and behavioral effects of chronic exposures at or below the recommended limit, the effects of tetrachloroethylene on animal fetuses of different species, and an understanding of the fate of absorbed tetrachloroethylene.

III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Tetrachloroethylene ($CCl_2 = CCl_2$), also known as perchloroethylene, is a colorless, clear, heavy liquid with an ethereal odor. [1] May determined an odor threshold of 50 ppm with a definite odor at 70 ppm. [2] However, some people may be able to smell it at lower concentrations. Leonardos et al [3] reported an odor threshold for their group of subjects of about 5 ppm. Methodological difficulties in odor detection may account for the discrepancies in these results. Some of the physical properties of tetrachloroethylene are tabulated in Table XII-1. [1,4-6]

Tetrachloroethylene is manufactured by at least eight companies in the United States. [7-9] Several manufacturing processes are utilized. [1,9] Its production in the US began in 1925. [1] In 1955, US production amounted to 178 million pounds, [10] and production increased steadily to 734 million pounds in 1972. [7,8,10-25]

The major uses of tetrachloroethylene are for commercial drycleaning and metal degreasing. Most workers in drycleaning establishments are exposed to it. [9]

Workers in at least 17 companies in the US are subject to tetrachloroethylene exposure in the formulation of a variety of products for home use and into veterinary anthelmintics. [26] Tetrachloroethylene is also prepared for grain fumigation by at least one company and some workers involved in grain fumigation are subject to exposure. [27]

NIOSH estimates 275,000 people are exposed to tetrachloroethylene in their work environment in the US.

Historical Reports

Tetrachloroethylene was studied as an anthelmintic by Hall and Shillinger, [28,29] who reported in 1925 the results of oral doses ranging from 0.05 to 15 ml/kg administered to 58 dogs. No deaths were observed in any healthy dogs that received the tetrachloroethylene, but dogs with clinical cases of distemper usually died 1-3 days after administration. Changes in the liver were reported for three healthy dogs receiving 0.2 ml/kg tetrachloroethylene and in one dog receiving 0.3 ml/kg. Degeneration of the parenchymatous cells, lobular hemorrhage and atrophy, and congestion of the central veins were observed.

Schlingman and Gruhzit [30] reported in 1927 that tetrachloroethylene produced different effects in various animal species. Chickens were notably resistant to single oral doses of 0.83 ml/kg or less. Cats, foxes, sheep, cattle, and horses, in that order, showed increasing susceptibility to tetrachloroethylene indicated by increased frequency of degeneration and necrosis of liver cells. Swelling and clouding of tubular epithelium of the kidneys was also observed.

In 1929, Lamson et al, [31] using thermal conductivity for analysis of gas samples, determined that a tetrachloroethylene concentration of 9,000 ppm was necessary to produce anesthesia in dogs. This concentration also caused secretion of 300 ml of saliva in 5 hours. The usual stages of anesthesia were reproduced, but it was almost impossible to obtain muscular relaxation except with nearly lethal concentrations.

The investigators [31] reported a series of animal experiments in which 116 animals, including dogs (adults and puppies), cats (adults and kittens), rabbits, and mice, were examined for pathologic changes in liver and kidneys 48 hours after administration of oral doses up to 25 ml/kg or after 5-6 hours of inhalation sufficient to maintain surgical anesthesia. In a few animals, principally puppies and kittens, there was a mild degree of fatty infiltration of the liver, but necrosis was absent in all instances. The fatty infiltration was found to be no more than in control animals on the same diet. In 10 dogs (5 by oral dosage, 5 by inhalation anesthesia) retention of phenoltetrachlorophthalein dye by the liver was essentially normal. In exposures of 35 dogs and 8 cats (oral and inhalation) tetrachloroethylene caused no change in the icteric index. A variety of a 185 animals were killed by lethal oral dose, and in every instance death was due to irreversible narcosis and not to any demonstrable pathologic change in internal organs. [31]

Lambert [32] in 1933 reported 46,000 administrations of tetrachloroethylene as a hookworm anthelmintic for humans on islands of the South Pacific. Dosages varied, but were usually between 2.8 and 4 ml. No deaths were reported but narcotic effects, exhilaration, and inebriation were observed.

The toxicity of anthelmintic doses of tetrachloroethylene was studied by Fernando et al [33] among 111 persons treated for hookworms. Liver functions were studied by sulfobromophthalein retention, icteric index, Van Den Bergh test, levulose tolerance test, and urobilin determinations in at least 40 individuals receiving from 1 to 8 ml of tetrachloroethylene. No significant variation was found between the liver function tests taken before the treatment and those taken after treatment. Cardiovascular, renal, and respiratory systems showed no toxic effects.

Narcotic properties of tetrachloroethylene were reported in 1911 by Lehmann [34] and again in 1936 by Lehmann and Schmidt-Kehl. [35] Cats were exposed to tetrachloroethylene concentrations ranging from 2,200 ppm (15 mg/l) to 16,500 ppm (112 mg/l). A cat exposed at 16,500 ppm began to salivate after 2 minutes, showed signs of equilibrium disturbance after 5 minutes, lay on its side after 10 minutes, and developed light narcosis after 85 minutes and deep narcosis after 145 minutes. These reactions were also seen at lesser concentrations but took longer to occur. Narcosis was not observed after 6 hours exposure at 2,200 ppm. [34]

Tetrachloroethylene was evaluated for anesthetic uses by Foot et al in 1943. [36] Fourteen patients were administered tetrachloroethylene sufficient to maintain surgical anesthesia. Only patients whose planned surgical procedure required a depth of anesthesia no greater than loss of consciousness were chosen. No patient was carried deeper than the second plane of the third stage of anesthesia. No systemic reactions were observed after administration, but several superficial burns to the face occurred, and there was irritation of the respiratory mucous membranes and the eyes. Tetrachloroethylene was not considered by the authors to be an effective anesthetic. [36]

Effects on Humans

(a) Neurologic Effects

In 1937 Carpenter and three of his colleagues subjected themselves to exposure to tetrachloroethylene vapor in concentrations of 500, 1,000, 2,000, and 5,000 ppm. [37] Vapor concentrations were measured by means of an interferometer to compare to refractive indices of known concentrations. The odor of tetrachloroethylene was detectable at 50 ppm. In a preliminary experiment, the subjects were able to detect the odor at 50 ppm whether they could detect the odor at lower concentrations was not tested. All subjects exposed at 500 ppm (475-680 ppm) for 30 minutes experienced increased salivation, metallic taste, slight eye irritation, increased perspiration of the hands, and tightness of the frontal sinuses. After eating a full course dinner, the subjects exposed themselves at 1,000 ppm (934-1,140) for 95 minutes and observed lassitude, a stinging sensation in the eyes, tightness of the frontal sinuses, and definite exhilaration after 45 minutes. Light narcosis was produced in all subjects after 7.5 minutes exposure at 2,000 ppm and for this reason they left the exposure chamber. No aftereffects were reported.

More recently, Rowe et al [38] exposed human volunteers at concentrations of tetrachloroethylene up to 1,185 ppm. Continuous analysis of vapor concentrations was made by a micro gas analyzer. Tetrachloroethylene vapor concentrations between 930 and 1,185 ppm were found to be markedly irritating to the eyes and upper respiratory tract in four subjects exposed 1-2 minutes. Two subjects experienced similar effects after a 10-minute exposure at 513-690 ppm. Dizziness, tightness and numbness around the mouth, and some loss of inhibition were experienced. Concentrated mental effort was necessary for motor effect to be comparable with nonexposure conditions.

Exposure at 280 ppm tetrachloroethylene for 2 hours resulted in lightheadedness, burning in the eyes, congestion of the frontal sinus, thickness of the tongue, and, in four subjects, motor coordination required additional mental effort.

Less severe but similar effects were experienced by four persons exposed for up to 2 hours at 216 ppm. Slight eye irritation was the only result of a 4-hour exposure of six individuals at 106 ppm (83-130 ppm). [38]

Stewart et al [39] in 1961 exposed six subjects, some more than once, to tetrachloroethylene. Exposures were separated by 4-week periods. Exposure concentrations ranged between 59 and 224 ppm with no exposure lasting longer than 187 minutes. A 1-4 minute exposure at 75-80 ppm caused a mild burning sensation of the eyes. Exposure at 100-120 ppm for 4-6 minutes resulted in dryness and irritation of the soft palate. Slight lightheadedness was noted after a 30-minute exposure at 210-244 ppm. Increased effort was necessary to maintain a normal Romberg test at this concentration. The authors reported that no other effects were found in the clinical or laboratory tests they performed. [39]

In 1970, Stewart et al [40] reported two experimental exposures of subjects to tetrachloroethylene. The subjects were healthy men ranging in age from 24 to 64 years. All were given a full medical examination prior to exposure. No control group was utilized. Two types of exposures were performed, a single 7-hour exposure of 15 subjects at a mean concentration of 101 ppm, and repeated 7-hour exposures of 5 subjects for 5 days, also at a mean concentration of 101 ppm tetrachloroethylene.

All subjects reported the odor of tetrachloroethylene to be moderately strong after 5 minutes of exposure and to be faint after 1 hour. The ability to perceive the odor progressively diminished in the group exposed over 5 days.

During the single 7-hour exposure, 25% of the subjects reported that they developed a mild frontal headache, 60% complained of mild eye, nose and throat irritation developing within the first 2 hours of exposure and usually subsiding before the 7 hours had elapsed. Twenty-five percent of the subjects complained of a sensation of blushing accompanied by slight lightheadedness. Forty percent of the subjects commented that they felt slightly sleepy and 25% reported some difficulty speaking. [40]

In the group that was repeatedly exposed, subjects had fewer subjective complaints. One subject, who had low-grade chronic sinusitis, developed a mild frontal headache throughout the exposures and two of the five subjects consistently reported mild eye and throat irritation. An abnormal response to the modified Romberg test was found with three of the subjects within the first 3 hours of exposure. With greater mental effort, however, the three subjects were able to perform a normal test when given a second chance. No other effects were found in other clinical, neurologic and behavioral tests. [40]

Stewart et al [41] in 1974 exposed 10 men and 11 women to tetrachloroethylene concentrations ranging from 20 to 150 ppm for specified periods 5 days/week for up to 5 weeks. To maintain the concentrations, the chamber was monitored with an infrared spectrometer, and a gas chromatograph equipped with an automatic sampling device. Test subjects were given, medical examinations before and after exposure and tests that included clinical chemistry, electrocardiograms (ECG), electroencephalograms (EEG), neurologic and behavior studies, and cardiopulmonary function. Blood, urine, and breath were sampled on a regular basis. No controls were used.

Subjective responses of 19 subjects exposed at several concentrations of tetrachloroethylene up to 150 ppm showed no relationship to dose level. Headaches were the most common response. The number of subjective responses reported under exposure did not show significant variations from each subject's preexposure state. [41]

Only preliminary qualitative analyses of EEG tracings of the experiment subjects were reported. The exposure to tetrachloroethylene resulted in a change in the EEG, characterized by a reduced overall wave amplitude and frequency. The change was most strikingly evident in occipital leads in which alpha wave acitvity (8-10 hertz, 10-50 μv amplitude) was generally replaced by delta or theta wave activity (3-5 Hz, 10-100 μv amplitude). [41]

The altered EEG patterns, similar to those of drowsiness or the first stages of anesthesia, were present in most subjects (three of four men and four of five women) exposed at 100 ppm tetrachloroethylene for 7.5 hours/day. Behavioral testing revealed that subjects exposed at 150 ppm showed impaired coordination after 7.5 hours of exposure. [41]

Central nervous system disturbances have been the most frequently reported result of occupational exposures to tetrachloroethylene. [42-49]

A sailor who used a tetrachloroethylene and water in solution (sic) for 1 month to clean gun parts experienced fatigue, vertigo, nausea, and vomiting. [42] He complained of a drunken feeling after working with the solution all day. Clinical and laboratory tests revealed no further abnormalities. Coworkers were not affected.

In 1957 Lob [43] reported 10 cases of tetrachloroethylene intoxication. One exposure resulted in a fatality. The death occurred when a worker was exposed for 3 weeks in an electrical plant where tetrachloroethylene was used as a solvent. The ventilation system was not in operation at the time. After 1 day of work, the man showed signs of nausea and inebriation, and vomited the following evening. The next day his symptoms became more severe and he became unconscious on the job. After an injection with a vasoconstrictor, he died suddenly during transport to his home. It is not clear whether these changes were the result of tetrachloroethylene alone or the administration of the vasoconstrictor. Post mortem examination revealed generalized edema of the lungs, bronchi, liver, spleen, kidneys, and cerebrum with multiple hemorrhages. The cause of death was diagnosed as asphyxia due to acute pulmonary edema. [43]

The nine cases of intoxication due to chronic exposure to tetrachloroethylene all showed similar symptoms. These included vertigo, headache, nausea, vomiting, anorexia, insomnia, and eye and throat irritation. In two of the cases involving 2-4 years of employment in an environment where tetrachloroethylene was used, severe neurologic disorders were observed. In one of these two cases, loss of memory, blindness in the left eye, pronounced dermographism and vestibular dysfunction were observed upon examination and persisted even after the man was given a new position. [43]

Headaches and vertigo occurred in another man 2 months after he began using tetrachloroethylene in his work. [43] Six months prior to his work with tetrachloroethylene, he had degreased metal parts with trichloroethylene. He worked with tetrachloroethylene for 9 months, enduring the situation until numbness of the fingers, difficulty in walking, trembling, exaggerated dermographism, and general weakness developed. There were mildly positive reactions for urobilin, urobilinogen and bilirubin in the urine.

Eberhardt and Freundt [44] reported two cases of poisoning due to tetrachloroethylene where there was neurologic involvement. In the first case, a 49-year-old man working for 2 months with tetrachloroethylene in a defatting operation experienced confusion, redness of the face, eye lids, and conjunctiva, and finally became unconscious on the job. The odor of solvent was noticeable on his breath.

The second case involved a 65-year-old woman who used tetrachloroethylene to clean metal parts in a watch factory. [44] After a 2-month exposure, she suffered from confusion and anorexia. She was hospitalized when feelings of confusion and dizziness became so strong that she could hardly walk. She recovered after 8 days. [44]

Peripheral neuropathy was the diagnosis in two cases where people had been working with tetrachloroethylene. These cases were found in the records of the California Department of Health for 1963-73 (E Baginsky, written communication, March 1975).

In one case, a 48-year-old female presser in a drycleaning operation became nauseated, cyanotic, and experienced coughing and tremors. A diagnosis of toxic peripheral neuritis was made by a neurologist. The duration and extent of exposure were not reported.

In the second case, a service man was splashed on the right side of his face with tetrachloroethylene while moving a drycleaning apparatus. On the following night, the man experienced numbness and inability to close the right eyelid fully. The diagnosis was toxic neuritis of the right facial nerve.

Neuropathies associated with exposure to chlorinated hydrocarbons were the subject of a report to the AMA Committee on Occupational Toxicology (HP Blejer, written communication, March 1975). Thirteen cases of neuropathy were reviewed. In one case, a 29-year-old woman developed optic atrophy attributed to tetrachloroethylene used as a garment spot remover.

A 1973 report from the USSR [45] indicated that 145 cases of various peripheral neuropathies resulted from a variety of unsaturated chlorinated hydrocarbon exposures that averaged more than 5 years duration.

Gold [46] reported in 1969 the effects of chronic exposure of a man to tetrachloroethylene. The man worked 6 days/week as a clerk and cleaner in a drycleaning plant. On the seventh day each week, the man cleaned vats containing tetrachloroethylene located in a small, poorly ventilated room where temperatures reached 120 F. On completion of the vat cleaning, the man always vomited, staggered, was confused and disoriented. He was employed for 3 years in the drycleaning plant before seeking medical care. He showed symptoms of increasing fatigue, dizziness, muscle cramps, memory difficulties, and increasing agitation and restlessness.

A physical examination revealed dry scaly forearms and hands while neurologic tests showed an absence of olfactory sensitivity on the right side (conceivably related to a septum deviation to the right) and conjunctivitis in the right eye. The patient performed poorly and had marked confusion in tasks requiring immediate concentration. Most signs and symptoms persisted during the followup year despite lack of further exposure. [46]

Acute pulmonary edema and coma were the result of a 7-hour occupational exposure to tetrachloroethylene. [47] In a laundry where tetrachloroethylene was used as the cleaning agent and reused after distillation, a man who worked alone forgot to turn on the cold water that cooled the last phase of distillation and the system overheated, giving off fumes which caused him to become dizzy. He lay down on a bed and shortly thereafter lost consciousness. He was rescued 7 hours later. Upon admission to the hospital he was in deep coma with acute pulmonary edema. Bubbling rales were heard over the entire lung field. Followup tests of liver and kidney function gave normal results.

Asthma induced by exposure to tetrachloroethylene has also been reported. [48] A 55-year-old woman working in a drycleaning establishment experienced an acute reaction from each of two massive exposures to tetrachloroethylene in a 2-year period. As a result of one exposure, she became unconscious. Both exposures were accompanied by asthmatic coughing attacks. After these incidents, she developed asthmatic attacks whenever she was in the shop. Diagnosis of asthma was supported by two indicators. The rate of exhaled air decreased 39% from 4.6 to 2.8 liter/second, and a positive reaction, indicating asthma, was obtained from an acetylcholine test.

Weiss [49] reported on two workers who became unconscious when high pressure tetrachloroethylene vapor at a temperature of about 200 C streamed out of a recovery apparatus in a drycleaning plant. The men received first and second degree burns on their faces, extremities and torsos and became unconscious after a few breaths. When the firemen arrived, the men were still unconscious. On hospitalization, urinary elimination of tetrachloroethylene was monitored in the patients for 26 and 31 days, respectively, beginning on the fourth day after exposure. Trichloroacetic acid was measured by a modified Fujiwara method once a day. The maximum elimination of trichloracetic acid, approximately 60 mg/l of urine, was recorded in both patients on the fifth day after the exposure. The investigator reported that the difference in the absolute amount of tetrachloroethylene eliminated by the patients probably was due to a difference in intake of tetrachloroethylene. This was supported by clinical evidence. The patient who was unconscious the longest and had the most extensive burns eliminated the highest amount of tetrachloroethylene. The tetrachloroethylene elimination in both patients showed an overall trend but fluctuated greatly from one day to the next. The investigator [49] had no explanation for this.

Tuttle et al [50] performed behavioral and neurological evaluations of workers exposed to tetrachloroethylene. The exposure occurred during the regular workday of 20 workers in five drycleaning plants. A group of 10 unexposed laundry workers was evaluated for comparison.

