criteria for a recommended standard....

OCCUPATIONAL EXPOSURE TO 1,1,2,2 TETRACHLOROETHANE

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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 1,1,2,2-tetrachloroethane by members of the NIOSH staff and the valuable constructive comments by the Review Consultants on 1,1,2,2-Tetrachloroethane, by the ad hoc committee of the American Occupational Medicine 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 1,1,2,2-tetrachloroethane. A list of Review Consultants appears on page vi.

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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 the recommended standard for 1,1,2,2-tetrachloroethane. The Division review staff for this document consisted of Richard A. Rhoden, Ph.D. (Chairman), Douglas L. Smith, Ph.D., and Paul E. Caplan, with Hervey B. Elkins, Ph.D., Ardith A. Grote (Division of Physical Sciences and Engineering), and Virginia J. Behrens (Division of Surveillance, Hazard Evaluations, and Field Studies).

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CRITERIA DOCUMENT:
RECOMMENDATIONS FOR AN OCCUPATIONAL
EXPOSURE STANDARD FOR 1,1,2,2-TETRACHLOROETHANE

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I. RECOMMENDATIONS FOR A 1,1,2,2-TETRACHLOROETHANE STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to 1,1,2,2-tetrachloroethane in the workplace be controlled by adherence to the following sections. The standard is designed to protect the health and safety of employees for up to a 10-hour work shift, 40-hour workweek, over a working lifetime. Compliance with all sections of the standard should prevent adverse effects of 1,1,2,2-tetrachloroethane on the health and safety of employees. The standard is measurable by techniques that are valid, reproducible, and available to industry and government agencies. Although the workplace environmental limits are considered to be safe levels based on current information, they should be regarded as the upper boundary of exposure and every effort should be made to maintain the exposure at levels as low as is technically feasible. The criteria and standard will be subject to review and revision as necessary.

These criteria and the recommended standard apply to exposure of workers to the symmetrical isomer of the chlorinated hydrocarbon compound, $CHCl_2 - CHCl_2$, referred to as 1,1,2,2-tetrachloroethane. Acetylene tetrachloride and sym-tetrachloroethane are synonyms. "Tetrachloroethane" will be used throughout this document to mean the symmetrical isomer unless otherwise stated. The "action level" is defined as one-half the recommended time-weighted average (TWA) environmental limit. "Occupational exposure to tetrachloroethane," because of systemic effects and dermal irritation produced by contact of tetrachloroethane with the skin, is defined as work in an area where tetrachloroethane is stored, produced,

processed, or otherwise used. If an employee is occupationally exposed to airborne concentrations of tetrachloroethane in excess of the action level, then all sections of the recommended standard shall be complied with; if the employee is occupationally exposed at or below the action level, then all sections of the recommended standard shall be complied with except Section 8. If exposure to other chemicals also occurs, provisions of any applicable standards for the other chemicals shall also apply.

Section 1 - Environmental (Workplace Air)

(a) Concentration

When skin exposure is prevented, occupational exposure to tetrachloroethane shall be controlled so that no employee is exposed to tetrachloroethane at a concentration greater than 1.0 part per million parts of air by volume (6.87 milligrams per cubic meter of air) determined as a TWA concentration for up to a 10-hour workday, 40-hour workweek.

(b) Sampling and Analysis

Procedures for the collection and analysis of environmental samples shall be as provided in Appendices I and II, or by any method shown to be at least equivalent in precision, accuracy, and sensitivity to the methods specified.

Section 2 - Medical

Medical surveillance shall be made available to all persons subject to occupational exposure to tetrachloroethane as described below.

(a) Preplacement medical examinations shall include at least:

(1) Comprehensive medical and work histories with special emphasis directed to symptoms related to the liver, kidneys, and nervous system. Information about exposure to other chemicals should be recorded, as should episodes of nausea, vomiting, dizziness, or headaches.

(2) A physical examination.

(3) Liver function tests, such as serum transaminase determinations, shall be performed, and screening tests of nervous system function should be considered by the responsible physician.

(4) Judgment of the worker's ability to use positive or negative pressure respirators.

(b) Periodic examinations shall be made available at least on an annual basis, or more frequently as determined by the responsible physician. These examinations shall include at least:

(1) Interim medical and work histories.

(2) A physical examination as described above for the preplacement examination.

(c) During examinations, applicants or employees having medical conditions which would be directly or indirectly aggravated by exposure to tetrachloroethane shall be counseled on the increased risk of impairment of their health from working with this substance.

(d) Initial medical examinations shall be made available to all workers within 6 months after promulgation of a standard based on these recommendations.

(e) If known or suspected exposure to tetrachloroethane vapor at a concentration above the TWA limit occurs, or if contact with the liquid

occurs, a physical examination, as described for preplacement examinations, and any other tests, as determined by the attending physician, shall be made available within a reasonable period of time.

(f) In an emergency involving tetrachloroethane, all affected personnel shall be provided with immediate first aid, followed by prompt medical evaluation and care. In the event of skin or eye contact with liquid tetrachloroethane, contaminated clothing and shoes shall be removed immediately, and eyes and skin shall be flushed with copious amounts of water. In all cases of eye contact or inhalation exposure, a physician shall be alerted. The medical attendants shall be informed of the possibility of central nervous system depression and, because of the severe toxicity of tetrachloroethane, persons so exposed shall be observed for a minimum of 24 hours after exposure. Examinations as described in paragraph (e) of this section should be made available as warranted by results of the 24-hour observation period.

(g) Pertinent medical records shall be maintained by the employer for all employees occupationally exposed to tetrachloroethane. Such records shall be retained for at least 30 years after termination of employment. These records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, and of the employer, employee, or former employee.

Section 3 - Labeling and Posting

(a) Labeling

All vessels containing tetrachloroethane shall carry in a readily visible location a label stating:

1,1,2,2-TETRACHLOROETHANE

(ACETYLENE TETRACHLORIDE)

WARNING!

HARMFUL IF INHALED
HARMFUL IF ABSORBED THROUGH SKIN

Avoid breathing of vapor.
Avoid contact with skin, eyes, and clothing.
Keep containers closed when not in use.
Use only with adequate ventilation.

(b) Posting

Areas where tetrachloroethane is present shall be posted with a sign reading:

1,1,2,2-TETRACHLOROETHANE

(ACETYLENE TETRACHLORIDE)

WARNING!

HARMFUL IF INHALED
HARMFUL IF ABSORBED THROUGH SKIN

Avoid breathing of vapor.
Avoid contact with skin, eyes, and clothing.
Keep containers closed when not in use.
Do not enter areas where used or stored unless adequate ventilation is provided.

All labels and warning signs shall be printed both in English and in the predominant language of non-English-reading employees. All employees shall be trained verbally and informed of the hazardous areas, with special instruction given to illiterate employees and employees reading only languages other than those used on labels and posted signs.

Section 4 - Personal Protective Equipment

Engineering controls shall be used if needed to maintain tetrachloroethane concentrations at or below the prescribed limit. When necessary, these shall be supplemented by the use of personal protective equipment. Requirements for personal protective equipment shall be in accordance with provisions of 29 CFR 1910, Subpart I.

(a) Eye Protection

Chemical safety goggles, face shields and goggles, or safety glasses with side shields shall be provided by the employer and shall be worn during any operation in which tetrachloroethane is present (29 CFR 1910.133).

(b) Skin Protection

Protective clothing, including gloves, aprons, suits, boots, and face shields (8-inch minimum) and goggles, made of a material resistant to tetrachloroethane, shall be worn where needed to prevent skin contact.

(c) Respiratory Protection

(1) Compliance with the permissible exposure limit may be achieved by the use of respirators only:

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

(B) During emergencies or during the performance of nonroutine maintenance or repair activities when air concentrations of tetrachloroethane may exceed the permissible environmental limit.

(2) When use of a respirator is permitted, it shall be selected and used pursuant to the following requirements:

(A) The employer shall establish and enforce a respiratory protective program meeting the requirements of 29 CFR 1910.134.

(B) The employer shall provide respirators in accordance with Table I-1 and shall ensure that the employee uses the respirator provided when necessary. The respiratory protective devices in conformance with Table I-1 shall comply with the standards jointly approved by NIOSH and the Mining Enforcement and Safety Administration (MESA, formerly Bureau of Mines) as specified under the provisions of 30 CFR 11.

(C) Respirators specified for use in higher concentrations of tetrachloroethane may be used in atmospheres of lower concentrations.

(D) The employer shall ensure that respirators are adequately cleaned and maintained, and that employees are trained and drilled, at least annually, in the proper use and testing for leakage of respirators assigned to them.

(E) Respirators shall be easily accessible, and employees shall be informed of their location.

TABLE I-1

RESPIRATOR SELECTION GUIDE

Concentrations of Tetrachloroethane	Respirator Type
Less than or equal to 10 ppm	(1) Chemical cartridge respirator with half-mask facepiece and organic vapor cartridge (2) Supplied-air respirator, demand type, with half-mask facepiece
Less than or equal to 50 ppm	(1) Chemical cartridge respirator with full facepiece and organic vapor cartridge (2) Gas mask with chin-style or front- or back-mounted organic vapor canister (3) Supplied-air respirator operated in demand mode with full facepiece (4) Self-contained breathing apparatus operated in demand mode with full facepiece
Less than or equal to 150 ppm	(1) Type C supplied-air respirator with full facepiece, helmet, hood, or suit and operated in continuous-flow mode (2) Type C supplied-air respirator with full facepiece operated in pressure-demand mode
Greater than 150 ppm	(1) Self-contained breathing apparatus with full facepiece operated in pressure-demand or other positive pressure mode (2) Combination Type C supplied-air respirator with full facepiece and auxiliary self-contained air supply operated in pressure-demand mode
Emergency or Entry (into an area of unknown concentration, eg, firefighting)	(1) Self-contained breathing apparatus with full facepiece operated in pressure-demand or other positive pressure mode (2) Combination Type C supplied-air respirator with full facepiece and auxiliary self-contained air supply operated in pressure-demand mode
Evacuation or Escape (from an area of unknown concentration)	(1) Any gas mask providing protection from organic vapors (2) Any self-contained breathing apparatus

Section 5 - Informing Employees of Hazards from 1,1,2,2-Tetrachloroethane

(a) The employer shall ensure that each employee occupationally exposed to tetrachloroethane is informed at the beginning of employment or on assignment to a tetrachloroethane area of the hazards, relevant symptoms of overexposure, appropriate emergency procedures, and proper conditions and precautions for the safe use of tetrachloroethane. This information shall also include a description of the general nature of the medical surveillance procedures and why it is advantageous to the workers to undergo these examinations. Employees engaged in maintenance and repair shall be included in these training programs. The employee shall be reinformed at least once annually. Each employee shall be advised of the availability of such relevant information, including the material safety data sheet which shall be kept on file.