Neurologic testing and medical examinations were performed at the beginning of the study. Several behavioral tests were administered to workers at the beginning and end of each workday. Breath samples were also collected at these times and every 2 hours during the day. The time-weighted average concentrations of tetrachloroethylene were also calculated. The environmental and breath analysis data are shown in Table XII-2. The TWA concentration ranged from 1.32 ppm for five counter workers to 37.2 ppm for five machine operators. The comparison group reportedly had no tetrachloroethylene exposure or exposure to other nervous system depressants. The only other apparent differences between the exposed and unexposed workers before testing was their mean age of 43.45 years for exposed workers and 34.44 years for unexposed. Differences in the neurologic examination between the exposed and unexposed workers included the proximal motor latency of the peroneal nerve, electrodiagnostic rating score, neurologic rating score, and total neurologic score. The results of behavioral tests showed no significant differences between performance of the two groups. Correlations significantly different from zero were found for years of tetrachloroethylene exposure and critical flicker frequency (CFF) and CFF-Mean. Correlations were shown between years of exposure and the Digit Symbol test, the Neisser Letter Search test, the Critical Flicker Fusion Frequency, and three Santa Ana finger dexterity scores. [50]

(b) Effects on the Liver

In a small plant where tetrachloroethylene was used as a degreaser, one of seven employees who used the solvent was found to have a definite case of cirrhosis of the liver. [51] This prompted an investigation of the other workers employed there 2-6 years. Medical histories were obtained and liver function tests and physical examinations were performed on all seven workers. Liver dysfunction was found in three of the workers, indicated by significant sulfobromophthalein (BSP) sodium dye retention at

30 minutes. Positive urinary urobilinogen was found in four workers. Only the man with cirrhosis of the liver showed a 3+ reaction to the cephalin-cholesterol flocculation test. Medical histories revealed no extensive alcohol consumption by any worker. The man with liver cirrhosis drank no alcohol whatsoever. Determinations of the environmental concentrations of tetrachloroethylene were made using a Halide meter. One of the degreasing operations, which operated for 8 hours twice weekly, resulted in 232-385 ppm of tetrachloroethylene. [51]

Hughes [52] reported a case of toxic hepatitis in a 25-year-old man who had worked for 11 weeks, 12-16 hours/day, sometimes 7 days a week, refilling drycleaning units with tetrachloroethylene. The work was performed in a hot, humid, poorly ventilated room. No protective clothes were worn and on one occasion the man spilled a pint of tetrachloroethylene on his shirt and trousers. On two or three occasions he became lightheaded when the tetrachloroethylene vapor concentration became high. The odor of tetrachloroethylene became increasingly distasteful to him. [52]

Two weeks before the onset of symptoms, the man suffered from excessive fatigue and difficulty in rising in the morning. He also had nausea, vomiting, jaundice, weakness, anorexia, dark urine, and light brown stools. On admission to the hospital, results of unspecified liver function tests were reported as grossly abnormal. The man had no history of heavy alcohol consumption or predisposing diseases of the liver. Recovery occurred after 4 weeks of hospitalization. Ten months after the illness, the man reported that he had again briefly worked near a tetrachloroethylene system and immediately experienced nausea on perception of the solvent. [52]

Hepatitis with hepatomegaly was reported in a 47-year-old woman employed for 2.5 months in a drycleaning establishment. [53] Two weeks before admission to the hospital, the woman was heavily exposed to tetrachloroethylene during cleaning of the machinery. On that day, she worked 10 hours and complained of dizziness, headache, and malaise, all lasting through the next day. A coworker, not exposed as long, suffered similar but milder symptoms. During the next 10 days, the first woman suffered from general weakness and loss of appetite. Two days before admission, she developed acholic stools, scleral icterus, nausea, vomiting, and generalized pruritus. When hospitalized, she had vague discomfort in the right upper quadrant of the abdomen, where a baseball-sized mass thought to be a distended gall bladder was found. Her liver was palpable 3.5 cm below the right costal margin. Alkaline phosphatase was elevated to 22.8 and 26.4 units repectively on the first and second day of hospitalization, compared to normal values of 2-9 units. Serum glutamic-oxaloacetic transaminase (SGOT) on these days was also elevated to 1,270 and 760 spectrophotometric units/ml respectively, compared to normal values of 8-10 units. Direct and total bilirubin and cephalin flocculation also showed values consistent with liver disease. A liver biopsy performed after 2 weeks of hospitalization showed central portions of the lobules to have obvious degeneration of parenchymal cells with exaggeration of the sinusoids and focal collections of mononuclear cells. Six months later, her liver was still enlarged. The patient had no history of alcohol use or of exposure to other factors predisposing the liver to hepatitis. [53]

Mild chemical hepatitis and marked CNS depression were experienced by a worker wearing a general purpose chemical gas mask while scrubbing the inside of a tank car with tetrachloroethylene. [54] After 5 minutes in the tank, the solvent odor became so strong inside the mask that he left the tank. Believing the mask to be faulty, he removed it and reentered the tank. He realized his error, left the tank, donned his mask and entered for a third time. Approximately 10 minutes later, he was discovered unconscious at the bottom of the tank. Physical examination revealed most vital signs to be normal. The man was drowsy but oriented. Results from a detailed neurologic test were normal except for the Romberg test. Infrared analysis of the patient's breath 1.5 hours after exposure showed 105 ppm tetrachloroethylene, confirming that the patient had been exposed at very high concentrations. SGOT was slightly increased on the third day after exposure and urinary urobilinogen was significantly elevated on the ninth day after exposure. After 10 days, all liver function tests had reverted to normal. [54]

Liver dysfunction, as evidenced by elevated SGOT, occurred in eight of nine firemen who were exposed for 3 minutes at unknown concentrations of tetrachloroethylene. [55] Immediately after the acute exposure, all nine men were reported to be "woozy" but once outside the drycleaning establishment where the exposure occurred, they felt well. All appeared normal the next day except two men, who showed moderate hypertension. Clinical examinations and laboratory tests were not performed until 12 days after the exposure. At that time the SGOT values were elevated in eight of the nine men. Hepatomegaly and splenomegaly were found in one man, and slight depression of total white blood count was seen in three others. Eventually all signs of illness ceased. [55]

Trense and Zimmerman [56] reported that a 33-year-old man who worked 4 months in a drycleaning establishment had died due to inhalation of tetrachloroethylene. During the middle of his fourth month of employment, he developed loss of appetite. A month later, he was hospitalized with respiratory distress, coughing, vomiting, and profuse sweating. Clinical examination revealed an increased respiratory rate, rales over most of the chest, tachycardia, paleness of the skin, and throat irritation with hyperemic mucous membranes. The liver was somewhat enlarged and slightly sensitive to palpation. Blood pressure was 165/65. Death from cardiac arrest occurred 2 days after admission to the hospital. Autopsy findings included hemorrhagic pneumonia and edema of the lungs, liver cell necrosis, and fatty degeneration of the heart muscle. Decomposition products, unspecified in amount or type, were reported in the cerebrum, but not in the lungs, liver, kidneys, or blood. [56]

The work area where the exposure took place was investigated by the authors. [56] Two reported measurements of tetrachloroethylene in workroom air showed 50 and 250 ppm. Clothes saturated with tetrachloroethylene were hung to dry in a poorly ventilated room. The drycleaning machine had a run-over cycle where warm tetrachloroethylene drained out into a bucket, often spilling on hot pipes and vaporizing. Tetrachloroethylene vapor was also released when the drycleaning machines were filled from 50-liter bottles of the solvent. During this procedure, no mask was worn. [56]

Moeschlin [57] described a case involving liver function impairment and gastrointestinal disturbances after 6 years of exposure to tetrachloroethylene. Symptoms of mild gastrointestinal and central nervous system disturbances were reported several times prior to hospitalization. Medical examination revealed the man was generally in good condition and good nutritional state. Mild hepatic damage was diagnosed on the basis of laboratory findings of serum bilirubin and iron values and BSP retention of 30% and 22%. After 20 days, he had no signs and symptoms of hepatic dysfunction. [57]

Two cases of hepato-nephritis due to occupational exposure to tetrachloroethylene were reported in the French literature in 1955 and 1964. [58,59] In both cases, the subjects were using tetrachloroethylene for degreasing metal parts. The atmospheric concentrations of the solvent were not measured but contact with the solvent was direct in one case and within a few meters in the other.

Vallud et al [58] reported the post mortem examination of one man after his death but gave no clinical description. Post mortem showed an average size liver, with "localized degenerations" and enlarged, yellowish kidneys with congestion in the pyramidal zone.

Dumortier et al [59] concluded that the case of hepato-nephritis they had diagnosed was due to occupational exposure to tetrachloroethylene. The patient experienced vomiting, jaundice, and anuresis within 1 week after he started using tetrachloroethylene to clean metal. There was no evidence of previous infectious disease or medication that would have been predisposing. However, the 34-year-old man had a history of alcoholism. Two years prior to the occupational exposure, hepatomegaly had been diagnosed. On admission to the hospital, the liver was found to be palpable four fingerwidths below the costal margin. Oliguria and arterial hypertension, albuminuria and uremia were also diagnosed. Treatment included blood dialysis with an artificial kidney machine. After a month of treatment kidney function was improved. [59]

A workman using solvent which consisted of 50% tetrachloroethylene and 50% Stoddard solvent experienced marked eye irritation and lightheadedness shortly after beginning work. [60] The work involved alternately cleaning steps and mixing cement in an area where solvent vapors were present. On three previous occasions, he had become dizzy and lightheaded and left the area 3-5 minutes while his head cleared. The work area was poorly ventilated. An auxiliary air hose was employed to circulate the air and this accounted for 1 air change/hour. However, because the air hose produced an annoying whistle, the workman turned it off. Thirty minutes later, he became unconscious and was carried from the area by fellow employees. The man had worked 3.5 hours and had used 1 gallon of solvent before becoming unconscious. Stewart et al [60] simulated the exposure conditions at the accident site and found that the average concentration of tetrachloroethylene for 3.5 hours was 393 ppm, but when the air hose was turned off, the concentration rose to 1,100 ppm. During the whole process of cleaning steps and mixing cement, the concentrations of tetrachloroethylene ranged from 25 to 1,470 ppm. The concentrations of Stoddard solvent ranged from 70 to 425 ppm.

The workman recovered consciousness the same day and showed no abnormalities on medical examination. The man was observed for 44 days after the episode. During observation, a variety of clinical laboratory studies were performed and tetrachloroethylene was measured in the expired air. Some liver function impairment became evident on the ninth day following exposure. Urinary urobilinogen and total serum bilirubin were elevated. Urinary urobilinogen was 1:320 dilution and total serum bilirubin was 3.2 mg %. These values returned to normal ranges by the 14th day, when the measurement for alkaline phosphatase showed an elevated value of 6.2 Bodansky units. On the 18th day, serum glutamic pyruvic transaminase (SGPT) was slightly elevated. Concentrations of tetrachloroethylene in the breath on days 1, 2, 3, 9, 10, 14, 16, 18, and 21 were 18, 8, 6, 2, 1.5, 0.7, 4.5, 0.4, and 0.2 ppm, respectively.

(c) Effects on the Skin

Skin burns, blistering, and erythema caused by direct contact with liquid tetrachloroethylene were reported in the case of a man in a drycleaning business who became unconscious and fell to the floor, where the solvent had been spilled as a result of faulty machines. [61] The man had worked in this environment about 5 hours before becoming unconscious. Recovery of consciousness occurred over the next 24 hours and the burns healed over the next 3 weeks.

A similar case was reported by Morgan [62] in which a 68-year-old man spilled a container of tetrachloroethylene on himself, soaking his clothes. He became unconscious and was found 30 minutes later lying on the floor. Clinical examination revealed erythema and blistering over 30% of his body. In 5 days, the erythema subsided and the blistering disappeared. Some dryness and irritation of the skin reportedly occurred thereafter.

Skin effects due to chronic tetrachloroethylene exposure have been reported in other studies. [46,63] Munzer and Heder [63] reported a case of eczema as a direct effect of exposure of a man in a drycleaning plant. Gold [46] reported that a drycleaner had severe neurologic disturbances and had dry, scaly forearms and hands.

Absorption of tetrachloroethylene through the skin of the thumb was studied by Stewart and Dodd. [64] Five subjects each immersed one thumb in tetrachloroethylene for 40 minutes, and the concentration of tetrachloroethylene in the exhaled air of the subjects was determined at 10, 20, and 30 minutes of immersion. The concentration ranges found in the breath of the three subjects were 0.02-0.06, μg/l at 10 minutes, 0.11-0.14 μg/l at 20 minutes and 0.17-0.17 (sic) μg/liter at 30 minutes. Five hours after exposure, tetrachloroethylene was still measurable and ranged from 0.16 to 0.26 μg/liter.

(d) Absorption, Metabolism, Excretion and Elimination

Stewart et al [41] determined tetrachloroethylene and its metabolites in breath, blood and urine of exposed volunteer subjects. Breath samples, taken at various times before and after exposure, were collected in plastic bags using a 30-second breath holding technique. All samples were analyzed for tetrachloroethylene using a gas chromatograph with a hydrogen flame ionization detector. The minimal amount of tetrachloroethylene detectable in breath by this method was 0.05 ppm with a reported accuracy of ±0.1 ppm. [41]

The body burden of exposure to tetrachloroethylene was indicated by the distribution in expired air, blood and urine. Breath analyses showed that tetrachloroethylene is excreted in the breath for long periods after exposure. At 21 hours after a 3-hour exposure at 100 ppm, mean breath concentrations of tetrachloroethylene for days 1 through 5 were 1.00, 2.63, 3.33, 3.07, 3.98 ppm, respectively. Tetrachloroethylene concentrations found in expired breath after exposure at 100 ppm for 7.5 hours/day are presented in Table XII-3.

Physical exercise during exposure increased the concentration of tetrachloroethylene in the expired air and blood considerably. Trichloroacetic acid was found in small amounts in the urine of exposed persons but not in amounts indicative of dose. No trichloroethanol was found. [41]

In 1972, Bolanowska and Golacka [65] exposed three men and two women to tetrachloroethylene at an average of 55 ppm (390 µg/l) for 6 hours with two 30-minute rest periods. Additionally there was a 6-hour exposure with no rest periods. Gas chromatographic determinations were made for tetrachloroethylene in the expired air during the exposure and for 40 hours after exposure. The purity of the tetrachloroethylene was not stated. Fujiwara analysis of the urine for trichloroacetic acid was performed on samples taken during the exposure and again 16 hours thereafter. To account for all the tetrachloroethylene that entered the body, the possibility of excretion through the skin was examined. Aluminum foil-covered polyethylene bags were placed on the hands of subjects at the middle and end of the exposure for 1 hour each time, and the amount of tetrachloroethylene was determined.

The investigators, using the summation method of Piotrowski, [66] determined that 25% of the inhaled tetrachloroethylene was contained in the expired air and the hourly excretion through the skin was only 0.02% of the dose. About 62% of the inhaled tetrachloroethylene was retained in the body, and presumably metabolized by some unknown pathway. [65]

Guberan and Fernandez in 1974 [67] exposed 25 subjects at 50-150 ppm of tetrachloroethylene for up to 8 hours. Concentrations of tetrachloroethylene were measured in expired air and these data were used in the development of a mathematical model to predict uptake and distribution of tetrachloroethylene in the body and its elimination in alveolar air. The tissues of the body were classified into four groups: the vessel-rich group (VRG) (corresponding to brain, heart, hepatoportal system, kidney, and endocrine glands), the muscle group (MG) (muscle and skin), the fat group (FG) (adipose tissue and yellow marrow), and vessel-poor group (VPG) composed of connective tissue (bone, cartilage, and ligaments). The mean values of the 25 experimental subjects were the physiological "parameters" of a "standard man" used in the model. The investigators thought that the predicted uptake of tetrachloroethylene by tissue groups was related to perfusion rates. Based on the mathematical model, the VRG becomes saturated and the partial pressure equilibrates with that in the arterial blood during the first 60 minutes of exposure. It was expected that a rapid depletion of the VRG would take place, followed more slowly by MG and VPG, and finally the FG, starting 8 hours after the end of exposure. Because tetrachloroethylene has a high fat solubility, it accumulated in adipose tissue with a predicted biologic half-life of 71.5 hours.

The investigators [67] concluded that the ratio of alveolar tetrachloroethylene to inhalation concentrations of tetrachloroethylene was a constant at any given time after exposure.

In another study performed by Fernandez et al [68] 24 volunteers were exposed for 1 to 8 hours in a chamber at concentrations of 100, 150 and 200 ppm. The tetrachloroethylene concentrations in the chamber were continuously monitored by gas chromatography and infrared spectroscopy techniques. The concentrations of tetrachloroethylene were determined in alveolar air during exposure of some subjects and every 15 minutes for the first 3 hours after exposure of others. Several subjects were also monitored 2 to 4 times daily during an 8-day post exposure period.

The concentration of tetrachloroethylene in the alveolar air at a given time was found to be directly proportional to the constant inspired concentration of tetrachloroethylene. Alveolar concentrations were not found to increase proportionally with the length of exposure.