(b) Required information shall be recorded on the "Material Safety Data Sheet" shown in Appendix III or on a similar form approved by the Occupational Safety and Health Administration, US Department of Labor.

Section 6 - Work Practices

(a) Engineering controls, such as process enclosure or local exhaust ventilation, shall be used as needed to maintain tetrachloroethane concentrations within the recommended environmental limit. Ventilation systems, if used, shall be designed to prevent the accumulation or recirculation of tetrachloroethane in the workplace, to maintain the tetrachloroethane concentrations within the limit of the recommended standard, and to effectively remove tetrachloroethane from the breathing zones of employees. Adequate, uncontaminated makeup air shall be provided.

Exhaust ventilation systems discharging into outside air must conform with applicable local, state, and federal air pollution regulations and must not constitute a hazard to employees or to the general population. Ventilation systems shall be subject to regular preventive maintenance and cleaning to ensure effectiveness, which shall be verified by airflow measurements taken at least every 3-6 months.

(b) Storage, Handling, and General Work Practices

(1) Containers of tetrachloroethane shall be kept tightly closed at all times when not in use. Only properly informed, trained, and equipped personnel shall be involved in storing, loading and unloading, or processing tetrachloroethane. Tetrachloroethane shall be stored in locations that are adequately ventilated and cool, and not in pits, depressions, or basements. Storage containers shall be periodically inspected for leakage and deterioration.

(2) Washing of hands, equipment, or structures with tetrachloroethane shall be prohibited.

(3) Prior to maintenance work, sources of tetrachloroethane and its vapor shall be eliminated to the extent feasible. If concentrations at or below the recommended workplace air limit cannot be assured, respiratory protective equipment shall be used during such maintenance work.

(4) Written operating instructions and first-aid procedures shall be formulated and posted by the employer where tetrachloroethane is handled or used.

(5) Tetrachloroethane containers and systems shall be inspected periodically for leaks. All tetrachloroethane equipment

including valves, fittings, and connections shall be checked for tightness and good working order. All newly made connections shall be checked for leaks immediately after tetrachloroethane is introduced. Needed repairs and adjustments shall be made promptly.

(6) An employee whose skin becomes contaminated with liquid tetrachloroethane shall immediately wash or shower. Clothing contaminated with the liquid shall be either disposed of or cleaned before reuse. Anyone handling or responsible for cleaning contaminated clothing shall be instructed as to the hazards, relevant symptoms of overexposure, appropriate emergency procedures, and proper conditions and precautions for the safe handling and use of tetrachloroethane. Some materials which cannot be effectively decontaminated, such as leather and rubber, shall be discarded.

(7) Transportation and use of tetrachloroethane shall comply with all applicable federal, state, and local regulations.

(c) Waste Disposal

Waste material contaminated with liquid tetrachloroethane shall be disposed of in a manner not hazardous to employees and conforming to all applicable local, state, and federal regulations. Incineration, properly conducted to prevent the release of hazardous combustion products such as hydrochloric acid and chlorine, is an acceptable means of disposal.

(d) Confined Spaces

(1) Entry into confined spaces, such as tanks, pits, tank cars, barges, process vessels, and tunnels, where tetrachloroethane has been present shall be controlled by a permit system. Permits signed by an authorized employer representative shall certify that preparation of the

confined space, precautionary measures, and personal protective equipment are adequate, and that precautions have been taken to ensure that prescribed procedures will be followed.

(2) Individuals entering confined spaces where they may be exposed to tetrachloroethane shall wear respirators as specified in Section 4.

(3) Confined spaces which have contained tetrachloroethane shall be inspected and tested for oxygen deficiency and for tetrachloroethane and other known or suspected contaminants and, prior to entry, shall be thoroughly ventilated and decontaminated.

(4) Accidental exposure to tetrachloroethane in confined spaces shall be prevented by disconnecting and blanking off tetrachloroethane supply lines.

(5) Confined spaces shall be ventilated while work is in progress therein to keep the concentration of tetrachloroethane at or below the workplace environmental limit and to prevent oxygen deficiency.

(6) When a person enters a confined space, another properly protected worker shall be on standby outside.

(e) Emergency Procedures

For all work areas where there is a reasonable potential for accidents involving tetrachloroethane, the procedures specified below shall be used, and any others appropriate for a specific operation or process shall be formulated in advance. Employees shall be instructed in their implementation.

(1) Procedures shall include prearranged plans for obtaining emergency medical care and for the transportation of injured

workers. Employees shall also be trained in administering immediate first aid and shall be prepared to render such assistance when necessary.

(2) Approved eye, skin, and respiratory protection as specified in Section 4 shall be used by persons who are involved in the cleanup operations at the accident site.

(3) Eyewash fountains and emergency showers shall be provided in accordance with 29 CFR 1910.151.

(4) Employees not essential to cleanup operations shall be evacuated from exposure areas during emergencies. Perimeters of hazardous exposure areas shall be delineated, posted, and secured. Employees in adjacent areas shall be informed of evacuation procedures in the event that their work areas become involved.

(5) Only personnel properly trained in emergency procedures and adequately protected against the attendant hazards shall be assigned to shut off sources of tetrachloroethane, clean up spills, and repair leaks.

(6) Spilled tetrachloroethane shall be cleaned up promptly. Small spills can be soaked up by absorbent material; larger spills, after being contained, can be pumped into drums or tanks. Waste disposal shall conform to Section 6(c) of this chapter.

Section 7 - Sanitation

(a) Plant sanitation shall meet the requirements of 29 CFR 1910.141.

(b) Food preparation, dispensing (including vending machines), and eating shall be prohibited in work areas where tetrachloroethane is present.

(c) Employees who handle liquid tetrachloroethane shall be instructed to wash their hands thoroughly with soap or mild detergent and water before eating, smoking, or using toilet facilities.

Section 8 - Monitoring and Recordkeeping Requirements

Within 6 months of the promulgation of a standard based on these recommendations, each employer who has a place of employment in which tetrachloroethane is present shall determine by an industrial hygiene survey if exposure to airborne tetrachloroethane at concentrations above the action level may occur. Records of these surveys, including the basis for concluding that air levels are at or below the action level, shall be maintained. Surveys shall be repeated at least once every year and within 30 days of any process change likely to result in an increase of airborne tetrachloroethane concentrations. If it has been decided that the environmental concentration of tetrachloroethane may exceed the action level, then the following requirements shall apply:

(a) Personal Monitoring

(1) A program of personal monitoring shall be instituted to identify and measure, or to permit calculation of, the exposure of all employees occupationally exposed to airborne tetrachloroethane. Source and area monitoring may be used to supplement personal monitoring.

(2) In all personal monitoring, samples representative of the exposure to airborne tetrachloroethane in the breathing zone of the employee shall be collected.

(3) For each TWA determination, a sufficient number of samples shall be taken to characterize employee exposures during each work

shift. Variations in work and production schedules, as well as employee locations and job functions, shall be considered in decisions on sampling locations, times, and frequencies.

(4) Each operation in each work area shall be sampled at least once every 3 months or as otherwise indicated by a professional industrial hygienist. If an employee is found to be exposed at a level in excess of the TWA environmental limit, the exposure of that employee shall be measured at least once every 30 days, control measures shall be initiated, and the employee shall be notified of the exposure and of the control measures being implemented. Such monitoring shall continue until two consecutive determinations, at least 1 week apart, indicate that employee exposure no longer exceeds the environmental limit. Quarterly monitoring may then be resumed.

(b) Recordkeeping

Records of environmental monitoring shall be maintained for at least 30 years. These records shall include the dates and times of measurements, job function and location of the employees within the worksite, sampling and analytical methods used, number, duration, and results of the samples taken, TWA concentrations estimated from these samples, type of personal protective equipment used, if any, and exposed employees' names. Employees shall have access to information on their own environmental exposures. These records shall be available to the authorized representatives of the Secretary of Health, Education, and Welfare, and of the Secretary of Labor. Pertinent medical records shall be retained for 30 years after termination of employment. 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 disease or injury arising from exposure to tetrachloroethane. 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 (NIOSH), after a review of data and consultation with others, formalized a system for the development of criteria from which standards can be established to protect the health of employees from exposure to hazardous chemical and physical agents. Any criteria and recommended standard should enable management and labor to develop better engineering controls resulting in more healthful work environments. Simple compliance with the recommended standard should not be the final goal.

These criteria for a standard for tetrachloroethane are part of a continuing series of documents published by NIOSH. The recommended standard applies only to the processing, manufacture, and use of tetrachloroethane 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 protect against the development of systemic toxic effects and local effects on the skin and eyes of workers and be measurable by techniques that are valid, reproducible, and available to industry and government agencies.

The major concerns in occupational exposure to tetrachloroethane are its potentials for causing hepatic, gastrointestinal, and neurologic effects. In addition, tetrachloroethane can cause central nervous system depression and mucosal irritation. Because the available evidence indicates that employees can be adversely affected by skin contact with tetrachloroethane, adherence to all provisions of the recommended standard except for environmental monitoring is required in all work areas in which tetrachloroethane is used regardless of its airborne concentration.

The development of the recommended standard for occupational exposure to tetrachloroethane revealed areas that require further research. Epidemiologic studies of workers exposed to tetrachloroethane are desirable to elucidate the effects of tetrachloroethane exposure at or below the recommended workplace environmental limit for extended periods. Experiments to assess the possible carcinogenic, mutagenic, and teratogenic potential of tetrachloroethane also are needed.

III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Tetrachloroethane ($CHCl_2 - CHCl_2$), also known as acetylene tetrachloride, is a colorless liquid at room temperature having a moderately strong, sweet, chloroformlike odor [1]. Compared to other chlorinated hydrocarbon solvents, tetrachloroethane has a low vapor pressure (5 mmHg at 21 C) and a high boiling point (146 C). Some important physical and chemical properties of tetrachloroethane are listed in Appendix IV [2,3,4].