Ikeda et al [69] surveyed seven workshops using tetrachloroethylene to determine the relationship between exposure and metabolites in the urine. The surveys were conducted during the latter half of the week. Urine samples were collected from 34 male workers and Fujiwara determinations were made for total trichloro-compounds (TTC), trichloroethanol (TCE), trichloroacetic acid (TCA) and creatinine. The workers were exposed to tetrachloroethylene for 8 hours/day, 6 days/week while supervising automatic dip-washing machines (connected with ovens for drying off the solvent) used in the removal of synthetic glue from Kimono silk. Concentrations of tetrachloroethylene ranging from 10 to 400 ppm were measured, using Kitagawa detection tubes. TCA and TCE concentrations increased in proportion to environmental concentrations up to 50 ppm. At that point, TTC, TCA or TCE no longer were proportional to exposure. [69]

Ikeda and Ohtsuji [70] used a modified Fujiwara reaction for analysis of the urine of 70 workers exposed to tetrachloroethylene. There were two groups of workers; one group of four workers was exposed at 20-70 ppm and another group of 66 workers was exposed at 200-400 ppm. The exposures were daily and intermittent. Vapor concentrations were determined using Kitagawa detection tubes. The group of four workers had 8-56 mg/liter total trichloro-compounds in the urine, 4-20 mg/liter trichloroethanol and 4-35 mg/liter trichloroacetic acid in the urine while the group of 66 workers had metabolites of 45-195, 21-100, and 32-97 mg/liter, respectively. [66]

Ogata et al [71] analyzed the urine of four volunteers exposed 3 hours at 87 ppm tetrachloroethylene for metabolites by a chromium oxidation method. Vapor concentrations were determined every half-hour by gas chromatography with flame ionization detection. During the last 2 hours of exposure, analysis of the expired air of the subjects was performed. Urine was collected for 67 hours after exposure. The two metabolites of tetrachloroethylene observed were trichloroacetic acid and an unidentified compound which formed trichloroacetic acid by oxidation with chromium oxide. [71] The excretion of trichloroacetic acid increased until 3 hours from the end of the exposure and nearly returned to normal 64 hours later. The excretion for the unknown chlorinated hydrocarbon followed a similar course. Only the equivalent of 2.8% of the tetrachloroethylene inhaled was recovered in the urine over 67 hours. [71]

Epidemiologic Studies

In 1969, Franke and Eggeling [72] reported the subjective complaints and results of medical examination and liver function tests of 113 workers in 46 drycleaning plants in Germany. The most frequent subjective complaints were headaches, insomnia, dizziness, and heart complaints reported in 35, 34, 29, and 20%, respectively, of the workers surveyed. Medical examination revealed hyperhidrosis, dermographism, and tremors in 40% of the workers and mucous membrane irritation in 33%. Environmental concentrations of tetrachloroethylene directly associated with these complaints were not given. The concentrations of tetrachloroethylene in the air of the workplaces were reported as the result of 326 discrete measurements in 46 plants. Of these measurements, 75% were less than 100 ppm. To determine fluctuations in air concentrations, measurements were also taken every 15 minutes for several hours in two plants. In one plant, measurements taken at various locations every 15 minutes during a 2-hour drying process showed that air concentrations of tetrachloroethylene never exceeded 80 ppm. In another plant, measurements taken during a spot removal operation revealed tetrachloroethylene concentrations of 175, 220, 100, 280, and 100 ppm. Determination of concentrations of tetrachloroethylene in the air were conducted by colorimetric analysis. [72]

Statistical analysis of data gathered from laboratory studies of the 113 workers and 43 controls revealed that only the thymol turbidity and bilirubin determinations were significantly affected by exposure to tetrachloroethylene. [72]

Munzer and Heder in 1972 [63] used a modified Fujiwara method to analyze the urine of 200 employees working in 55 drycleaning plants where tetrachloroethylene was used. Trichloroacetic acid was found in the urine of 124 employees. The employees were classified in groups of 1-10, 11-20, 21-30, 31-40 and over 40 mg/l of trichloroacetic acid in the urine; the number of workers in each group was 53, 54, 11, 4, and 2, respectively. The investigators considered values of trichloroacetic acid up to 10 mg/l tolerable but did not explain the basis for this. Laboratory tests, and examinations were performed and medical histories were recorded on 40 of the 71 people with more than 10 mg/l of trichloroacetic acid in their urine. Of the group of 40 workers, 23 were men and 17 were women. Hyperactivity of the autonomic nervous system as indicated by hyperhidrosis, dermographism, and tremors of the fingers and eyelids was found in 12 of the 23 men and 10 of the 17 women. Laboratory tests including erythrocyte sedimentation rate, SGOT, SGPT, and thymol turbidity determinations showed no differences between the exposed group and an unexposed control group. [63]

Tetrachloroethylene was measured at various positions in drycleaning plants and during different processes. The methods of sampling and measuring were not reported. During an operation where tetrachloroethylene was brushed on fabrics, 150-300 ppm tetrachloroethylene were found in the workroom air. Measurements taken behind drycleaning machines ranged from 100 to 400 ppm. The general room air contained 200-300 ppm. When windows were open and cool air streamed in, vapor concentrations of tetrachloroethylene were 25 ppm at 30 cm above the floor, 150-200 ppm at head height, and 400 ppm at ceiling height. When a floor suction apparatus was in operation, 50 ppm were found at shop tables and 150 ppm in the rooms with machines; when suction was turned off, these concentrations increased to 100 and 300 ppm, respectively. [63]

An association between workroom air concentrations and trichloroacetic acid levels was not made. It was reported that generally women were most involved in the brushing operations while the men worked directly with the machines. [63]

Animal Toxicity

(a) Effects on the Nervous System

The neurophysiological effects of single and chronic exposures to tetrachloroethylene were reported by Dmitrieva. [73] Rats were exposed at concentration levels between 15 and 1,500 ppm (0.1 and 10 mg/l) tetrachloroethylene, 4 hours daily, for 15-30 days. After 20 minutes of exposure at 1,500 ppm, rats exhibited an intensified motor reaction which subsequently weakened. No description was given of how motor reaction was measured. There were also distinct alterations of the EEG such as increased frequency of rapid (up to 30-45/minute) and slow (up to 10-15/minute) graphic spikes, and an increase in the amplitude of the slow spike to 220 (u)v. The impedance of cerebral tissue increased 10-15% after 20 minutes and 30-40% after 4 hours. Biopotentials, as indicated by an electromyogram, were decreased as was EEG voltage. An unspecified decrease in activity of blood acetycholinesterase was reported. It was not specified whether this was serum or erythrocyte acetylcholinesterase but serum seems more likely because of its relationship to nervous function. Similar effects were also reported after 4-hour exposures at 600 and 300 ppm (4 and 2 mg/liter) and also after 2 and 4 weeks of repeated 4-hour daily exposures at 140 and 70 ppm. As a result of the repeated exposures, the delta-index of EEG increased to 80-90%, and the animals lost the capacity for assimilation of a preset rhythm. Electrical impedance of cerebral tissue increased 5-8%.

Exposures of 46 rats at 15 and 1.5 ppm for 5 hours daily for 5 months were performed by Dmitrieva and Kuleshov. [74] Concentrations were maintained "spectrophotometrically." Behavior and body weights did not differ from controls during or after the experiments. Effects on the EEG were observed after 2 weeks' exposure at 15 ppm. The frequency of rapid oscillations was up to 50 cycles/second higher in the experimental rats and the amplitude increased 30-50%. The pattern of EEG waves subsequently changed as slow delta-waves with a frequency of 1-4 cycles/second and amplitude of 100-150 μv appeared. Electrical conductivity and impedance of cerebral tissue were also effected by exposure. Conductivity decreased 10-15% after 1 month of exposure with corresponding increased impedance. The EEG of the exposed animals displayed uniform differences from those of the control animals.

Histologic examination of rats exposed at 15 ppm tetrachloroethylene revealed swelling of the protoplasm of some cerebral cortical cells in addition to the presence of isolated cells with vacuoles in the protoplasm and isolated cells with signs of karyolysis. Fatty infiltration of isolated cells of the liver was also observed. The activity of serum acetylcholinesterase decreased from 3.8 μM of acetic acid/ml of blood to 1.2 μmoles after 5 months of exposure. One month after the exposures were completed, only the EEG pattern was different. [74]

The exposure of rats at 1.5 ppm of tetrachloroethylene resulted in a slight decrease in acetylcholinesterase activity as well as unspecified changes in impedance of the cerebral tissue. [73]

Dmitrieva and Kuleshov [74] also studied the effect of tetrachloroethylene on 29 male rats. A comparison group of 24 rats was also studied. The exposures occurred 5 hours/day, 6 days/week for 5 months at concentrations of 15 and 1.5 ppm (0.1 and 0.01 mg/l). The number of animals exposed at each concentration was not reported.

Electroencephalographs of the rats were taken before exposure and once monthly during the exposure period with the aid of implanted silver and platinum electrodes. Assimilation of rhythmic photic stimulus of constant intensity and pulse duration was the criteria for evaluation. The electrical conductivity of the cerebral tissue was determined by use of the same electrodes used in the EEG tests attached to a conductivity meter. [74]

Distinct changes of the EEG waves developed after 5 months of exposure at 15 ppm. These included inhibition of electric activity evidenced by the appearance of the slow delta-rhythm (1-3 cps) that became dominant. The capacity for assimilation of an imposed rhythm was lacking. There also was a reduction of electrical conductivity by 24-40% after 5 months of exposure.

Microscopic investigation revealed swollen and vacuolized protoplasm in some cells, but these occurred only sporadically, most cells being normal. One to two months after exposure, the EEG and electric conductivity were only slightly or not at all different from controls. The 5-month exposure at 1.5 ppm resulted only in a slightly higher impedance of the cerebral tissue than was found with the controls. [74]

(b) Effects on Liver and Kidneys

Carpenter [37] attempted to discover the highest concentration of tetrachloroethylene vapors that would not anesthetize rats exposed for 8 hours. Rats exposed at 31,000 ppm (3.1%) died after a few minutes of exposure and after 30 to 60 minutes when exposure was 19,000 ppm (1.9%). Some rats survived exposure at 19,000 ppm but their livers showed congestion and granular swelling. Similar liver effects were found after exposure at 9,000 ppm. In addition, there was marked granular swelling of the kidneys. No deaths were reported after a single exposure at 9,000, 4,500, or 2,750 ppm (0.7, 0.45, 0.275%). Post mortem examinations of rats exposed to those concentrations showed a slight increase in the prominence of liver and kidney markings.

Carpenter [37] performed experiments involving chronic exposure of rats to tetrachloroethylene. Three groups of albino rats were exposed at vapor concentrations which averaged 70, 230 and 470 ppm for 8 hours/day, 5 days/week for up to 7 months. A group of 18 unexposed animals served as controls.

Exposures of 150 days at 470 ppm followed by a 46-day rest period resulted in cloudy and congested livers with swelling but no evidence of fatty degeneration or necrosis; increased secretion, cloudy swelling and desquamation of kidneys; and congested spleens with increased pigment. Pathologic changes were similar but less severe in the rats exposed at 230 ppm. However, in most of the rats, no pathologic effects were found. In some instances, there was congestion and light granular swelling of the kidneys after 21 exposures. After 150 exposures at 130 ppm and a 20-day rest, congestion was found in kidneys and the spleens. The livers showed reduced glycogen storage. No microscopic evidence of damage was discerned in rats exposed at 70 ppm for 150 exposures totaling 1,200 hours. No effects were noted after microscopic examination of heart, brain, eye or nerve tissue in any of the chronic exposures. [37]

Laboratory tests including icteric index, van den Bergh test for bilirubin, and blood and urine analyses, showed no abnormalities as a result of the exposures. Fertility of female rats was increased slightly after repeated exposures at 230 and at 470 ppm. [37]

Rowe et al [38] exposed four animal species to tetrachloroethylene vapor for 7 hours, 5 days/week for up to 6 months. The exposure concentrations varied from 100 to 2,500 ppm. Rabbits, monkeys and rats showed no effects of repeated exposures at concentrations up to 400 ppm; no effects on growth, liver weight or lipid content, gross or microscopic anatomy were observed in any animal. Guinea pigs however showed marked susceptibility to exposure to tetrachloroethylene, the authors reported. After 132 7-hour exposures at 100 ppm, the liver weights of female guinea pigs significantly increased. At 200 ppm, there was a slight depression of growth in female guinea pigs and increased liver weights in both males and females. Slight to moderate fatty degeneration of the liver was also observed. These effects were more pronounced in guinea pigs that received 169 7-hour exposures at 400 ppm. At this concentration, there also were increased amounts of neutral fat and esterfied cholesterol in livers. Gross and microscopic examination of the tissues revealed slight to moderate fatty degeneration in the liver with slight cirrhosis. [38]

Kylin et al [75] in 1963 studied the hepatotoxic effect of a single inhalation exposure of mice to tetrachloroethylene for 4 hours. The experiments were performed in female albino mice of a single strain with a mean weight of 23 g. The mice were exposed to tetrachloroethylene concentrations of 200, 400, 800 and 1,600 ppm for 4 hours and killed 1 or 3 days after exposure and the tissues were studied microscopically. Evaluation was limited to assessing the extent of necrosis and the degree of fat infiltration of the liver. Mice exposed at 200 ppm for 4 hours and killed 1 day later showed moderate infiltration of fat in the liver but there was no evident increase in mice killed 3 days after the same exposure. Moderate to massive infiltration was observed in mice killed 1 or 3 days after exposure at 400 ppm or more, but no cell necrosis was observed even after 4 hours exposure at up to 1,600 ppm tetrachloroethylene.

Kylin et al [76] in 1965 exposed four groups of 20 albino mice at 200 ppm. Each group was exposed for 4 hours/day, 6 days/week, for 1, 2, 4, or 8 weeks. Microscopic examinations were performed on livers and kidneys of the exposed mice and controls. Fatty degeneration of the liver was graded in accordance with the following criteria:

(1) Fatty degeneration involving a thin cell layer, up to two to three cells in width, usually at the periphery of the lobules;

(2) Same as in (1), but involving a layer of three to five cells in width;

(3) Pronounced infiltration of fat, either peripheral or central, involving about one-third of the lobules;

(4) Massive infiltration of fat, usually central, involving at least half of the lobules.

Fatty degeneration was particularly marked and tended to be more severe with longer exposure to tetrachloroethylene. [76]

In addition to histologic examination, chemical determination of the liver fat content was also performed. Correlation between the histological and the concentration of fat extraction was ±0.74. The fat content of livers of the exposed animals was between 4 and 5 mg/g body weight compared to 2-2.5 mg/g for controls. The actual fat content of the livers did not increase with duration of exposure as did the extent of the fatty infiltration. No liver cell necrosis was observed nor were there reported effects on the kidneys. [76]

Mazza [77] exposed 15 male rabbits, 4 hours/day, 5 days/week for 45 days at 2,790 ppm tetrachloroethylene, to determine the specific location of initial liver injury and to obtain serum enzymes associated with tetrachloroethylene intoxication. This was accomplished using the Schmidt Index, which is the sum of serum glutamic-oxaloacetic transaminase (SGOT) and glutamic-pyruvic transaminase (SGPT) divided by the serum glutamate dehydrogenase (GDH). The Schmidt Index was used by the investigators as an indication of hepatic disorders. Enzymatic determinations were made before the exposure and 15, 30, and 45 days after the exposure. Activities of all three serum enzymes under study showed an increase but the GDH increased the most, reducing the Schmidt Index from 6.70 to 1.79. The investigators concluded that this reduction shows the prevalence of mitochondrial injury over cytoplasmic injury in the liver.

Mazza and Brancaccio [78] exposed 10 rabbits for 4 hours/day, 5 days/week for 45 days at 2,790 ppm of tetrachloroethylene. The effects of these exposures on the suprarenal tissues were determined by measuring urinary and plasmatic concentrations of hormones of the cortex and suprarenal medulla and mandelic acid before and after exposure at various intervals. The investigators found a moderate but not statistically significant increase of cortical and medullar hormones as well as an increase in the elimination of 3-methoxy-4-hydroxymandelic acid.

Klaassen and Plaa [79,80] estimated the ED50 for liver and kidney damage in dogs and mice. The ED50 values for organ dysfunction were measured by BSP, SGPT, glucose, protein and phenolsulfonephthalein (PSP). They also determined the potency ratio, which they defined as the ratio of the LD50 to the ED50. All effects were observed after single intraperitoneal doses. After administration, effects on the liver and kidneys were determined by microscopic examination and by determination of SGPT elevation for the liver and PSP excretion for the kidneys.

The acute lethality and effective liver and kidney doses for dogs and mice are shown in Table XII-4.

(c) Effects on the Heart

Christensen and Lynch [81] observed depression of the heart and respiration in five dogs each given a single oral dose ranging from 4 to 5.3 cc/kg tetrachloroethylene. Autopsy showed fatty infiltration of both heart and liver tissue. In every case the small intestine was extremely shriveled and showed marked inflammation.

Barsoum and Saad [82] determined the greatest dilution of tetrachloroethylene that would have a depressant effect on an isolated toad's and rabbit's hearts were 1:3,000 and 1:4,000, respectively.

Reinhardt et al [83] studied the effect of tetrachloroethylene inhalation for 10 minutes on heart responses of 17 dogs injected with epinephrine. Tetrachloroethylene concentrations of 5,000 and 10,000 ppm were used. Tetrachloroethylene did not sensitize the hearts of any of the dogs to epinephrine. In the same study, sensitization occurred with 1,1,1-trichloroethane, trichloroethylene and trichlorotrifluoroethane. However, the investigator noted the possibility that tetrachloroethylene has the potential for cardiac sensitization but to a lesser degree than other chlorinated hydrocarbons. [83]

(d) Carcinogenicity, Mutagenicity, Teratogenicity

Schwetz et al [84] exposed 17 rats and 17 mice 7 hours daily at 300 ppm tetrachloroethylene on days 6 through 15 of gestation. The exposure was associated with a decrease in the maternal weight gain among rats, and an increase in the maternal relative weight of the liver in mice. There was an increase in the incidence of fetal resorptions in rats, and in fetal mice there were decreased body weights and increased incidences of subcutaneous edema, delayed ossification of skull bones, and split sternebrae.

Leong et al [85] gave an interim report in 1975 on the results of chronic inhalation in rats of tetrachloroethylene after 24 months. A tetrachloroethylene formulation was analyzed for composition by gas chromatography and introduced into a 3.7 cu m stainless steel chamber. The vapor concentration of tetrachloroethylene in the chamber was calculated from the ratio of material delivery rate to the total chamber air flow rate. The concentration was verified at regular intervals by infrared spectrophotometry. Two groups of rats, each consisting of 96 males and 96 females, were exposed at 300 or 600 ppm of tetrachloroethylene for 6 hrs/day, 5 days/week for 52 weeks. Food and water were witheld during exposure. A control group of 192 male and 192 female rats was not subjected to solvent exposure but was deprived of food and water on the same schedule as the experimental group. The investigators measured body weight, RBC count, HB concentration, packed cell volume, differential white count, and urinalysis for pH, specific gravity, sugar and albumic concentrations, presence of ketone bodies, and bilirubin. All animals were observed until moribund or dead. Representative specimens of all major organs and glands were microscopically examined. Behavioral signs indicative of CNS depression, such as hypoactivity, were sought. The investigators reported that, starting from the fifth month of exposure, the mortality of male rats exposed at 600 ppm was significantly higher than that of control. The cause of death was not stated. There was no difference in mortality rates in male rats exposed at 300 ppm or female rats exposed at 300 or 600 ppm. The investigators reported that spontaneous tumors appeared with comparable frequency in both exposed and nonexposed animals after 29 months.

The National Cancer Institute is currently conducting a study of the carcinogenic potential of tetrachloroethylene. The results of this study will be evaluated when they become available.