Tetrachloroethane was the first chlorinated hydrocarbon solvent produced in high tonnage before World War I [3]. Because of its powerful solvent properties, it found industrial use as a solvent for cellulose acetate, fats, waxes, greases, rubber, and sulfur [3,5]. However, because of its toxicity, tetrachloroethane has been largely replaced since World War II by other, less toxic solvents. Its current use is quite limited; in 1975, Hooker Chemicals and Plastics Corporation was the only manufacturer in the United States [6 (p 1)]. The manufacturing process for tetrachloroethane involves the chlorination of acetylene [6 (p 4)]. Most of the tetrachloroethane produced by the one company (production figures not available) is used at the same location as an intermediate in the manufacture of trichloroethylene and tetrachloroethylene. Prior to 1967, tetrachloroethane was the primary starting material for producing these other chlorinated hydrocarbon solvents but, since that time, a process involving chlorination of ethylene has predominated. A small percentage of the tetrachloroethane produced is used as a carrier or reaction solvent in

the manufacturing processes for other chemicals. Tetrachloroethane is used also by a number of textile manufacturers as an analytical reagent in polymer characterization tests [6 (p 1)].

NIOSH estimates that 5,000 workers in the United States are potentially exposed to tetrachloroethane.

Historical Reports

The adverse health effects from exposure to tetrachloroethane first became apparent at the beginning of World War I with reports [7,8] of numerous poisonings of workers in the aircraft industries of several European countries. Tetrachloroethane was the solvent in the varnish or "dope" used to make airplane wing surfaces impervious to moisture and air. The chemical was chosen because of its low cost, limited solubility in water, incombustibility, and its unique ability to tighten the stretched fabric forming the wings [8].

In 1914, Heffter [7] reported that inhalation of tetrachloroethane was responsible for an increasing incidence of poisoning among Germany's aircraft factory workers. Heffter was a member of a commission that investigated the illnesses of 12 of 15 workers who regularly used two varnishes containing 30 and 50% tetrachloroethane by weight; 2 of the 12 afflicted workers had died. Heffter classified the patients by signs and symptoms into two groups: one group showed mainly gastrointestinal disturbances, jaundice, and enlarged livers; the second group had neurologic disturbances such as hand tremors, sensations of deafness, paresthesias in the extremities, reduced patellar reflexes, and headaches, in addition to anorexia and nausea. Animal experiments [7] designed to

verify suspicions that tetrachloroethane was the varnish constituent responsible for the illness showed that tetrachloroethane and the two varnishes produced similar gastrointestinal and hepatic effects in dogs. The neurologic effects seen in the humans were not found in the dogs. The German commission recommended banning the use of all varnishes containing tetrachloroethane. Before the end of World War I, there were numerous poisonings attributed to tetrachloroethane in the aircraft industries of Germany, France, England, and Holland; in England alone, there were 70 reported cases with 12 deaths [9].

A 1917 study by Hamilton [10] of 18 domestic airplane factories revealed no severe overexposures to tetrachloroethane. Noting only complaints of headache, drowsiness, and nausea, Hamilton concluded that the absence of serious hepatic symptoms was due to the limited production and to the short exposure time for workers in the American factories compared with those in European plants.

Effects on Humans

As a result of the numerous occupational poisonings attributed to overexposure to tetrachloroethane, much clinical data have been presented in medical reports [5,8,11-14]. Most of these overexposures occurred before World War II. Although none of the reports contained quantitative exposure data, they consistently indicated primary involvement of the liver and of the nervous and gastrointestinal systems.

Most of the reported poisoning cases had a clinical picture characterized by gastrointestinal and hepatic symptoms. Browning [9] described this form of tetrachloroethane poisoning in four progressive

stages, as follows:

(a) Prejaundice - anorexia, constipation, drowsiness, exhaustion, and nausea.

(b) Jaundice without toxemia - jaundice with pale stools and bile-stained urine, increased exhaustion, albuminuria, and vomiting.

(c) Jaundice with toxemia - increased vomiting and jaundice accompanied by other toxic manifestations such as delirium and convulsions.

(d) Fatal - severe jaundice of the entire body.

Willcox et al [8], in 1915, reported 14 poisonings, 4 of which were fatal, and all were of the gastrohepatic type associated with exposure to tetrachloroethane. The 14 victims, 11 men and 3 women between the ages of 17 and 58, were employed in three separate aircraft factories in Great Britain. The authors stated that there were additional poisonings, but these 14 cases were the only ones detailed in clinical reports. The varnishes used in the three plants all contained about 12% tetrachloroethane by weight; acetone, benzene, methylated spirit, and cellulose acetate were the other constituents. From autopsies of rats subjected to inhalation exposures to the individual constituents of the varnishes, the authors [8] concluded that tetrachloroethane was the primary liver poison in the varnish. The poisoned workers included several "dopers" who applied the varnish and probably had dermal contact in addition to inhalation exposure, as well as several workers who did not handle the varnish but were exposed by inhalation.