(e) Absorption, Metabolism, Excretion and Elimination

Curves depicting the concentrations of tetrachloroethylene in expired air were developed by Boettner and Muranko [86] who exposed Sprague-Dawley rats at various concentrations of tetrachloroethylene ranging from 50 to 500 ppm for up to 40 hours. Samples of the expired air of the rats were taken at various intervals after exposure using plastic bags. The series of curves was constructed to indicate the concentration of tetrachloroethylene in the expired air when duration of exposure and concentration of solvent were varied. The curves showed that the amount of tetrachloroethylene in the breath with constant exposure time (3 hours) was proportional to the exposure concentration.

Yllner [87] determined the urinary metabolites of C 14-labeled tetrachloroethylene in five female mice exposed for 2 hours to vapor in doses of 1.3 mg/g bodyweight. In 4 days, 90% of the absorbed tetrachloroethylene was excreted or metabolized, 70% in expired air, 20% in urine, and less than 0.5% in feces. Using chromatographic, radiographic, isotope dilution methods and, in part, Jondorf's method, the following metabolites were identified in the urine according to the percentage of total urinary activity: trichloroacetic acid, 52%; oxalic acid, 11%; and traces of dichloroacetic acid.

Daniel [88] studied the partition of Cl 36-labeled tetrachloroethylene in urine, feces and expired air of rats. Wistar rats were administered 1.75 μci or 13 μci of the labeled tetrachloroethylene by stomach tube. The half-life of expiration of tetrachloroethylene was found to be 8 hours, and 97.9% of the radioactivity was found in the expired air 48 hours after administration of the labeled tetrachloroethylene. After 18 days, 1.6-2.1% of the radioactivity was found in the urine. No radioactivity was found in the feces. Trichloroacetic acid and inorganic chloride were the only metabolites detected in the urine. On the addition of silver nitrate to the urine, 25% of the total urinary chlorine was precipitated as chloride. The remaining urinary radioactivity was accounted for by trichloroacetic acid. Oxalic acid was not found. [88]

The toxicity of trichloroacetic acid, a metabolite of tetrachloroethylene, has been the subject of some reports in the literature. [89,90] Woodard et al [89] reported the LD50 to be 3.32 g/kg for rats and 4.97 g/kg for mice. The consequences of chronic excretion of trichloroacetic acid were considered by Frant and Westendorp. [90] Trichloroacetic acid is a strong organic acid which may be neutralized in the body by sodium or potassium. Whether this constant elimination of fixed alkali will result in acidosis or diminution of the carbon dioxide-combining power of the blood has not been studied.

Dmitrieva [91] performed a number of experiments to identify the metabolites of tetrachloroethylene. In two series of chronic exposures, 24 rats were exposed 5 hours/day for 5 months at 15 and 1.5 ppm (0.1 and 0.01 mg/l) tetrachloroethylene. Concentrations were maintained by spectrophotometric monitoring. Trichloroacetic acid and ethylene glycol were found in the urine of the exposed rats but nzt in a group of eight controls. Oxalic acid was found in both exposed and not exposed animals.

Daniel [88] also exposed seven male and seven female rats at 1,000 ppm tetrachloroethylene to determine the effect on liver lipid content. The exposures were for three successive periods of 6 hours each. In the exposed female rats, 8.0 ± 1.5 mg lipid/100 mg dry liver weight was found compared to 10.7 ± 2.2 in controls, but this was not considered significant. In the exposed males, 11.3 mg lipid/100 mg dry liver weight was found compared with 11.2 for the controls.

Van Dyke and Wineman [92] found that little chloride was liberated from tetrachloroethylene in vitro by their dechlorinating enzyme system. The enzyme system was located in hepatic microsomes and required NADPH, oxygen, and a factor present in the 105,000 G supernatant. It was inducible by phenobarbital or benzpyrene, but not by methylcholanthrene.

Cornish and Adefuin [93] studied the effect of administering ethanol to rats 16-18 hours before exposing them to different chlorinated hydrocarbons. Two groups of rats, 6 each, were treated with chlorinated hydrocarbons and one of these groups was also pretreated with alcohol. Tetrachloroethylene exposure concentrations of 4,000 ppm for 6 hours, 5,000 ppm for 4 hours, 10,000 ppm for 2 hours, and 15,000 ppm for 2 hours were studied. Alcohol ingestion did not potentiate the toxicity of tetrachloroethylene under any of these conditions. Serum enzyme levels (SGOT, SGPT and serum isocitric dehydrogenase), lipid stains of liver sections, and other histologic findings in liver, kidney, lung, adrenal gland and spleen were similar to controls in all cases. In this study, ingestion of ethanol enhanced the toxicity of carbon tetrachloride and trichloroethylene.

Cornish et al [94] studied the potentiating effects in rats of 50 mg/kg phenobarbital injected ip 2 days and 1 day before ip administration of different chlorinated hydrocarbons. Four animals were used in each group. Marked potentiation of carbon tetrachloride and chloroform toxicity were found. However there was no potentiation of the toxicity of the other chlorinated hydrocarbons studied including tetrachloroethylene.

Plaa and Larson [95] injected 10 mice ip with tetrachloroethylene at 2.5 ml/kg and 10 others at 5.0 ml/kg and found 100 mg% or more of protein in the urine of 1 of 6 surviving mice injected with the lower dose and in 2 of 4 survivors of the higher dose. The investigators found less than 150 mg% of glucose in the urine of all 10 mice. The urine was sampled 24 hours after the injection of tetrachloroethylene. The kidneys of the mice given the lower dose were examined microscopically. The proximal convoluted tubules were swollen in all animals and necrotic in one.

The metabolism of hexachlorethane, widely used as an anthelmintic in cattle and sheep, was studied by Fowler. [96] He found that pentachloroethane and tetrachloroethylene were major metabolites of hexachloroethane. He also administered tetrachloroethylene orally in doses of 0.3 ml/kg to two sheep. No adverse clinical response of the sheep to the administered tetrachloroethylene was observed, but there were some plasma enzyme changes. Ornithine carbamoyl transferase did not change, glutamate dehydrogenase increased eight-fold in one animal and three-fold in the other, and sorbitol dehydrogenase was doubled.

Correlation of Exposure and Effect

Occupational exposure to tetrachlorethylene has caused signs and symptoms of acute effects on the central nervous system including loss of consciousness, dizziness, lightheadedness, inebriation, and difficulty in walking. [43,49,60] With prolonged exposures, signs and symptoms of chronic effects on the central, autonomic and peripheral nervous systems have been reported. These signs and symptoms included confusion, impaired memory, numbness of extremities and peripheral neuropathy including impaired vision. [43,46,51,63,72,85] Involvement of the liver in occupational tetrachloroethylene poisoning has been indicated by jaundice and enlarged livers, by clinical findings of impaired liver function and elevated serum enzymes, and by microscopic evidence of tissue changes. [51,53,55-57,59,72] In addition to these effects of absorbing tetrachlorethylene into the body, workers have experienced eye, nose and throat irritation and have developed lesions of the skin. [43,44,46,49,63]

In many of the reports of occupational exposure, environmental concentrations were not reported. [43,44,47,49] However, the conditions of work usually were described and from these descriptions it is possible to identify some of the conditions under which the effects occurred.

(a) Nervous System Effects

The only concentration measurements of tetrachloroethylene associated with unconsciousness in a work situation were reported in a study by

Stewart et al. [60] They reported a situation in which a workman was rendered unconscious while alternately cleaning steps with a solvent mixture (50% tetrachlorothylene and 50% Stoddard solvent) and mixing cement in an area where very high concentrations of the solvent vapor were present. In an attempt to determine the concentration at which the man was exposed, Stewart et al re-enacted the 3.5-hour exposure at the work site under the same conditions. They found 25 to 1,470 ppm tetrachloroethylene (average 393 ppm) and 70 to 425 ppm of Stoddard solvent.

Carpenter et al [37] reported that exposure at 2000 ppm would cause light nacrosis after 7.5 minutes and unconsciousness soon after. The lowest concentration that will produce unconsciousness has not been determined. At 1000 ppm, four subjects experienced tightness of the frontal sinuses, stinging sensation of the eyes, lassitude, slight mental fogginess, increased salivation. Similar but less severe signs and symptoms were reported by subjects in two different studies where exposures were 400-600 ppm. [37,38]

In a study of drycleaning plants where concentrations of tetrachloroethylene ranged from 25-400 ppm, Munzer and Heder found some type of hyperactivity of the autonomic nervous system in 20 of 40 workers examined. This was indicated by hyperhidrosis, dermographism and tremor of the fingers and eyelids. [63]

Lob [43] reported on a man using tetrachlorothylene as a solvent in an electrical plant where the exhaust system had not worked for 3 weeks. After work one day, he experienced nausea, inebriation and vomiting. The next day these effects were more severe and the man finally became unconscious. In another reported case, [44] a 49-year-old man was exposed to tetrachloroethylene for 2 months while working in a degreasing operation. During this time he experienced redness of the face, irritation of the conjunctiva and eyelids, confusion and finally became unconscious on the job. In another case, [47] a 7-hour exposure in a laundry resulted in unconsciousness of a worker who forgot to turn on the cooling unit of a distillation system for recycling the tetrachloroethylene. The system overheated, causing the man to become dizzy and eventually unconscious. Two similar cases were reported by Weiss. [49] Two workers in a drycleaning plant were overcome when tetrachlorothylene heated to 200 C streamed out of a recovery apparatus. The men were burned on the face and extremities and became unconscious after a few breaths of the vapor.

Neurologic involvement has been a frequent result of occupational exposures to tetrachloroethylene where concentrations were not reported but where unconsciousness did not occur. [43,44-46,85] Lob [43] reported that, in nine cases of chronic exposure to tetrachloroethylene, all workers showed similar symptoms of vertigo, headache, nausea, vomiting, and eye and throat irritation. In two of these cases involving 2-4 years employment, more severe neurologic disorders were observed. In one worker, these included loss of memory, blindness in the left eye, and vestibular dysfunction. The other worker experienced numbness of the fingers, difficulty in walking and trembling of the extremities.

Signs of neurologic response were reported in workers in a degreasing operation where tetrachloroethylene concentrations ranging from 230 to 385 ppm occurred 2 days a week for 2.5 to 6 years. [51] All of 7 workers exhibited lightheadedness, memory impairment, headache, staggering gait, and an inebriation-like state. Effects on the liver were also observed: these are discussed later.

In a survey of 46 drycleaning plants in Germany, Franke and Eggeling [72] found that 40% of 113 workers had either hyperhidrosis, dermographism, or tremors and 33% had mucous membrane irritation. Subjective complaints such as headaches, insomnia, dizziness, and heart complaints (otherwise undescribed), were made by 35, 34, 29, and 20% of the workers, respectively. Tetrachloroethylene concentrations in the air of these work places were reported as the result of 326 measurements; 75% were less than 100 ppm. In one of two additional plants, measurements taken every 15 minutes for several hours never exceeded 80 ppm.

Most of the reports of the effects of tetrachloroethylene at known low concentrations were experimental studies. They were performed at concentrations usually between 100 and 200 ppm. Preliminary signs of narcosis, as indicated by the overall reduction of the amplitude and frequency of EEG waves, were found in three of four men and four of five women exposed at 100 ppm of tetrachloroethylene for 7.5 hours/day. [41] Behavioral tests revealed that subjects exposed at 150 ppm showed impaired coordination after 7.5 hours of exposure.

In an earlier experiment, Stewart et al [40] found that, in a group of 15 male subjects exposed for one 7-hour period at a mean concentration of 101 ppm, 60% complained of mild eye, nose and throat irritation during the first 2 hours which subsided by the end of the experiment; 40% of the subjects felt slightly sleeply and 25% felt lightheadedness, developed mild frontal headaches or had some difficulty speaking.

Similar symptoms were found in a group of five of these subjects exposed at 101 ppm 7 hours/day for 5 days. Mild eye and throat irritation were consistently reported by two of the five subjects, and three of the five had an abnormal Romberg test on the first attempt. No control group was utilized. [40]

(b) Effects on the Liver

Tetrachloroethylene has been reported to produce effects on the liver, but the concentration at which such effects occur has not been determined.

Liver dysfunction, indicated by increased sulfobromophthalein sodium dye retention and positive urobilinogen, was found in three and four workers, respectively, out of a total of seven workers using tetrachloroethylene as a degreaser. [51] Liver cirrhosis was found in one worker. All men had been employed for at least 2 years. Concentrations of tetrachloroethylene in the workplace ranged from 220 to 385 ppm.

Out of 10 cases of tetrachloroethylene intoxication reported by Lob [43] in 1957, there was one case of liver involvement.

Liver cell necrosis was part of the pathologic diagnosis from an autopsy of a 33-year-old man who died from exposure to tetrachloroethylene. [56] The man had been working in a drycleaning establishment for 4 months. The investigators made two measurements of tetrachloroethylene and reported the concentrations of 50 and 250 ppm. The acute exposures occurred when tetrachloroethylene periodically spilled out of the drycleaning machine and fell on hot pipes, when it vaporized. Exposure also occurred when machines were being filled with tetrachloroethylene.

Bilirubin and thymol turbidity determinations were significantly affected in the 113 exposed workers studied by Franke and Eggeling [72] when compared with 43 unexposed workers.

Elevated SGOT was found in eight of nine firemen 12 days after a 3-minute exposure at an unknown concentration of tetrachloroethylene. [55] An enlarged liver and spleen were found in one man upon examination. At the time of exposure, all nine men became "woozy" for a few minutes. Results of examination of the livers of animals exposed to tetrachloroethylene at various concentrations have been reported in a number of studies. [31,37,38,75] Studying the toxicity of anthelmintic doses of tetrachloroethylene, Lamson et al [31] found no necrosis in a series of 400 animals administered doses up to 25 ml/kg or after 5-6 hours of inhalation of anesthetic concentrations.

Kylin et al [75] exposed mice at concentrations of 200, 400, 800 and 1,600 ppm for 4 hours. No liver cell necrosis was observed. However, fatty infiltration of the liver was evident at all concentrations and its extent was associated with the concentration of tetrachloroethylene.

Four groups of 20 mice were exposed by Kylin et al [76] at 200 ppm for 1,2,4 or 8 weeks. Microscopic examination revealed that fatty degeneration was particularly marked and tended to be more severe as the duration of exposure increased.

Carpenter [37] found no liver damage in rats exposed 150 times at 70 ppm tetrachloroethylene. Cloudy and congested livers with swelling were observed after exposures at 470 ppm for 8 hours/day 5 days/week for up to 150 days. Similar but less severe changes were observed after exposure at 230 ppm.

Rowe et al [38] found no effects in the livers of monkeys, rabbits and rats after repeated 7-hour exposures at concentrations up to 400 ppm. However, effects on the liver were evident in guinea pigs. After 132 7-hour exposures at 100 ppm, liver weights of female guinea pigs were increased; slight to moderate fatty infiltration of the liver was noted after exposure at 200 ppm and was more pronounced after exposure at 400 ppm; and slight cirrhosis was observed in guinea pigs exposed 7 hours/day for 169 days at 400 ppm.

(c) Carcinogenicity, Mutagenicity, Teratogenicity

The potential of tetrachloroethylene to produce carcinogenic, mutagenic or teratogenic effects has not been studied conclusively.

The effects of tetrachloroethylene in pregnant animals and their offspring were reported in two studies. [37,84] Carpenter [37] reported that fertility of rats increased slightly after exposure at 230 or 470 ppm for up to 7 months. Schwetz et al [84] found that mice and rats exposed at 300 ppm tetrachloroethylene for 7 hours/day on days 6 through 15 of gestation showed an increase in the relative maternal liver weights of mice, decrease in maternal body weights of rats, and increase in incidence of fetal resorptions in rats. In fetal mice, there were decreased body weights and increased incidences of subcutaneous edema, delayed ossification of skull bones, and split sternebrae.

Most of the effects found in the study by Schwetz et al [84] represent fetal and maternal toxicity. Only the delayed ossification of skull bones and split sternebrae could be considered as possible teratogenic effects. These occurred in mice but not in rats. The number of animals used in this study was too few to establish the significance of these findings, since the incidences of the abnormalities in large samples of these strains of rats and mice are not known. Whether these effects would occur in other species including humans has not been determined. This is an important requirement of further research.

(d) Metabolism

The metabolic pathways of tetrachloroethylene are still questions for investigation. Trichloroacetic acid and trichloroethanol have been found in the urine of humans and animals. [41,65,69,71] Additionally, oxalic acid, dichloracetic acid and ethylene glycol have been reported in the urine of exposed animals. [74,87,88]

The effects of tetrachloroethylene at various exposure levels are presented in Table XII-5.

IV. ENVIRONMENTAL DATA AND BIOLOGIC EVALUATION OF EXPOSURE

Environmental Concentrations and Engineering Controls

Smyth and Smyth [97] in 1935 studied concentrations of tetrachloroethylene at which workers were exposed in two drycleaning plants. Samples were collected in 35 and 77 minutes in the two plants, respectively. In the first plant, the average concentration found was 47 ppm with a peak of 2,960 ppm. In the other plant, an average concentration of 280 ppm was found with a peak of 4,636 ppm. Closed drycleaning machines were used in both plants. The concentrations were determined with a 50-cm portable interference refractometer as close as possible to the workmen's noses.

An extensive study of tetrachloroethylene concentrations in drycleaning plants was made in southwestern Ohio and southeastern Indiana in 1971 by Kerr. [98] Twelve commercial plants that daily cleaned 100-1,000 lbs of clothing and four coin-operated plants were studied. Six of the commercial plants were studied on only one occasion; the others were studied two or three times. The mean concentration of the 30 field studies conducted was 104 ppm. Nineteen of the 30 studies conducted in comercial package plants resulted in a mean concentration of 92 ppm ranging from 31 to 270 ppm. Most measurements were obtained with a halide meter, but some use was made of colorimetric indicator tubes. Average concentrations are summarized in Tables XII-6 and XII-7. The proportion of the sampling time that concentrations exceeded 200 and 300 ppm is summarized in Tables XII-8 to XII-11. Peak concentrations near 1,000 ppm were found in some plants. [98]

Kerr [98] reported that the greatest single factor to influence tetrachloroethylene vapor concentrations in the drycleaning operations studied was ventilation. In one of the drycleaning plants he found that a mean concentration of 100 ppm was accompanied by an air movement of 125 to 205 feet/minute while a 270 ppm mean concentration was observed when no air movement was recorded.

In evaluating the results of the study Kerr observed that the design of the solvent recovery systems in many of the plants surveyed was based on invalid concepts regarding the behavior of tetrachloroethylene vapor in the air. While tetrachloroethylene has a pure vapor density of 5.22-5.83 g/l, the low vapor pressure limits the amount of vapor that can exist in air without condensation to about 3% at 77 F. The density of this "saturated" (3%) air is considered to be 1.11 compared to air at 1.0. Such a vapor and air mixture would certainly not sink to the floor but would immediately disperse.