The first indications of effects from tetrachloroethane on the workers [8] were complaints of general malaise, drowsiness at work, anorexia, nausea, retching in the morning, unpleasant taste in the throat,

constipation, and headache. Two of the workers complained of these early symptoms immediately or soon after the start of exposure; the other 12 were exposed for 2-4 months before becoming ill. These nonspecific symptoms lasted several days or even weeks before definite jaundice, often accompanied by pale stools, biliuria, and vomiting, developed. According to the authors [8], this was the stage at which most of the affected employees left work. In early stages of the illness, there was often slight liver enlargement but no accompanying abdominal pain; as the illness progressed, the liver diminished in size. Workers who were removed from tetrachloroethane exposure when they showed the early stages of poisoning recovered fairly promptly, although it was usually several weeks before the jaundice was no longer evident. As the disease progressed, the workers became mentally confused, stuporous or delirious, and finally comatose. Purpuric rash, suppression of urine, hematemesis, and convulsions were also noted in the later stages.

Post-mortem examinations were performed on three of the four workers who died [8]. Examination of the first victim revealed pathologic changes predominantly in the liver, although some changes in the heart and kidney tissues also were observed. The heart showed fatty degeneration, as did the kidneys which were enlarged and bile-stained. The liver was reduced in size, soft, wrinkled, and deeply bile-stained throughout. Microscopic examination revealed extreme liver destruction, large portions of liver tissue having been replaced by fibrous tissue. The livers of the other two victims were greatly reduced in size with large areas of necrotic liver cells; however, no fibrous replacement tissue was yet apparent. The authors suggested that death had occurred more quickly in these patients

than it had in the first, before regeneration of the liver had begun.

Symptoms involving the nervous system occurred in a second group of occupational poisoning cases [5,12,13]. These usually started with a sensation of numbness and loss of feeling in the toes and fingers, paresthesias, hand tremors, and plantar pain. Two such examples reported by Leri and Breitel [13] in 1922 involved two young women, a 16-year-old and a 17-year-old, who had been exposed to tetrachloroethane while employed at a plant manufacturing artificial pearls. Both women were assigned to dipping artificial pearls into a varnish composed of an oil made from "ablet" shells that had been dissolved in tetrachloroethane and small amounts of alcohol and cellulose acetate. The onset of poisoning occurred after 2 years of employment for the 17-year-old and after only 3 months for the other; however, the latter had the additional responsibility of stirring the varnish, which she did with her hands. The initial effects consisted of vertigo and a feeling of inebriation for the older woman, while diarrhea, colic, amenorrhea, and the inability to control evacuative functions were reported for the younger woman. In spite of these initial differences, the advanced clinical pictures in the women were similar--difficulty in walking, paresis of the last phalanges of their toes and fingers, severe hypoesthesia of the ends of the toes, tingling sensations in the toes and terminal phalanges of the fingers, and paresis of the soft palate with an absence of pharyngeal reflex. The only reported difference was that the 17-year-old developed paresis of the sphincter muscles of the eyelids and lips, whereas the other did not. The signs and symptoms were quite persistent and were still present, although diminished, 1 year after the women had left the factory.

Similar neurologic disturbances in German aircraft workers during World War I were reported by Grimm et al [12]. In several cases reported by Schultze [11], Zollinger [5], and Fiessinger and Wolf [14], gastrointestinal and hepatic effects, as well as neurologic signs and symptoms, occurred simultaneously during the course of the disease.

There have been several reports of nonoccupational poisonings from tetrachloroethane consumed with suicidal intent. Two similar cases, one described by Hepple [15] in 1927 and another by Elliott [16] in 1933, involved a 21-year-old man and a 43-year-old member of the British Armed Forces, respectively. Shortly after drinking an unknown quantity of silk cleaning fluid containing tetrachloroethane, each subject lost consciousness and, when examined after hospitalization, showed complete absence of corneal reflexes. Elliott [16] reported marked cyanosis in the older man, while Hepple [15] described progressive respiratory difficulty leading to Cheyne-Stokes respiration (periods of hyperpnea alternating with periods of apnea) in the younger man. Neither subject regained consciousness despite efforts at resuscitation; the older man died within 12 hours and the younger man died 20 hours after exposure. Forbes [17] and Lilliman [18] documented the deaths of two other men who had consumed unknown volumes of tetrachloroethane. Signs and symptoms were consistent with those previously described, ie, early loss of consciousness, further CNS depression, and death. Forbes [17] reported that a 33-year-old man died 6 hours after ingesting tetrachloroethane; according to Lilliman's report [18], death occurred after approximately 9 hours. Gross and microscopic post-mortem examinations of the four victims [15-18] revealed no remarkable changes except "tissue congestion" and hyperemia.

A case reported by Lynch [19] in 1967 involved a 67-year-old man who, having ingested an unknown quantity of tetrachloroethane, collapsed in the street and was taken to the hospital already comatose. He did not respond to unspecified stimuli and, although breathing rapidly and regularly, he was cyanotic; his condition rapidly deteriorated until death 8 hours after hospital admission. Histologic examination showed small droplets of fat in the hepatic cells and in the cells lining the proximal and distal renal tubules. Although the victim, an active gardener, had used a tetrachloroethane spray for whiteflies, the likelihood of inhalation effects could not be determined from the information given. Moreover, the recovery of 4 ml of tetrachloroethane from the victim's stomach indicated that death was primarily due to ingestion.