A study of 96 professional drycleaning institutions in the Denver area was made by the Department of Health and Hospitals in 1974-75. Halide meters were used to determine concentrations of tetrachloroethylene representative of the workers' breathing zones in machine service areas, such as loading, unloading, and maintenence of machines. Sampling times varied from 10 to 30 minutes. The levels of tetrachloroethylene found ranged from 5 to 125 ppm and averaged 41 ppm. Of 96 professional drycleaners, 68 had concentrations of tetrachloroethylene in worker breathing zones of 50 ppm or less. In most of these cases the air velocity at the face of the washer was greater than 100 feet/minute. (T Bullock, written communication, July 1975).

Coler and Rossmiller [51] used a halide meter to measure tetrachloroethylene concentrations in the breathing zone of an operator in a degreasing operation. Concentrations of 232-385 ppm were found.

Morse and Goldberg in 1943 [99] studied 108 degreasing units of the condensing and noncondensing types. A portable micro-furnace, which they developed and described, was used to make the atmospheric determinations. Tanks employing either trichloroethylene or tetrachloroethylene were included in the study. The data were summarized in ppm of solvent without distinguishing between the two solvents. Average concentrations were 96 ppm total solvent for the ventilated tank of the condensing type, and 221 ppm total solvent for the nonventilated, noncondensing units. Tetrachloroethylene is usually used with noncondensing units. The results of 402 determinations are presented in Table XII-12. [96]

In degreasing operations, equipping solvent vapor type degreasers with a "vapor level control" should serve to control the concentration of tetrachloroethylene in air. This device is a sensitive bulb-type thermostat with the sensitive bulb set at a temperature 10 F to 15 F below the vapor temperature (BP) of the solvent in use. The device is activated by an increase in vapor height of 3 to 4 inches above normal. Another means of reducing emissions is the use of a free board buffer which is basically a pair of refrigerated coils installed in the free board area of a degreaser. The cooling effect of these coils and the establishment of a cold air blanket above the solvent vapors results in reducing solvent emissions in the range of 35 to 50%. (TJ Kearney, written communication, April 1975)

The use of appropriate local exhaust systems is recommended for drycleaning and degreasing operations. Local exhaust systems should be designed and operated in conformance with American National Standard, *Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2-1971*. [100]

Environmental Sampling and Analytical Methods

(a) Sampling Methods

Most analytical methods are dependent on the effectiveness and reproducibility of the uptake of tetrachloroethylene by different collection media. Air samples are usually collected and transported to a laboratory, desorbed or chemically treated, and analyzed quantitatively.

Silica gel, which has been used as a collection medium, [101,102] is a polar adsorbent and shows pronounced selectivity in adsorbing polar molecules, particularly water. [103] A laboratory study indicated that water vapor could displace tetrachloroethylene when sampling more than three liters of air through 1-inch diameter silica gel tubes. [103]

Activated charcoal has been used as a collection medium in conjunction with gas chromatography. [104] It is nonpolar and will generally adsorb organic vapors in preference to water vapor, resulting in less interference from atmospheric moisture than with silica gel. [103]

Williams and Umstead [105] reported the use of porous polymer beads as a collection medium. With this method, the same column is used for sample collection and gas chromatographic analysis. This method consolidates collection and analysis into one operation, but only one analysis can be made on each sample. This method has not been developed for field use.

Liquids have been used to collect chlorinated hydrocarbons from contaminated atmospheres. Midget impingers containing m-xylene have been used for collection with gas chromatographic analysis. [106] Bubble bottles containing a pyridine solution have been used for collection in conjunction with colorimetric analysis. [107] Success in the 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 directly in a variety of containers ranging from plastic bags to hypodermic syringes. [108]

(b) Desorption Methods

When solid collection media are used it is necessary to desorb the collected contaminant from the medium. Desorption from charcoal was studied by Otterson and Guy. [108] They recommended the use of different desorbing agents depending on the comparative gas chromatograph retention times for the desorber and the contaminant. The investigators determined carbon disulfide to be the best desorbent for tetrachloroethylene collected in charcoal tubes.

(c) Analysis

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

(1) Chemical Methods

The three chemical methods that have been used extensively are: (A) dechlorination of collected vapor samples with strong alkalis followed by titration of the chloride ion (alkaline hydrolysis) [109]; (B) colorimetric measurement of the reaction products of tetrachloroethylene and pyridine heated in alkali solution (Fujiwara reaction) [110]: and (C) direct reading colorimetric indicators. [111]

(A) The dechlorination method (alkaline hydrolysis) requires collection of the tetrachloroethylene contaminated atmosphere by a suitable collection medium followed by alkaline hydrolysis in isopropyl alcohol, and titration of the liberated chloride with silver nitrate. [109] The percent of chlorine hydrolyzed is determined by comparison between samples and known controls. A disadvantage of this method is the difficulty of achieving hydrolysis and the inconsistent hydrolysis of the compound. Another disadvantage is that it is not specific for tetrachloroethylene.

(B) In the colorimetric analytical method based on the Fujiwara reaction, a stream of air containing tetrachloroethylene is passed through a bottle containing pyridine. [110] Potassium hydroxide (KOH) is then added to a portion of the sample, which is heated in a boiling water bath and cooled during a fixed time period. After coloring with a benzidene solution, absorption coefficients are determined with a spectrophotometer. This method requires less time than the dechlorination method, but the problem of specificity with mixtures of chlorinated hydrocarbons remains.

(C) The third chemical method utilizes direct reading detector tubes. [111] These are glass tubes packed with solid chemicals that change color when a measured and controlled flow of air containing tetrachloroethylene passes through the packed material. Depending on the type of detector tube, the air can be drawn directly through the tube and compared with a calibration chart, or the air may be drawn into a pyrolyzer accessory prior to the detection tube. [111] In either case, the analysis is not specific for tetrachloroethylene since liberated halogen ions produce the stain and any halogen or halogenated compounds will interfere. Regulations on detector tubes (42 CFR 84.50) provide that measurements with colorimetric indicator tubes shall be correct within ±25% of the values read. Tubes that meet these specifications have been evaluated and are available. [112]

(2) Physicochemical Methods

Photodetection (halide meters) [113], infrared spectrometry, [114] and gas chromatography [115] are among the analytical methods based on the physicochemical properties of tetrachloroethylene.

(A) Halide meters are made to detect the increased brightness of an arc across metal electrodes when they are enveloped by an atmosphere contaminated with halogenated hydrocarbons. These instruments are sensitive to all halogens and halogenated compounds and consequently they are not specific for tetrachloroethylene. Halide meters are suitable for continuous monitoring if tetrachloroethylene is the only halogenated contaminant present in the sampled air. [113]

(B) An infrared spectrophotometer in conjunction with a suitable recorder can be used to measure instantaneous concentrations or to record continuously. With this method, concentrations are measured directly and it is not necessary to collect individual samples or to transport them to a laboratory for analysis. Infrared spectrophotometry has been used for continuous monitoring of industrial operations for chlorinated hydrocarbons. [114] The atmosphere of relevant work stations must be sampled, and such samples must correspond to the breathing zone of the workers at the work stations. Infrared analysis is subject to interferences from other air contaminants and these interferences are not easily detected or resolved without substantial knowledge of infrared spectrophotometry.

(C) Gas chromatography provides a quantitative analytical method which can be specific for different chlorinated hydrocarbons. [104] Every compound has a specific retention time in a given chromatograph column, but several compounds in a mixture may have similar retention times. This problem can be overcome by altering the stationary phase of the chromatograph column or by changing the column temperature or other analytical parameters. Altering conditions will usually change the retention times and separate the components.

A mass spectrometer can be used subsequent to gas chromatography to identify the substance present in a gas chromatographic peak more positively. Linked gas chromatograph-mass spectrometer instruments perform this identification automatically. A charcoal capillary tube has been used to trap and transfer the material associated with a gas chromatographic peak to a mass spectrometer for qualitative identification when only unlinked units are available. [116]

(d) Conclusions and Recommendations

(1) Compliance Method

Based on review of air sampling and analytical methods, it is recommended that tetrachloroethylene in air samples be collected with activated coconut shell charcoal, desorbed with carbon disulfide, and analyzed by gas chromatography. Although the indirect system of measurement requiring collection and desorption prior to analysis is a disadvantage, this sampling and analytical method has the following attributes:

(A) Charcoal tubes are easy to prepare, ship, and store.

(B) Estimation of exposure with personal samplers is easily achieved.

(C) Desorption with carbon disulfide is effective and reproducible. However, carbon disulfide is a hazardous substance and should be handled in a chemical hood without sources of heat.

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

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

(F) Sampling tubes and personal pumps are commercially available.

(2) Monitoring Methods

Exposure to tetrachloroethylene associated with its continuous and constant use can be monitored by infrared spectrophotometry, or if it is the only halogenated hydrocarbon in the workroom air, halide meters can be used. Air from representative work sites can be drawn directly into the infrared spectrophotometer or halide meter by a multiprobe sampling apparatus. A time-location study of the workroom at the different probe locations can be used to estimate TWA exposures to tetrachloroethylene.

Direct reading colorimetric tubes (gas detection tubes) can be used as an inexpensive way to monitor tetrachloroethylene concentrations. The tubes must be used as instructed by the manufacturer. They are not suitable for determining compliance with the standard, but may be useful for determining exposure areas.

Biologic Evaluation of Exposure

Evaluation of some types of exposure to tetrachloroethylene, using breath analysis data, is feasible because nearly all the material is excreted through the lungs. [41,68,87,88] Data have been gathered from experiments where concentration and duration of exposure have been set at a variety of levels. The resultant alveolar concentrations were plotted according to time during and after exposure. From these data a map of breath concentrations resulting from an array of exposure conditions could be constructed to allow reasonable estimation of past exposures, provided the end point of the last exposure was known.

The alveolar concentration of tetrachloroethylene has been shown to be proportional to the concentration in the inspired air, and does not increase in proportion to the length of exposure. [68] Where the environmental conditions are such that the inspiration concentrations are fairly constant, breath analysis would be applicable for evaluation of exposure.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

There was little information on which to base early standards for occupational exposure to tetrachloroethylene. Hamilton, [117] in 1934, had only to say that it was a new solvent about which little was known. The first report found in the literature of an attempt to set a standard was from the Commonwealth of Massachusetts. [118]

The Subcommittee on Fumes of the Massachusetts Dust and Fume Code Committee prepared a list of proposed maximum allowable concentrations of industrial fumes in 1937. [118] No basis was given for the proposed value for tetrachloroethylene of 200 ppm.

The Subcommittee on Threshold Limits of the National Conference of Governmental Industrial Hygienists (NCGIH) published a list in 1942 entitled "Maximum Permissible Concentrations of Atmospheric Contaminants as Recommended by Various State Industrial Hygiene Units." [119] Eight states were listed as recommending 200 ppm for tetrachloroethylene, and Michigan was listed as recommending 100 ppm. The material was presented without comment other than that the tabulated values were not to be construed as recommended safe concentrations.

A list of maximum allowable concentrations of atmospheric industrial contaminants was compiled by Cook [120] in 1945 from the following governmental agencies: California Industrial Accident Commission, Connecticut Bureau of Industrial Hygiene, Massachusetts Department of Labor and Industries, New York State Department of Labor, Oregon State Board of Health, Utah Department of Health, and the United States Public Health Service.

All of these agencies recommended 200 ppm which was considered allowable for prolonged exposures, usually assuming a 40-hour workweek. [120]

Cook [120] also presented a list of accepted and tentative values based on industrial experience, animal experimentation, sensory responses of persons, or a combination of these. In this tabulation, he listed 200 ppm for tetrachloroethylene and cited the animal experiments of Carpenter. [37] Cook suggested that until more evidence was available on human exposures under industrial conditions, workers exposed at concentrations in the vicinity of the suggested allowable limit of 200 ppm should be under medical observation. [120]

The American Conference of Governmental Industrial Hygienists (ACGIH), formerly the National Conference of Governmental Industrial Hygienists, adopted a list of "Maximum Allowable Concentrations of Air Contaminants for 1946" which was prepared by the Subcommittee on Threshold Limits. [121] The selected value of 200 ppm for tetrachloroethylene was based on the recommendation of Cook [120] and the values tabulated by the NCGIH Subcommittee on Threshold Limits in 1942. [119]

The ACGIH Committee on Threshold Limits recommended, and the ACGIH adopted, a threshold limit value (TLV) of 100 ppm for tetrachloroethylene in 1947. [122,123] No basis for this change was given. The 1947 TLV for tetrachloroethylene was restored to 200 ppm in 1953. [124] The basis given for the change was information received from conference members that was not elaborated upon.

A preface to future tables of threshold limits proposed by the TLV Committee and adopted by the ACGIH in 1953 defined the values as "maximum average atmospheric concentration of contaminants to which workers may be exposed for an 8-hour working day without injury to health." [124] The preface was modified in 1958, and included the statement that "They [Threshold Limit Values] represent conditions under which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect." [125]

The first Hygienic Guide for tetrachloroethylene, published in 1960, gave 200 ppm as the recommended maximum atmospheric concentration for 8 hours. [126] This was believed to be a maximum which should not be exceeded in repeated daily exposure. It was not to be used as an integrated average concentration, and it was suggested that 100 ppm would be better for this purpose. The basis of the recommendation was given as human experience and the report of Rowe et al. [38]

The Committee on Threshold Limits proposed, and the ACGIH adopted, a TLV of 100 ppm for tetrachloroethylene in 1961. [127] This value, recommended on the basis of prevention of minimal narcotic effects in man, was supported by the reports of Carpenter, [37] Stewart et al, [39] Rowe et al, [38] and Smyth [128] in the first "Documentation of Threshold Limit Values" published in 1962. [129]

A standard of 4.4 ppm (0.03 mg/l) was proposed in 1965 as the maximum permissible concentration of tetrachloroethylene in air of industrial premises in Russia by Dmitrieva. [73] This recommendation was based on EEG and ECG changes in rats from chronic exposure at 15 ppm (0.1 mg/l). Similar changes were not found when the exposure concentration was 1.5 ppm (0.01 mg/l). [73,74]

The Hygienic Guide for tetrachloroethylene was revised in 1965. [130] The recommended maximum atmospheric concentration for 8 hours of 100 ppm was based on ACGIH recommendations.

American National Standard Acceptable Concentrations of Tetrachloroethylene (ANSI Z37.22-1967) [131] published in 1967 gave an acceptable time-weighted average for protection of health, assuming an 8-hour workday, of 100 ppm, an acceptable ceiling concentration of 200 ppm if the time-weighted average was below 100 ppm, and a maximum peak above the ceiling of 300 ppm for not more than 5 minutes of every 3 hours. This standard was based on the reviews by von Oettingen, [132] and Irish, [5] and the reports of Rowe et al, [38] Stewart et al, [60] and Stewart et al. [39]

Tables of "Permissible Levels of Toxic Substances in the Working Environment" for many countries were published by the International Labour Office in 1970. [133] The USSR values are absolute values never to be exceeded. They are set at a value believed not to produce, in any of the persons exposed, any deviation from normal, or any disease. Standards for several other countries are listed in Table V-1.

The most recent documentation of the threshold limit values was published by the ACGIH in 1971. [134] The reports of Carpenter, [37] Rowe et al, [38] Stewart et al, [60] Stewart et al, [39] Stewart et al, [40] Coler and Rossmiller, [51] Meckler and Phelps, [53] Dumortier et al, [59] and Lob, [43] were used to support the TLV of 100 ppm adopted in 1961. It was believed by the TLV Committee that 100 ppm would prevent serious narcotic effects, and that chronic intoxication involving hepatic or central nervous system effects would be unlikely if concentrations were maintained below this level. [134]

TABLE V-1

STANDARDS FOR SEVERAL COUNTRIES

Country	Standard		Qualifications
	mg/cu m	ppm	
Bulgaria	50	7.5	Ceiling
Finland	670	100	8 hours continuous exposure
Hungary	50	7.5	8-hour average
Hungary	250	37	30 minutes
Japan	670	100	None stated
Poland	200	29	None stated
UAR and SAR	67	10	None stated
USSR	10	1.5	Ceiling
Yugoslavia	670	100	None stated

Adapted from reference [133]

The Occupational Safety and Health Administration, US Department of Labor, adopted ANSI standard Z37.22-1967 [131] as the federal standard for tetrachloroethylene (29 CFR 1910.1000). This standard is 100 ppm for an 8-hour TWA exposure, with an acceptable ceiling exposure concentration of 200 ppm, and an acceptable maximum peak above the acceptable ceiling concentration for an 8-hour shift of 300 ppm for 5 minutes in any 4 hours.

Basis for Recommended Standard

(a) Environmental limits

Exposure to tetrachloroethylene has resulted in effects on the central nervous system, mucous membranes, eyes, lungs, liver, kidneys, heart, and skin. [31,33,36-38,41-44,46,50,55,56]

The most frequent effects have been on the nervous system. Tetrachloroethylene is a central nervous system depressant. Unconsciousness, dizziness, headache, vertigo or light narcosis has occurred after many occupational exposures. [43,44,49,63,72]

Experimental exposures to tetrachloroethylene at concentrations greater than 2,000 ppm have resulted in unconsciousness in humans after acute exposures. [37] At lower concentrations, such as those reported in the study of German drycleaners by Munzer and Heder, workers exposed at concentrations between 25 and 400 ppm showed signs of effects on the autonomic nervous system as indicated by hyperhidrosis, dermographism, and tremor of the fingers and eyelids. [63] The average environmental concentrations were not reported so it is difficult to determine at what concentrations these workers were exposed.

Similar signs and symptoms were reported by Franke and Eggeling [72] in their survey of 46 drycleaning plants in Germany. They reported concentrations resulting from 326 samples taken at random and 16 measurements taken at 15-minute intervals. Seventy-five percent of the measurements were less than 100 ppm. The maximum reported concentration was 400 ppm. Various subjective complaints among 113 workers were reported, including headaches, 35%: insominia, 34%: dizziness, 29%: and unspecified heart complaints, 30%. Tremors, hyperhidrosis, and dermographism were found in 40% of the surveyed workers.

In the studies by Munzer and Heder [63] and by Franke and Eggeling [72] concentrations reportedly ranged to 400 ppm. Workers surveyed or examined showed no irreversible neurologic effects of chronic tetrachloroethylene exposure. Irreversible neurologic effects have been reported in other studies but in most cases the concentrations were not known. [43,45,46, and E Baginsky, written communication, March 1975]

In nine cases of chronic exposure to tetrachloroethylene, symptomatology included vertigo, headache, nausea, vomiting, anorexia, insomnia, and eye and throat irritation. [43] In two of the cases involving 2-4 years of employment in an environment where tetrachloroethylene was used, severe neurological disorders were observed. In the case of one man working for 4 years in a poorly ventilated environment, loss of memory, blindness in the left eye, pronounced dermographism and vestibular dysfunction were observed upon examination. These disorders persisted even after the exposure had been discontinued.

Mild central nervous disorders were found in another man 2 months after he began using tetrachloroethylene in his work. However, 6 months prior to his work with tetrachloroethylene, he had degreased metal parts with trichloroethylene. He worked with tetrachloroethylene for 9 months, enduring the symptoms until they progressed to include numbness of the fingers, difficulty walking, trembling, exaggerated dermographism, and general weakness. Slight but positive reactions for urinary urobilinogen were also found. [43]

Gold [46] reported that a man who worked for 3 years in a drycleaning operation presented symptoms of increasing fatigue, dizziness, muscle cramps, memory difficulties, and restlessness. Neurological examination revealed an absence of olfactory sensitivity, deviation of the septum, and conjunctivitis, all on the right side. Most signs and symptoms persisted during the follow up year after exposure had ceased.

Peripheral neuropathies have also been reported resulting from tetrachloroethylene exposures (E Baginsky, written communication, March 1975).

The failure to find irreversible neurologic changes in the two studies of German drycleaning plants where concentrations ranged to 400 ppm was consistent with studies by Rowe et al [38] of four animal species. Rats, rabbits, monkeys and guinea pigs were exposed at up to 400 ppm for 7 hours/day, 5 days/week for up to 6 months. No neurologic changes were observed.

There is little information on the effects of chronic exposures to tetrachloroethylene at 0-200 ppm. Studies of acute exposures show effects consistent with the action of a central nervous system depressant.

Rowe [38] found that four subjects exposed at 216 ppm tetrachloroethylene for 2 hours required mental effort to maintain motor coordination. Similarly, in studies by Stewart et al in 1961, [39] and 1970, [40] at concentrations of 210-244 ppm for 30 minutes and 101 ppm for 3 hours, respectively, subjects experienced difficulty in maintaining a normal Romberg test.

Stewart et al [40] also found that of 15 subjects exposed for 7 hours at 101 ppm tetrachloroethylene, 25% reported mild frontal headaches, 60% complained of mild eye, nose and throat irritation developing within the first 2 hours, 25% experienced some difficulty speaking, and 40% felt slightly sleepy. No control group was provided.

Stewart et al [41] reported that results from the Flanagan coordination test indicated impaired motor coordination after 7.5 hours of exposure to tetrachloroethylene at 150 ppm. [41] Clinical evidence of central nervous system depression has not been reported with exposure concentrations below 150 ppm, [38,41] but there is preliminary evidence in EEG tracings of subclinical central nervous system response to repeated 7.5-hour daily exposures of humans at 100 ppm. [41] There is also evidence that these changes were maintained for at least 3 days after four 5-day weeks of 7.5-hours/day exposures at average concentrations of 20-150 ppm. [41] Data were not presented nor discussed for the results of EEG tracings during the week of exposure at 20 ppm of tetrachloroethylene. [41] The EEG tracings obtained with 100 ppm exposures indicated that the preliminary signs of narcosis were present in most subjects exposed at 100 ppm for 7.5 hours/day. [41]

The alteration of EEG tracings (increased delta wave activity), and subjective responses such as headaches, reported by Stewart et al, [40,41] after exposures at 100 ppm for 7.5 hours/day, were the only effects found at this concentration. While these alterations may be a preliminary subclinical response to tetrachloroethylene exposure, their appearance can result from various other factors unrelated to exposure. Stewart et al [41] reported no EEG alterations for subjects exposed at 20 ppm.

The data on human exposures at less than 100 ppm is sparse. Tuttle et al [50] reported neurologic and behavioral examinations of 22 workers in drycleaning operations with a mean of 7.47 years of exposure to tetrachloroethylene. The average TWA exposure for machine operators was 37.2 ± 24.96 ppm with an average ceiling of 214.90 ± 179.44 ppm. The investigators could identify no behavioral effects in workers exposed to tetrachloroethylene compared to an unexposed group. Differences in the neurologic examinations existed between the exposed and unexposed workers in proximal motor latency of the peroneal nerve, electrodiagnostic rating score, neurologic rating score and total neurologic score. The significance of these findings is in doubt because of the mean age of the exposed workers was 43.45 years and of the controls it was 34.44 years. The results of this study could easily have been confounded with the differences due to age.

Neurologic effects were not found in humans either from exposures at 20 ppm for 1 week, 7 hours/day by Stewart et al, [41] or at 55 ppm for 6 hours in the metabolism studies of Bolanowska and Golacka. [65] Studies of acute and chronic exposure at or near 100 ppm indicated that slight signs and symptoms of central nervous system depression may result. These effects are reversible and have been not shown to be painful or dysfunctional. There is very little evidence to indicate that exposures at less than 100 ppm will result in effects on humans.

Tetrachloroethylene is slowly eliminated from the body. [39,41,67] With repeated daily exposures it builds up in the blood and tissues, especially adipose tissues. [41,67] It is slowly metabolized. [58,69,70] All aspects of the metabolism are not known. Various metabolites have been found with tetrachloroethylene exposure. Trichloroacetic acid has been frequently determined in the urine. [69-71] Other metabolites of lesser urinary concentrations include trichloroethanol, oxalic acid, dichloracetic acid and ethylene glycol. [65,69-71,74,87,88]

It is recommended that the environmental limit for tetrachloroethylene be a time-weighted average concentration of 50 ppm. This limit should prevent neurologic effects as well as eye and respiratory tract irritation. No evidence of liver damage at or near the recommended limit has been reported.

Human exposures at concentrations between 100 and 300 ppm have resulted in neurologic effects such as difficulty maintaining a normal Romberg test and impaired motor coordination on the Flanagan test. To protect against temporary neurologic dysfunction, it is recommended that ceiling exposures be limited to 100 ppm as determined by sampling periods of 15 minutes.

It is recognized that many workers handle small amounts of tetrachloroethylene 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. Therefore, environmental monitoring and recordkeeping is recommended for those work situations which involve exposure above one-half the recommended limit, to delineate work areas that do not require the expenditure of health resources for control of inhalation hazards. One-half the environmental limit has been chosen on the basis of professional judgment rather than on quantitative data that delineate nonhazardous areas from those in which a hazard definitely exists.

Tetrachloroethylene has caused abnormalities in fetal animals. [84] These included an increased incidence of subcutaneous edema, delayed ossification of skull bones, and split sternebrae in fetal mice. There was also an increased incidence of fetal resorptions in rats. In both species, exposures occurred on days 6 through 15 of gestation for 7 hours a day at 300 ppm. The significance of these findings and their applicability to human workers is still in question. However, since the effects observed in the animals studied reflect in part maternal effects that the recommended environmental limits are expected to prevent, it is not recommended that additional considerations for exposure be given to females of child bearing age. Further investigations are warranted and discussed in Chapter VII. Additional considerations for protecting women of child bearing age will be recommended if indicated by results of additional research.

Other information which may affect the recommended environmental limit are the results of the National Cancer Institute study of carcinogenesis which is currently in progress. When this information is made available it will be evaluated and the recommended standard will be revised if necessary.

(b) Medical Monitoring

It is recommended that all workers be given preplacement and annual medical examinations. The preplacement examinations may identify workers that might be susceptible, due to predisposing conditions, to exposure to tetrachloroethylene below the recommended environmental limit. Examinations given prior to employment will provide data for evaluating workers after various lengths of exposure. The annual medical examination has been recommended to supplement the environmental monitoring which is not continuous. These examinations should provide additional evaluation of the effectiveness of the recommended environmental limit. The medical examinations should be general with emphasis on the hepatic and nervous systems, which have been reported to be the most effected systems. [38,43,55] Since information on the effects of tetrachloroethylene on pregnant women and offspring is inconclusive it is recommended that physicians report any spontaneous abortions or fetal abnormalities that might result from exposure to tetrachloroethylene. The annual schedule for the examinations will provide the opportunity for early detection of effects on the health of the workers.

(c) Sampling and Analytical Methods

It is recommended that tetrachloroethylene in air samples be collected with activated coconut charcoal, desorbed with carbon disulfide, and analyzed by gas chromatography. [104] The basis for this is discussed in Chapter IV and Appendices I and II. These methods have been chosen because of the availability of components, specificity of the method, and relative ease of use.

Since tetrachloroethylene is used in many small scale operations, such as drycleaning, it is recommended that direct reading colorimetric detector tubes be used to supplement the primary method of sampling and analysis for tetrachloroethylene. [111,112]

(d) Work Practices

Exposure to tetrachloroethylene will be minimized by adherence to the work practices recommended in Chapter I and discussed in Chapter VI. The basis of these practices is the avoidance of tetrachloroethylene by confinement of the material, and by personal protection of the worker.

Tetrachloroethylene is confined by various storage containers, tanks, pipes and valves. These are maintained by periodic inspection. Tetrachloroethylene can linger in confined spaces and concentrations may build up. For this reason, entry into confined spaces shall not occur until the appropriate ventilation procedures and respiratory protective measures recommended in Chapter I are instituted. Table I-1 shows the concentrations for which various types of respirators are effective. These should be used in confined spaces under conditions specified in Chapter I.

Eyes and skin are vulnerable to tetrachloroethylene. [38,40,44,46,61,63,64] It is recommended that goggles be worn in activities where splashing is possible.

VI. WORK PRACTICES

The manufacture of tetrachloroethylene requires large amounts of chlorine. [1,9] Information on safe handling of chlorine is available. [135] Other chlorohydrocarbons may be used as starting materials or may be formed as coproducts. Caution must be taken to avoid exposure to these substances as well as any hydrocarbons which may be used as starting materials.

Further information concerning specific work practices for tetrachloroethylene can be found in the Manufacturing Chemists Association Safety Data Sheet SD-24, and in various other publications. [6,136,138]

(a) Transport, Handling, and Use

Tetrachloroethylene may be stored in mild steel, cast iron or galvanized iron containers. Commercial grades are stabilized to prevent decomposition in air or light up to 140 C (284 F). It is nonflammable, but since it can be decomposed to toxic and corrosive compounds such as phosgene and hydrochloric acid by contact with open flame or red-hot surfaces, it should be appropriately stored and handled to prevent such contacts. [1,6,9] Damaged drums or other storage or transporting containers should not be welded until thoroughly purged with steam, flushed with water, and air dried. [139]

All piping and valves at the loading or unloading station should be of tetrachloroethylene-resistant material and should be carefully inspected prior to connection to the transport vehicle and periodically during the operation. Personal protective clothing must be provided during both inspection and connection. Eye wash and safety shower installations should be readily available in the immediate area. Signs indicating the location of safety showers and eye wash facilities should be prominently displayed throughout the work area. Unloading areas must be posted "Danger: loading or unloading tetrachloroethylene."

Tetrachloroethylene has been found to cause effects on the skin. Prolonged or repeated exposure of skin to tetrachloroethylene should be avoided to prevent cutaneous effects.

Due to the toxicity of tetrachloroethylene, processes in which it is used in large quantities should be carried out in closed systems. Well designed hoods and ventilation systems should be used to maintain exposures at or below concentrations specified by this standard. Further protective measures include the use of personal protective equipment and clothing and purging of equipment prior to and during servicing and maintenance.

Tetrachloroethylene is a component of some insecticidal fumigants and conventional work practice guidelines are inappropriate to protect agricultural workers from the hazards of exposure. For these uses, fumigants containing tetrachloroethylene must be used in a manner consistent with their labeling requirements. These usually specify allowable time limits before a fumigated area or space may be reentered, and safe practices for the application of the particular pesticide. Consideration must be given to the wearing of personal protective equipment including a long-sleeved shirt, long-legged pants (or suitable coveralls), a hat, shoes, socks, and solvent-resistant gloves. Specific requirements of worker protection standards for agricultural pesticides may be found in 40 CFR 170.

Where a fumigant is applied to a crop in confined storage, hazardous concentrations may be encountered and entry to such areas must not be made without proper personal protective equipment including a self-contained breathing apparatus.

Safety showers and eye wash facilities are necessary in areas where tetrachloroethylene is handled. In locations where such facilities are not available, a container of water for emergency use must be kept with the first aid supplies.

(b) Equipment Maintenance

All equipment used for handling tetrachloroethylene must be emptied and purged prior to entry or disassembly. Steaming followed by washing with water is recommended for purging tanks and other containers which have held tetrachloroethylene. [6] Pipe lines should be disconnected and capped. Under conditions where it is necessary to enter or otherwise work with tetrachloroethylene contaminated equipment, maintenance personnel must use either a self-contained breathing apparatus of the pressure-demand mode, with an impervious protective suit, or a combination supplied-air suit with auxiliary self-contained air supply. Ventilation should still be continued during this time by blowing or drawing fresh air through the system. Safety precautions for emergency rescue require that all maintenance personnel be informed of the toxic properties of tetrachloroethylene and be instructed on the necessity of wearing personal protective equipment. [6] Constant observation of anyone entering a tank should be maintained in case rescue work is necessary.

(c) Emergencies

Spills must be anticipated. Storage tanks should be diked to contain the contents of the tank. Drum storage areas must also be diked to contain the tetrachloroethylene in the drums, preventing release to other areas. Areas where major spills are likely to occur should be constructed so that they may be closed until properly protected personnel can ventilate, enter, and clear the area. Warning signs must be posted so that unauthorized personnel will not enter the area. Normal work should not be continued until the concentration of tetrachloroethylene has been reduced to that prescribed by this standard. Any high temperature operations must be stopped until the spill is cleared. Disposal of tetrachloroethylene must be done in compliance with local, state, and federal waste disposal regulations. Consideration should be given to pumping the diked spill to another tank. In addition, it is advisable to have facilities for transfer of the contents of a leaking tank to another suitable tank.

Areas in which spills have occurred should be evacuated and well ventilated. Small, portable exhaust fans may be used in confined areas where local exhaust ventilation is not feasible. Workers should not return to any work area if the odor of tetrachloroethylene is still perceptible without first determining the concentration.

(d) Respiratory Protection

For adequate respiratory protection against the multiplicity of conditions which may be encountered in individual operations, many types of respirators have been developed and approved. Each have particular applications and limitations from the viewpoint of protection, as well as advantages and disadvantages from the viewpoint of operational procedures and maintenance. Detailed information on the selection and use of respirators can be obtained from the respiratory protection devices manual [140] published by the AIHA and the ACGIH in 1963. The American National Standards Practices for Respiratory Protection, ANSI Z88.2-1969, [141] also classifies, describes, and gives the limitations of respirators.

There are three categories of respirators: atmosphere-supplying respirators, air-purifying respirators, and combination atmosphere-supplying and air-purifying respirators.

One factor that affects the overall performance of demand-type (negative pressure) respirators is the variability of the face seal. Facepiece leakage is the major limitation of half-mask and quarter-mask facepieces operated with a negative pressure.

For purposes of uniform regulations covering the many face sizes and shapes of the US population, NIOSH recommends that the half-mask or quarter-mask facepieces operated with a negative pressure not be used for protection above 10 times the TWA limit, although the majority of wearers can obtain protection in atmospheres of higher tetrachloroethylene concentrations. On the same basis, NIOSH recommends that the full facepiece, operated with negative pressure, may be used up to 50 times the TWA limit.

These maximum use concentration guides do not take into account the service life of the filters and/or absorbent canisters which also affect the performance of air-purifying respirators. The approval tests (30 CFR 11) for these two devices specify only carbon tetrachloride for the service life test. Based on recent tests by Nelson and Harder, [142] who tested standard respirator cartridges against many types of industrial organic solvents, it is now possible to estimate the service life of approved organic vapor canisters or cartridges against tetrachloroethylene. With a test concentration of 1,000 ppm of tetrachloroethylene, they reported that the standard organic vapor cartridge has a service life of 129 minutes before a breakthrough of 100 ppm of tetrachloroethylene. Under the same test conditions, a service life of 90 minutes for carbon tetrachloride was obtained. The standard industrial size gas mask canister is tested against 20,000 ppm of carbon tetrachloride and it must have a service life of 12 minutes before a breakthrough of 5 ppm. Since it has been shown that charcoal can adsorb 0.7 times as much carbon tetrachloride as tetrachloroethylene, it can be estimated that the service life for an industrial size canister is 340 minutes in an atmosphere of 1,000 ppm tetrachloroethylene.

NIOSH periodically issues a list of approved or certified respiratory protective devices. All devices approved by the Bureau of Mines are listed in Information Circular 8559 and supplements. All types of devices certified by the Testing and Certification Laboratory of NIOSH are listed in a separate publication. These are available from the Testing and Certification Laboratory, NIOSH, Morgantown, West Virginia, 26505.

VII. RESEARCH NEEDS

There is a need for data concerning the long-range effects of chronic exposures to tetrachloroethylene at or below the recommended environmental limit. Of particular concern is the area of behavioral and neurological effects. A preliminary study showed that certain behavioral and neurological tests will reflect tetrachloroethylene exposure. [50]

While the results of the study are inconclusive due to small numbers of subjects and differences between exposed and unexposed groups, the approach is valid and should be studied further. Additional research could be conclusive if the number of subjects is increased and the experiment is more rigorously designed.

Another area of needed research concerns the fetotoxic and teratogenic effects of tetrachloroethylene. The study by Schwetz et al [84] is the only study that provides information on teratogenesis. The design of this study did not take into consideration the effects of chronic exposure to tetrachloroethylene prior to breeding. Therefore the effects on organogenesis of the fetus of chronic exposure of the mother to tetrachloroethylene or its metabolites are not known. Studies should be designed to provide this information. The findings reported in the study by Schwetz et al [84] should be confirmed by other investigators and extended to other species including primates. Studies of whether tetrachloroethylene has mutagenic potentials were not found in the literature. Such studies should be performed.

The metabolic pathways for tetrachloroethylene are subject to question. Various metabolites have been found after tetrachloroethylene exposure. The process, products, and disposition of inhaled tetrachloroethylene should be determined.

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IX. APPENDIX I

SAMPLING PROCEDURE FOR COLLECTION OF TETRACHLOROETHYLENE

General Requirements

(a) Air samples representative of the breathing zones of workers must be collected to characterize the exposure from each job or specific operation in each work area.

(b) Samples collected must be representative of exposure of individual workers.

(c) Suggested records:

(1) The date and time of sample collection.