There were two incidents in Africa, where tetrachloroethane was mistaken for tetrachloroethylene and given as a treatment for hookworms. In 1953, Sherman [20] reported that eight adults each received 3 ml tetrachloroethane orally with 1 oz of magnesium sulfate and water. Within 2 hours, the three who were hospital patients became comatose, but were revived with enemas and methedrine injections; the five outpatients were found in various stages of semiconsciousness, but revived without treatment. None of the eight experienced any adverse aftereffects during a 3-month observation period. A similar incident in which a young man, a young woman, and a 12-year-old girl were erroneously given 3, 3, and 2 ml of tetrachloroethane, respectively, was described by Ward [21] in 1955. The man and woman became comatose but they were revived by gastric lavage and iv injections of nikethamide, a stimulant. The girl was induced to

vomit with a strong emetic and did not lose consciousness or suffer other ill effects.

In 1970, Morgan et al [22] reported their use of a radioactive tracer method to study the absorption and excretion rates of inhaled tetrachloroethane. A gas chromatograph with a radioactivity detector was used to isolate and quantitate 38Cl-labeled tetrachloroethane, which was eluted directly into a collection tube. All subsequent monitoring was done by gamma-ray scintillation spectrometry. A volunteer deeply inhaled 2.5 mg of 38Cl-labeled tetrachloroethane vapor from a 150-ml bulb. Measurement of residual radioactivity in the bulb indicated that almost all of the labeled tetrachloroethane was inhaled. After holding the breath for 20 seconds, the subject exhaled through an activated-charcoal trap. He then inhaled room air and exhaled through the trap a second time. The radioactivity of the trapped material was then measured, and it was determined that about 97% of the inhaled tetrachloroethane was retained in the lungs. The subject continued to breathe room air and to exhale for 1 hour through charcoal traps that were changed periodically. Analysis of the radioactive material on these traps indicated that only 3.3% of the initially retained tetrachloroethane was exhaled in 1 hour.

After performing in vitro experiments, Morgan et al [22] reported the partition coefficient, KD (concentration in liquid/concentration in gas), of tetrachloroethane between blood and air to be 72.6 and between serum and air to be 78.2. The KD's for tetrachloroethane were much higher than those for the other chlorinated hydrocarbons tested, eg, the blood-air and serum-air KD's were 9.5 and 5.9, respectively, for trichloroethylene and 44.2 and 37.1, respectively, for trichloroethane. These experiments were performed

at 40 C. Because of tetrachloroethane's high KD values in spite of its poor solubility in water, the authors [22] postulated that its KD's between blood and air and between serum and air actually represented the solubility of tetrachloroethane in blood and serum lipids. A later report by these authors [23], in 1972, supported their earlier findings when they reported the partition coefficient of tetrachloroethane between olive oil and air to be 1,110 as compared to 220 between serum and air (at 25 C). Inhalation and partition-coefficient experiments [22] with several other halogenated hydrocarbons indicated a definite correlation between their absorption and retention and their respective KD values. Of the compounds tested, tetrachloroethane had the highest KD values, one of the highest rates of absorption, and one of the lowest rates of elimination by exhalation. The measured absorption of 94% (total of 6% exhaled in 1 hour) may not be directly applicable to acute occupational exposure because in the experiments there was optimum absorption efficiency (holding the breath for 20 seconds).

Barrett et al [24] reported in 1939 that one of the authors voluntarily for 10 minutes inhaled vapor which was generated from an open vessel of tetrachloroethane heated to 50 C. No specific information on the exposure concentration was given. The subject stated that the sensations produced were less pleasant than the sweetish taste and very slight euphoria that were experienced with trichloroethylene inhalation. No noticeable aftereffects were reported, and direct urinalysis for chlorinated hydrocarbons by the Fujiwara test [25] was negative. Two hours after the exposure, the first 5 cc of steam distillate obtained from 25 cc of urine gave a faintly positive Fujiwara reaction; at 24 hours, analysis

of the distillate for chlorinated hydrocarbons was negative.

The results of this qualitative experiment were consistent with those reported for dogs, rats, guinea pigs, and rabbits in the same study [24], as described in this document in Animal Toxicity. Because no chlorinated hydrocarbon compounds were found in the urine, Barrett et al [24] concluded that, contrary to their speculation, tetrachloroethane was not initially metabolized to trichloroethylene, a compound which does produce chlorinated hydrocarbons (ie, trichloroacetic acid) in the urine.

In 1936, Lehmann and Schmidt-Kehl [26] reported the effects of acute inhalation of tetrachloroethane in two male volunteers. At the beginning of each experiment, a technician sprayed tetrachloroethane into a 10-cu m exposure chamber either with a hand sprayer or an atomizer with oxygen as the propellant. The tetrachloroethane concentration was measured by absorption on calcium oxide, hydrolysis in alcohol, and chloride determination by the Volhard method [27]. The eight reported test concentrations were determined as exposure periods began; however, measurements showed that concentrations decreased only by about 10% during exposure. The two men were exposed simultaneously at concentrations ranging from 0.02 to 2.3 mg/liter (2.9-335 ppm) for exposure periods up to 30 minutes. The men did not complain of any effects during 10-minute periods of exposure to tetrachloroethane at concentrations of 0.02, 0.03, or 0.09 mg/liter (2.9, 4.4, or 13 ppm). A detectable odor was reported, even at the lowest concentration; at 13 ppm, the odor was discernibly stronger. After exposure at 0.8 mg/liter (116 ppm) for 20 minutes, the men experienced dizziness and mild vomiting. Initially, the odor was even stronger than at the previous concentration but was not discernible by the