(2) Sampling duration.

(3) Total sample volume.

(4) Location of sampling.

(5) Temperature, pressure, and relative humidity at time of sampling.

(6) Other pertinent information.

Sampling

(a) Samples should be collected as near as practicable to the faces of workers without interfering with freedom of movement.

(b) Samples should be collected to permit determination of TWA workday and ceiling exposures for every job involving exposure to tetrachloroethylene in sufficient numbers to express the variability of the exposures in the work situation.

(c) Apparatus for Charcoal Tube Sampling

(1) Pump, battery-operated, complete with clip for attachment to the worker. Airflow through the pump shall be within 5% of the desired rate.

(2) Charcoal tubes: glass tube with both ends flame-sealed, 7 cm long, 6-mm O.D. and 4-mm I.D., containing two sections of 20/40 mesh activated coconut shell charcoal separated by a 2-mm portion of urethane foam. The first is the adsorbing section and contains 100 mg of charcoal from coconut shells. The second, or reserve section, contains 50 mg. A 3-mm portion of urethane foam is placed between the outlet of the tube and the reserve section. A plug of glass wool is placed in front of the adsorbing section. The pressure drop across the tube when in use must be less than 1 inch of mercury at a flowrate of 1 liter/min.

(d) Calibration of Sampling Instruments

(1) Air sampling instruments shall be calibrated with a representative charcoal tube in line, over a normal range of flowrates (25-1,000 ml/min). Calibration curves must be established for each sampling pump and shall be used in adjusting the pump prior to and during each field use. New calibration curves should be established for each sampling pump after making any repairs on modifications to the sampling system.

(2) The flowrate through the sampling system should be spot checked and the proper adjustments made before and during each study to ensure obtaining accurate airflow data.

(e) Collection and Handling of Samples

(1) Immediately before sampling, break both ends of the tube to provide openings at least one-half the internal diameter of the tube (2 mm).

(2) The smaller section of charcoal is used as a reserve and should be positioned nearest the sampling pump.

(3) The charcoal tube should be placed in a vertical position during sampling.

(4) Tubing may be used to connect the back of the tube to the pump, but air being sampled should not be passed through any hose or tubing before entering the charcoal tube.

(5) The sample can be taken at flowrates of 25-1,000 ml/min, depending on the pump. Total sample volumes of 1-12 liters are recommended, eg, a sample could be collected at 200 ml/min for 15 minutes to give a total sample of 3 liters, or at 25 ml/min for 8 hours to give a total sample volume of 12 liters. However, it is also recommended that each sample be collected in 4 hours or less.

(6) Samples should be collected over 15-minute periods at times when the highest exposure is expected. The TWA determination can be made from collecting a series of 15-minute samples.

(7) The charcoal tubes should be capped with inert plastic caps immediately after sampling. Under no circumstances should rubber caps be used.

(8) One charcoal tube, to serve as an analytical blank, should be handled in the same manner as the sample tube (break, seal, and transport) except that no air is sampled through this tube.

X. APPENDIX II

ANALYTICAL PROCEDURE FOR DETERMINATION OF TETRACHLOROETHYLENE

Principle of the Method

(a) A known volume of air is drawn through a charcoal tube to trap the tetrachloroethylene vapor.

(b) The tetrachloroethylene is desorbed from the charcoal with carbon disulfide.

(c) An aliquot of the desorbed sample is injected into a gas chromatograph.

(d) The area of the resulting peak is determined and compared with areas obtained from the injection of standards.

Range and Sensitivity

(a) The lower limit for detection of tetrachloroethylene on a gas chromatograph with a flame ionization detector is 2 μg/sample.

(b) The upper limit value for tetrachloroethylene is 4.0 mg/sample. This is the estimated amount of tetrachloroethylene which the front section will hold before this compound breaks through to the reserve section of charcoal. If a particular atmosphere is suspected of containing a high concentration of tetrachloroethylene, it is recommended that a smaller volume of air be sampled.

Interferences

(a) Tetrachloroethylene will not be trapped when the amount of water in the air is so great that condensation occurs in the charcoal sampling tube.

(b) Any compound which has the same retention time as tetrachloroethylene with the chromatographic conditions described in this method could interfere. These may be eliminated by altering operating conditions of the gas chromatograph using a different column packing or using a selective detector, ie, electron capture.

Advantages of the Method

(a) This method provides one basic method for determining many different organic compounds.

(b) The sampling device is small, portable, and involves no liquids.

(c) The analysis of the tubes can be accomplished rapidly.

Disadvantages of the Method

(a) The amount of sample which can be taken is limited by the weight of tetrachloroethylene which the tube will hold before overloading.

(b) When the sample value obtained for the reserve section of charcoal exceeds 25% of that found on the front section, the possibility of appreciable sample loss exists.

(c) Other organic compounds in high concentrations may displace tetrachloroethylene from the charcoal.

Apparatus

(a) Gas chromatograph equipped with a flame ionization detector.

(b) Stainless steel column (20 ft x 1/8 in) with 10% free fatty acid polymer (FFAP) stationary phase on 80/100 mesh Chromosorb W (or equivalent), acid-washed and treated with dimethyldichlorosilane.

(c) A recorder and some method for determining peak area.

(d) Glass stoppered microtubes of 2.5-ml capacity or 2-ml vials that can be sealed with inert caps.

(e) Microsyringe of 10-μl capacity, and convenient sizes for making standards.

(f) Pipets 0.5-ml delivery pipets or 1.0-ml pipets graduated in 0.1-ml increments.

(g) Volumetric flasks of 10-ml capacity or convenient sizes for making standard solutions.

Reagents

(a) "Spectroquality" carbon disulfide.

(b) Tetrachloroethylene, preferably "chromatoquality" grade.

(c) Bureau of Mines Grade A helium.

(d) Prepurified hydrogen.

(e) Filtered compressed air.

Analysis of Samples

(a) All equipment used in the analysis should be washed in detergent followed by appropriate tap and distilled water rinses.

(b) Preparation: Each charcoal tube is scored with a file in front of the first section of charcoal and broken open. The glass wool is removed and discarded. The charcoal in the first (larger) section is transferred to a small stoppered test tube. The separating foam is removed and discarded; the second section is transferred to another similar tube or vial. These two sections are analyzed separately. Prior to analysis, 0.5 ml of carbon disulfide is pipetted into each test tube to desorb tetrachloroethylene from the charcoal. Do not pipette by mouth.

> EXTREME CAUTION MUST BE EXERCISED AT ALL TIMES WHEN USING CARBON DISFULIDE BECAUSE OF ITS HIGH TOXICITY AND FIRE AND EXPLOSION HAZARDS. IT CAN BE IGNITED BY HOT STEAM PIPES. ALL WORK WITH CARBON DISULFIDE MUST BE PERFORMED UNDER AN EXHAUST HOOD.

(c) Typical chromatographic operating conditions:

(1) 40 ml/min (70 psig) helium carrier gas flow.

(2) 65 ml/min (24 psig) hydrogen gas flow to detector.

(3) 500 ml/min (50 psig) airflow to detector.

(4) 200 C injector temperature.

(5) 200 C manifold temperature (detector).

(6) 80 C isothermal oven or column temperature.

(d) Injection: The first step in the analysis is the injection of the sample into the gas chromatograph. To eliminate difficulties arising from blowback or distillation within the syringe needle, the solvent flush injection technique is employed. The 10-μl syringe is first flushed with carbon disulfide several times to wet the barrel and plunger. Three μl of carbon disulfide are drawn into the syringe to increase the accuracy and reproducibility of the injected sample volume. The needle is removed from the carbon disulfide solvent, and the plunger is pulled back about 0.2 μl to separate the solvent flush from the sample, with a pocket of air to be used as a marker. The needle is then immersed in the sample,, and a 5-μl aliquot is withdrawn, taking into consideration the volume of the needle, since the sample in the needle will be completely injected. After the needle is removed from the sample and prior to injection, the plunger is pulled back a short distance to minimize evaporation of the sample from the tip of the needle. Duplicate injections of each sample and standard should be made. No more than a 3% difference in area is to be expected.

(e) Measurement of area: The area of the sample peak is determined and preliminary sample results are read from a standard curve prepared as discussed below.

Determination of Desorption Efficiency

It is necessary to determine the percentage of tetrachloroethylene on the charcoal that is removed in the desorption process. This desorption efficiency is determined once for a given compound provided the same batch of charcoal is always used.

Activated charcoal, equivalent to the amount in the first section of the sampling tube (100 mg), is measured into a 2-inch long tube, with an inside diameter of 4 mm, flame-sealed at one end. This charcoal must be from the same batch used in obtaining the samples and can be obtained from unused charcoal tubes. The open end is capped with inert plastic. A known amount of the compound is injected directly into the activated charcoal with a microliter syringe, and the tube is capped with inert plastic.

A minimum of six tubes are prepared in this manner and allowed to stand at least overnight to ensure complete adsorption of tetrachloroethylene onto the charcoal. These six tubes will be referred to as the "desorption samples." A parallel blank tube should be treated in the same manner except that no tetrachloroethylene is added to it. The desorption samples and blanks are desorbed and analyzed in exactly the same manner as previously described.

Two or three desorption standards are prepared for analysis by injecting the same volume of tetrachloroethylene into 0.5 ml of carbon disulfide with the same syringe used in the preparation of the desorption samples. These are analyzed with the desorption samples.

The desorption efficiency equals the difference between the average peak area of the desorption samples and the peak area of the blank divided by the average peak area of the desorption standards, or

$$\text{desorption efficiency} = \frac{\text{area of sample} - \text{area of blank}}{\text{area of standard}}$$

Calibration and Standards

It is convenient to prepare standards in terms of mg tetrachloroethylene/0.5 ml of carbon disulfide because samples are desorbed in this amount of carbon disulfide. To minimize error due to the volatility of carbon disulfide, 20 times the weight can be injected into 10 ml of carbon disulfide. For example, to prepare a 0.3 mg/0.5 ml standard, 6.0 mg of tetrachloroethylene is injected into exactly 10 ml of carbon disulfide in a glass stoppered flask. The density of tetrachloroethylene (1.623 g/ml) is used to convert 6.0 mg into microliters for easy measurement with a microliter syringe. A series of standards is prepared, varying in concentration over the range of interest and analyzed under the same gas chromatographic conditions and during the same time period as the unknown samples. Curves are established by plotting concentration versus average peak area.

Calculations

(a) The weight in mg corresponding to the peak area is read from the standard curve. No volume corrections are needed, because the standard curve is based on mg tetrachloroethylene/0.5 ml carbon disulfide, and the volume of sample injected is identical to the volume of the standards injected.

(b) Separately determine the weights of tetrachloroethylene on the front and reserve sections of the charcoal tube.

(c) Corrections must be made to the tetrachloroethylene weights determined on both the front and reserve sections for the weights of the respective sections of the blank charcoal tube.

(1) Subtract the weight of tetrachloroethylene found on the front section of the blank charcoal tube from the weight of tetrachloroethylene found on the front section of the sample charcoal tube to give a corrected front section weight.

(2) Subtract the weight of tetrachloroethylene found on the reserve section of the blank charcoal tube from the weight of

tetrachloroethylene found on the reserve section of the sample charcoal tube to give a corrected reserve section weight.

(3) Add the corrected amounts of tetrachloroethylene present on the front and reserve sections of the sample tube to determine the total measured tetrachloroethylene in the sample.

(4) Divide this total weight by the determined desorption efficiency to obtain M, the total mg per sample.

(d) Convert the liters of air sampled (V) to volume (V') at standard conditions of 25 C and 760 mm Hg, as follows:

$$V' = \frac{298VP}{760(T+273)} = \frac{0.392VP}{(T+273)}$$

Where:

V' = volume of sampled air in liters at 25 C and 760 mm Hg

V = measured volume of sampled air in liters

P = barometric pressure in mm Hg, measured at time of sampling

T = temperature of air in degree celsius, measured at time of sampling

(e) The concentration of tetrachloroethylene in the sampled air can be expressed in various ways using M, the weight of tetrachloroethylene obtained in (c)(4), and V', the standardized sample volume, obtained in (d), as follows:

(1) mg/liter = M/V'

(2) mg/cu m = µg/liter = 1,000 M/V'

(3) ppm = 147.4 M/V'

XI. APPENDIX III - MATERIAL SAFETY DATA SHEET

General instructions for preparing a Material Safety Data Sheet (MSDS) are presented in this chapter. The examples used in the text are for illustrative purposes and are not intended to apply to any specific compound or product. Applicable information about a specific product or material shall be supplied in the appropriate block of the MSDS.

The product designation is inserted in the block in the upper left corner of the first page to facilitate filing and retrieval. Print in upper case letters as large as possible. It should be printed to read upright with the sheet turned sideways. The product designation is that name or code designation which appears on the label, or by which the product is sold or known by employees. The relative numerical hazard ratings and key statements are those determined by the guidelines in Chapter V, Part B, of the NIOSH publication, An Identification System for Occupationally Hazardous Materials. The company identification may be printed in the upper right corner if desired.

(a) Section I. Product Identification

The manufacturer's name, address, and regular and emergency telephone numbers (including area code) are inserted in the appropriate blocks of Section I. The company listed should be a source of detailed backup information on the hazards of the material(s) covered by the MSDS. The listing of suppliers or wholesale distributors is discouraged. The trade name should be the product designation or common name associated with the material. The synonyms are those commonly used for the product, especially formal chemical nomenclature. Every known chemical designation or competitor's trade name need not be listed.

(b) Section II. Hazardous Ingredients

The "materials" listed in Section II shall be those substances which are part of the hazardous product covered by the MSDS and individually meet any of the criteria defining a hazardous material. Thus, one component of a multicomponent product might be listed because of its toxicity, another component because of its flammability, while a third component could be included both for its toxicity and its reactivity. Note that a MSDS for a single component product must have the name of the material repeated in this section to avoid giving the impression that there are no hazardous ingredients.

Chemical substances should be listed according to their complete name derived from a recognized system of nomenclature. Where possible, avoid using common names and general class names such as "aromatic amine," "safety solvent," or "aliphatic hydrocarbon" when the specific name is known.

The "%" may be the approximate percentage by weight or volume (indicate basis) which each hazardous ingredient of the mixture bears to the whole mixture. This may be indicated as a range or maximum amount, ie, "10-40% vol" or "10% max wt" to avoid disclosure of trade secrets.

Toxic hazard data shall be stated in terms of concentration, mode of exposure or test, and animal used, ie, "100 ppm LC50 rat," "25 mg/kg LD50-skin-rabbit," "75 ppm LC man," or "permissible exposure from 29 CFR 1910.1000," or, if not available, from other sources of publications such as the American Conference of Governmental Industrial Hygienists or the American National Standards Institute Inc. Flammable or reactive data could be flash point, shock sensitivity, or other brief data indicating nature of the hazard.

(c) Section III. Physical Data

The data in Section III should be for the total mixture and should include the boiling point and melting point in degrees Fahrenheit (Celsius in parentheses); vapor pressure, in conventional millimeters of mercury (mm Hg); vapor density of gas or vapor (air = 1): solubility in water, in parts/hundred parts of water by weight; specific gravity (water = 1): percent volatiles (indicated if by weight or volume) at 70 degrees Fahrenheit (21.1 degrees Celsius); evaporation rate for liquids or sublimable solids, relative to butyl acetate; and appearance and odor. These data are useful for the control of toxic substances. Boiling point, vapor density, percent volatiles, vapor pressure, and evaporation are useful for designing proper ventilation equipment. This information is also useful for design and deployment of adequate fire and spill containment equipment. The appearance and odor may facilitate identification of substances stored in improperly marked containers, or when spilled.

(d) Section IV. Fire and Explosion Data

Section IV should contain complete fire and explosion data for the product, including flash point and autoignition temperature in degrees Fahrenheit (Celsius in parentheses); flammable limits, in percent by volume in air; suitable extinguishing media or materials; special firefighting procedures; and unusual fire and explosion hazard information. If the product presents no fire hazard, insert "NO FIRE HAZARD" on the line labeled "Extinguishing Media."

(e) Section V. Health Hazard Information

The "Health Hazard Data" should be a combined estimate of the hazard of the total product. This can be expressed as a time-weighted average (TWA) concentration, as a permissible exposure, or by some other indication of an acceptable limit. Other data are acceptable, such as lowest LD50 if multiple components are involved.

Under "Routes of Exposure," comments in each category should reflect the potential hazard from absorption by the route in question. Comments should indicate the severity of the effect and the basis for the statement if possible. The basis might be animal studies, analogy with similar products, or human experiences. Comments such as "yes" or "possible" are not helpful. Typical comments might be:

> Skin Contact--single short contact, no adverse effects likely; prolonged or repeated contact, irritation, and cracking. Readily absorbed through the skin with severe systemic effects.
>
> Eye Contact--some pain and mild transient irritation; no corneal scarring.

"Emergency and First Aid Procedures" should be written in lay language and should primarily represent first aid treatment that could be provided by paramedical personnel or individuals trained in first aid.

Information in the "Notes to Physician" section should include any special medical information which would be of assistance to an attending physician including required or recommended preplacement and periodic medical examinations, diagnostic procedures, and medical management of overexposed workers.

(f) Section VI. Reactivity Data

The comments in Section VI relate to safe storage and handling of hazardous, unstable substances. It is particularly important to highlight instability or incompatibility to common substances or circumstances such as water, direct sunlight, steel or copper piping, acids, alkalies, etc. "Hazardous Decomposition Products" shall include those products released under fire conditions. It must also include dangerous products produced by aging, such as peroxides in the case of some ethers. Where applicable, shelf life should also be indicated.

(g) Section VII. Spill or Leak Procedures

Detailed procedures for cleanup and disposal should be listed with emphasis on precautions to be taken to protect workers assigned to cleanup detail. Specific neutralizing chemicals or procedures should be described in detail. Disposal methods should be explicit including proper labeling of containers holding residues and ultimate disposal methods such as "sanitary landfill," or "incineration." Warnings such as "comply with local, state, and federal anti-pollution ordinances" are proper but not sufficient. Specific procedures should be identified.

(h) Section VIII. Special Protection Information

Section VIII requires specific information. Statements such as "Yes," "No," or "If Necessary" are not informative. Ventilation requirements should be specific as to type and preferred methods. Specify respirators as to type and NIOSH or US Bureau of Mines approval class, ie, "Supplied air," "Organic vapor canister," "Suitable for dusts not more toxic than lead," etc. Protective equipment must be specified as to type and materials of construction.

(i) Section IX. Special Precautions

"Precautionary Statements" shall consist of the label statements selected for use on the container or placard. Additional information on any aspect of safety or health not covered in other sections should be inserted in Section IX. The lower block can contain references to published guides or in-house procedures for handling and storage. Department of Transportation markings and classifications and other freight, handling, or storage requirements and environmental controls can be noted.

(j) Signature and Filing

Finally, the name and address of the responsible person who completed the MSDS and the date of completion are entered. This will facilitate correction of errors and identify a source of additional information.

The MSDS shall be filed in a location readily accessible to workers potentially exposed to the hazardous material. The MSDS can be used as a training aid and basis for discussion during safety meetings and training of new employees. It should assist management by directing attention to the need for specific control engineering, work practices, and protective measures to ensure safe handling and use of the material. It will aid the safety and health staff in planning a safe and healthful work environment and suggesting appropriate emergency procedures and sources of help in the event of harmful exposure of employees.

MATERIAL SAFETY DATA SHEET

I PRODUCT IDENTIFICATION

MANUFACTURER'S NAME	REGULAR TELEPHONE NO. EMERGENCY TELEPHONE NO.
ADDRESS	
TRADE NAME	
SYNONYMS	

II HAZARDOUS INGREDIENTS

MATERIAL OR COMPONENT	%	HAZARD DATA

III PHYSICAL DATA

BOILING POINT, 760 MM HG		MELTING POINT
SPECIFIC GRAVITY (H_2O=1)		VAPOR PRESSURE
VAPOR DENSITY (AIR=1)		SOLUBILITY IN H_2O, % BY WT
% VOLATILES BY VOL		EVAPORATION RATE (BUTYL ACETATE=1)
APPEARANCE AND ODOR		

IV FIRE AND EXPLOSION DATA

FLASH POINT (TEST METHOD)		AUTOIGNITION TEMPERATURE			
FLAMMABLE LIMITS IN AIR, % BY VOL.	LOWER		UPPER		
EXTINGUISHING MEDIA					
SPECIAL FIRE FIGHTING PROCEDURES					
UNUSUAL FIRE AND EXPLOSION HAZARD					

V HEALTH HAZARD INFORMATION

HEALTH HAZARD DATA

ROUTES OF EXPOSURE

INHALATION

SKIN CONTACT

SKIN ABSORPTION

EYE CONTACT

INGESTION

EFFECTS OF OVEREXPOSURE

ACUTE OVEREXPOSURE

CHRONIC OVEREXPOSURE

EMERGENCY AND FIRST AID PROCEDURES

EYES

SKIN

INHALATION

INGESTION

NOTES TO PHYSICIAN

VI REACTIVITY DATA

CONDITIONS CONTRIBUTING TO INSTABILITY

INCOMPATIBILITY

HAZARDOUS DECOMPOSITION PRODUCTS

CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION

VII SPILL OR LEAK PROCEDURES

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED

NEUTRALIZING CHEMICALS

WASTE DISPOSAL METHOD

VIII SPECIAL PROTECTION INFORMATION

VENTILATION REQUIREMENTS

SPECIFIC PERSONAL PROTECTIVE EQUIPMENT

RESPIRATORY (SPECIFY IN DETAIL)

EYE

GLOVES

OTHER CLOTHING AND EQUIPMENT

IX SPECIAL PRECAUTIONS

PRECAUTIONARY
STATEMENTS

OTHER HANDLING AND
STORAGE REQUIREMENTS

PREPARED BY

ADDRESS

DATE

XII. TABLES

TABLE XII-1

PHYSICAL PROPERTIES OF TETRACHLOROETHYLENE

Chemical Abstract's serial number	000127184
Synonyms	Tetrachloroethylene Perchloroethylene Tetrachloroethene Ethylene tetrachloride
Molecular formula	CCl 2 = CCl 2
Molecular weight	165.84
Boiling point	121.2 C (250 F) (760 mm Hg)
Melting point	-22.35 C (-8 F)
Vapor density	5.76 (air = 1)
Specific gravity	1.623 (20 C), (water = 1.000 at 4 C)
Solubility	0.015g/100g water at 25 C; soluble in ethyl ether, ethyl alcohol, benzene chloroform
Density of saturated air	1.12 (air = 1)
Concentration of saturated air	2.43% by volume at 25 C
Flammable (explosive) limits	None
Flash point	"
Autoignition temperature	"

TABLE XII-1 (CONTINUED)

PHYSICAL PROPERTIES OF TETRACHLOROETHYLENE

Vapor pressure	Temp F	Temp C	mm Hg
	50	10	8
	68	20	14
	77	25	19
	86	30	25
	104	40	41
Conversion factors, 25 C 760 mm Hg	1 mg/liter = 1 g/cu m = 147.4 ppm 1 ppm = 6.78 mg/cu m = 6.78 μg/liter		

Adapted from references 5,6,7

TABLE XII-2

EXPOSURE DATA FOR PARTICIPANTS IN A STUDY OF NEUROLOGICAL AND BEHAVIORAL EFFECTS OF TETRACHLOROETHYLENE

POSITION	No.	AVERAGE TWA CONCENTRATION ppm		AVERAGE PEAK CONCENTRATION ppm		AVERAGE BREATH SAMPLE CONCENTRATION ppm	
		MEAN	SD	MEAN	SD	MEAN	SD
Machine Operator	5	37.2	± 24.96	214.90	± 179.44	20.47	± 18.21
Presser	2	11.43	± 6.82	51.85	± 64.56	4.48	± .39
Counter	5	1.32	± .97	2.61	± 1.87	.95	± .62
Miscellaneous	7	3.03	± 2.09	27.45	± 46.02	2.04	± 2.29

Adapted from Tuttle el al [50]

TABLE XII-3

BREATH CONCENTRATION OF TETRACHLOROETHYLENE AFTER EXPOSURE FOR 7.5 HOURS AT 100 ppm

Four Male Subjects
Week 4

	DAY				
	1	2	3	4	5
		Mean and standard deviations in ppm			
Preexposure	2.90				
	±0.94				
Postexposure					
1 minute	36.43	35.24	37.18	37.55	38.77
	±4.01	±1.52	±4.17	±2.92	±2.16
10 minutes	30.10	29.43	32.33	30.52	32.55
	±3.36	±1.41	±1.65	±3.35	±2.61
20 minutes	27.79	23.92	29.31	27.10	29.59
	±2.90	±2.42	±2.66	±3.92	±2.63
30 minutes	22.90	23.33	27.05	25.67	26.12
	±0.71	±2.31	±1.67	±2.19	±2.52
1 hour	17.48	19.49	22.42	21.48	24.49
	±0.74	±2.07	±1.54	±0.66	±2.43
3 hours	10.26	11.95	11.10	10.56	12.92
	±2.64	±2.37	±3.57	±0.71	±7.15
16-1/2 hours	5.76	6.37	7.76	7.96	9.76
	±0.45	±0.27	±0.75	±0.76	±1.00

Adapted from Stewart et al [41]

TABLE XII-4

24-HOUR MEDIAN LETHAL AND EFFECTIVE DOSES OF TETRACHLOROETHYLENE
(mg/kg)

Species	LD50	BSP Retention	SGPT	PSP Retention
Mouse	2.9	2.9	2.9	Not Determined
Dog	2.1	Not Determined	0.74	1.4

Adapted from Klaassen and Plaa [79,80]

TABLE XII-5

SUMMARY OF EFFECTS OF TETRACHLOROETHYLENE

Exposure Concentration and Reference	Exposure Variables	Effects
	Human Data	
20-70 ppm [70]	Intermittent daily exposures	4-20 mg/liter trichloroethanol and 4-35 mg/liter trichloroacetic acid in urine
75-80 ppm [39]	1-4 minutes	Very slight eye irritation and mild burning sensation
83-130 ppm 106 ppm average [55]	4 hours	Slight eye irritation
100 ppm [41]	7-1/2 hours/day	EEG indicated preliminary signs of narcosis in most subjects
100-120 ppm [38]	4-6 minutes	Dryness and irritation of soft palate
150 ppm [69]	7-1/2 hours/day	Impaired coordination
10-400 ppm [69]	8 hours/day, 5 days/week	Urine concentrations of trichloroacetic acid and trichloroethanol proportional to exposure concentrations up to 100 ppm
216 ppm [38]	2 hours	Responses similar to those at 280 ppm, but less severe
50-250 ppm [56]	Drycleaning plant	Central nervous symptom disorders in 3 workers
50-250 ppm [56]	Drycleaning plant 4 months	Urinary trichloracetic acid 20, 23 and 25 mg/liter loss of appetite

TABLE XII-5 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHYLENE

Exposure Concentration and Reference	Exposure Variables	Effects
	Human Data	
50-250 ppm [56] (continued)	Drycleaning plant 5 months	Respiratory distress, coughing, vomiting, cardiac failure and death with hepatic necrosis and fatty degeneration of the heart
210-244 ppm [39]	30 minutes	Slight lightheadedness, increased effort to maintain normal Romberg test
280 ppm [38]	2 hours	Burning eyes, congestion of frontal sinus, lightheadedness, mental effort required for motor coordination
232-385 ppm [51]	8 hours twice weekly	Liver injury in 7 de-degreaser operators
200-400 ppm [70]	Intermittent daily exposures	21-100 mg/liter trichloroethanol and 32-97 mg/liter trichloroacetic acid in urine
25-1,470 ppm average 393 ppm 70-425 ppm of Stoddard solvent [60]	3-1/2 hours	Marked eye irritation, light headedness, dizziness, unconsciousness, rapid recovery, evidence of liver injury 9 days later
475-680 ppm average 500 ppm [37]	1/2 hour	Increased salivation, metallic taste, slight eye irritation, increased perspiration of the hands, tightness of frontal sinuses

TABLE XII-5 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHYLENE

Exposure Concentration and Reference	Exposure Variables	Effects
	Human Data	
513-690 ppm [38]	10 minutes	Eye and respiratory tract irritation, dizziness, tightness and numbness around mouth, loss of some inhibitions, increased mental effort required to maintain motor ability
930-1,185 ppm [38]	1-2 minutes	Markedly irritating to eyes and upper respiratory tract
934-1,140 ppm average 1,000 ppm [37]	95 minutes	Lassitude, stinging sensation in eyes, tightness of the frontal sinuses, definite exhilaration after 45 minutes
2,000 ppm [37]	7-1/2 minutes	Light narcosis
	Animal Data	
15 ppm [73]	4 hours/day 5 months	Rats, EEG changes and protoplasmal swelling of cerebral cortical cells, some vacuolated cells and signs of karyolysis
70 ppm [37]	8 hours/day 5 days/week 150 exposures	Rats, no pathological findings
73 and 147 ppm [73]	4 hours/day 4 weeks	Rats, EEG and electromyogram changes: decreased acetylcholinesterase activity

TABLE XII-5 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHYLENE

Exposure Concentration and Reference	Exposure Variables	Effects
	Animal Data	
100 ppm [38]	7 hours/day, 5 days/week 132 exposures	Guinea pigs, increased liver weights in females
200 ppm [38]	7 hours/day, 5 days/week	Guinea pigs, increased liver weights with some fatty degeneration in both males and females
200 ppm [75]	4 hours single exposure	Mice, moderate liver fatty infiltration 1 day after exposure but not 3 days after
230 ppm [37]	8 hours/day, 5 days/week 150 exposures	Rats, similar but less severe pathological findings as with 470 ppm
300 ppm [84]	7 hours/day, days 6-15 of gestation	Rats, decreased maternal weight gains, increased fetal resorptions
300 ppm [84]	7 hours/day, days 6-15 of gestation	Mice, maternal liver weights increased relative to body weight; increased incidences of fetal subcutaneous edema, delayed ossification of skull bones, and split sternebrae
100-400 ppm [38]	7 hours/day, 5 days/week 6 months	Rats, rabbits, monkeys, no abnormal growth, organ function or histopathologic findings

TABLE XII-5 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHYLENE

Exposure Concentration and Reference	Exposure Variables	Effects
	Animal Data	
400 ppm [38]	7 hours/day, 5 days/week 169 exposures	Guinea pigs, more pronounced liver changes than at 200 ppm, slight cirrhosis was observed
470 ppm [37]	8 hours/day, 5 days/week 150 exposures	Rats, congested livers, no evidence of fatty degeneration or necrosis: evidence of kidney injury
1,000 ppm [88]	6 hours 3 exposures	Rats, no increase in liver lipid
3,000 ppm [34,35]	4 hours	Cats, no anesthesia
4,000-15,000 ppm [93]	2-6 hours single exposures with and without ethanol pretreatment	Rats, ethanol did not potentiate effects of tetrachloroethylene
5,000 and 10,000 ppm [83]	10 minutes	Dogs, tetrachloroethylene did not sensitize the hearts to epinephrine
9,000 ppm [31]	5-6 hours	Dogs, anesthesia
14,600 ppm [34,35]	1-2 hours	Cats, anesthesia
2,750-9,000 ppm [37]	Single exposure	Rats, no deaths
19,000 ppm [37]	30-60 minutes	Rats, congested livers with granular swelling, some deaths

TABLE XII-6

CONCENTRATIONS OF TETRACHLOROETHYLENE IN COMMERCIAL DRYCLEANING PLANTS

Establishment No.	Date	Mean Concentration, ppm	Concentration Range, ppm	Sampling Time, Minutes
10	9-15-71	270	32-808	490
6	12-18-71	239	55-514	242
10	12-15-71	166	19-990	493
15	9-13-71	120	32-689	328
11	12-20-71	107	19-428	519
10	7-28-71	106	9-514	482
12	9-8-71	103	24-514	402
7	12-16-71	76	13-416	501
3	7-20-71	72	9-440	353
1	9-17-71	64	9-689	444
3	7-12-71	54	9-428	485
1	6-24-71	54	19-514	321
22	7-30-71	54	5-514	484
9	7-27-71	50	13-122	554
4	7-21-71	47	9-416	417
9	8-16-71	46	13-150	441
4	7-13-71	44	0-404	482
2	7-15-71	36	9-188	400
2	7-1-71	31	9-141	239

Adapted from Kerr [98]

TABLE XII-7

TETRACHLOROETHYLENE CONCENTRATIONS AROUND COIN-OPERATED DRYCLEANERS

Establishment No.	Date	Concentrations, ppm		
		Composite Sample	Maintenance Area	Customer Area
23	12-22-71	264	378	121
23	8-24-71	155	260	82
18	9-7-71	139	178	40
18	8-23-71	126	195	35
5	9-10-71	111	155	33
5	9-6-71	110	195	39
18	8-10-71	104	176	31
21	9-9-71	97	153	51
21	9-14-71	93	150	34
21	8-2-71	87	93	39
5	8-31-71	87	144	28

Adapted from Kerr [98]

TABLE XII-8

PROPORTION OF SAMPLING TIME DURING WHICH CONCENTRATIONS EXCEEDED 200 ppm, COMMERCIAL PLANTS

Establishment No.	Date	Proportion of Sampling Time >200 ppm	Mean Sample Concentration, ppm
10	9-15-71	89.2%	270
6	12-18-71	79.7%	239
10	12-15-71	44.8%	166
10	7-28-71	36.5%	106
15	9-13-71	32.9%	120
12	9-8-71	29.3%	103
3	7-20-71	22.1%	72
11	12-20-71	19.1%	107
1	9-17-71	16.4%	64
7	12-16-71	14.6%	76
22	7-30-71	13.6%	54
3	7-12-71	12.6%	54
4	7-21-71	11.8%	47
1	6-24-71	10.6%	54
4	7-13-71	9.7%	44

Adapted from Kerr [98]

TABLE XII-9

PROPORTION OF SAMPLING TIME DURING WHICH CONCENTRATIONS EXCEEDED 200 ppm, COIN-OPERATED MAINTENANCE AREAS

Establishment No.	Date	Proportion of Sampling Time >200 ppm	Mean Sample Concentration, ppm
23	12-22-71	70.5%	378
23	8-24-71	51.8%	260
18	8-23-71	47.2%	195
5	9-6-71	42.1%	195
18	8-10-71	40.7%	176
18	9-7-71	39.4%	178
21	9-14-71	33.5%	150
5	9-10-71	30.8%	155
5	8-31-71	28.5%	144
21	9-9-71	28.1%	153
21	8-2-71	6.5%	93

Adapted from Kerr [98]

TABLE XII-10

PROPORTION OF SAMPLING TIME DURING WHICH CONCENTRATIONS EXCEEDED 300 ppm, COMMERCIAL PLANTS

Establishment No.	Date	Proportion of Sampling Time >300 ppm	Mean Sample Concentration, ppm
10	9-15-71	39.2%	270
6	12-18-71	35.9%	239
10	12-15-71	20.5%	166
10	7-28-71	16.8%	106
15	9-13-71	13.4%	120
12	9-8-71	10.9%	103
1	9-17-71	6.5%	64
3	7-20-71	6.5%	72
11	12-20-71	5.6%	107
4	7-13-71	5.2%	44
7	12-16-71	4.7%	76

Adapted from Kerr [98]

TABLE XII-11

PROPORTION OF SAMPLING TIME DURING WHICH CONCENTRATIONS EXCEEDED 300 ppm, COIN-OPERATED MAINTENANCE AREAS

Establishment No.	Date	Proportion of Sampling Time >300 ppm	Mean Sample Concentration, ppm
23	12-22-71	58.9%	378
23	8-24-71	38.4%	260
18	8-23-71	26.9%	193
5	9-6-71	26.0%	195
18	8-10-71	23.9%	176
5	9-10-71	19.6%	155
18	9-7-71	19.1%	178
5	8-31-71	17.4%	144

Adapted from Kerr [98]

TABLE XII-12

CONCENTRATIONS OF TETRACHLOROETHYLENE AND TRICHLOROETHYLENE FOUND IN DEGREASING OPERATIONS

Range of Concentration ppm	Ventilated Tanks		Nonventilated Tanks		Noncondensing Tanks*	
	No.	%	No.	%	No.	%
0 - 50	69	46.9	29	15.4	11	16.9
51 - 100	29	19.7	58	30.8	10	15.1
101 - 150	15	10.2	47	24.8	6	9.0
151 - 200	10	6.8	17	8.9	9	13.8
201 - 300	20	13.6	25	13.2	14	21.2
301 - 400	4	2.8	7	3.8	8	12.1
401 - 500	-	-	2	1.0	3	4.5
501 - 600	-	-	1	0.5	2	3.0
601 - 700	-	-	0	-	2	3.0
701 - 800	-	-	1	0.5	0	-
801 -900	-	-	2	1.1	1	1.4

* Noncondensing tanks usually contain tetrachloroethylene
Adapted from Morse and Goldberg [99]

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