subjects after 10 minutes. At 0.9 mg/liter (131 ppm), the men experienced dizziness after 10 minutes and the exposure was terminated. The exposure at 1.0 mg/liter (146 ppm) lasted 30 minutes, although the subjects experienced dizziness after 10 minutes, mucosal irritation at 12 minutes, and fatigue after 20 minutes. A 10-minute exposure at 1.8 mg/liter (262 ppm), resulted in dizziness and mucosal irritation of the mouth, eyes, and nose. The odor produced a repulsive bitter-sweet taste which disappeared after 5 minutes. The highest exposure concentration, 2.3 mg/liter (335 ppm), initially produced a stronger odor which was not discernible after 3 minutes. Tetrachloroethane at this concentration produced dizziness in 3 minutes and fatigue and mucosal irritation at 10 minutes at which time the exposure was ended. Although the subjects also experienced weakness in the knees, they said that they did not feel faint. This report [26] of effects on humans experimentally exposed to tetrachloroethane is one of the few found and indicates that although the odor of tetrachloroethane was detected at even the lowest concentration used, 0.02 mg/liter (2.9 ppm), odor is an unreliable indicator of tetrachloroethane exposure because workers may become inured to its presence.

Lehmann and Schmidt-Kehl [26] also measured tetrachloroethane in the expired breath of the two subjects during exposures at five concentrations ranging from 0.8 to 2.3 mg/liter (116-335 ppm). The only detail reported was that the two subjects exhaled into a bottle of air that had been warmed for 3 minutes in a 37 C water bath, probably to deter condensation and thus allow an accurate measurement of the expired tetrachloroethane concentration. These determinations indicated that 45-62% of the inspired tetrachloroethane was not exhaled.

Epidemiologic Studies

In 1957, Jeney et al [28] reported the findings from a 3-year study of the effects of tetrachloroethane on workers in a penicillin factory in Czechoslovakia. Tetrachloroethane was used in this plant as a solvent for extracting the penicillin from the fermentation liquid. The process included two different liquid-liquid extractions; the resulting emulsions were separated with equipment designated as "separators." When the workers routinely dismantled these separators to clean and rinse the parts, much higher concentrations of airborne tetrachloroethane resulted than during normal operation. Workers were required to wear gas masks with filters while dismantling and cleaning the separators; the efficiency of these protective devices was not reported. The workers spent about 90% of their 6- to 8-hour workday in the extraction room, with approximately 60 hours/month spent cleaning the separators. The ventilation system used in the work area was improved twice during the course of the study. In April 1954, two exhaust vents were added to the system after it had been evaluated as inadequate in 1953. The entire extraction system was moved in March 1956 to another building where the concentration of tetrachloroethane in the air was initially higher than it had been in the first plant. Eventually, the new ventilation system was greatly improved. Also, the work shifts were shortened from 8 hours to 6 hours, and the workers started to wear overalls that were periodically changed. The authors [28] did not mention whether or not dermal contact had any importance in the exposure of workers to tetrachloroethane.

During the study [28], from 34 to 75 workers were employed at the factory at any given time. They were between 20 and 50 years of age, were

of average body weight, and had no apparent liver ailment, anemia, gastric disorder, or alcoholism. Because liver disorders appeared in workers soon after production started at the factory in 1952, physical examinations, every other month, were instituted in July 1953. Several blood and urine tests to measure liver function were included with general physical examinations. All prospective employees were also given this screening examination.

The authors [28] reported that area air samples taken at various locations within the plant were collected with bubblers containing amyl alcohol and analyzed for tetrachloroethane by a method utilizing alkaline dechlorination followed by titration of the liberated chloride. The measured concentrations of tetrachloroethane in 170 air samples were from 0.01 to 1.7 mg/liter (1.5 to 247 ppm). The concentration ranges for each of four processes with three different ventilation systems are shown in Table III-1. More specific sampling results were not reported. The decrease in the tetrachloroethane concentration was greatest in the area of sludging, a part of the cleaning process, where the maximum concentrations were reduced from 247 to 36.4 ppm.

During the first year after the screening examinations were initiated, 31% of the workers had adverse signs and symptoms, particularly digestive organ complaints. These were loss of appetite, bad taste in the mouth, epigastric pain, and sensations of pressure in the liver area for 66% of these workers; headaches, general debility, and lack of stamina for 29%; lost body weight for 4%; and painful prurigo for 1%. During the second year, only 13% of the workers had such symptoms, and this percentage

TABLE III-1

CONCENTRATIONS OF TETRACHLOROETHANE (PPM) IN THE AIR DURING PENICILLIN MANUFACTURING

Process	Ventilation System		
	Original 1953 - March 1954	Improved April 1954 - February 1956	New Plant
First separation	2.3- 14.6	1.5- 14.6	1.5-21.8
Second separation	4.4- 58.2	1.5- 46.6	1.5-29.1
Sludging (elutriation)	11.6-247	4.4-124	1.5-36.4
Disk rinsing	10.2- 58.2	7.3- 29.1	1.5-36.4

Adapted from Jeney et al [28]

had decreased to 2% the third year. These results are shown in Table III-2, as are other signs that were detected in the periodic examinations. As a direct consequence of the results of these examinations, 18-21 workers were transferred each year to other work areas where there was considerably less exposure to tetrachloroethane. Palpable livers disappeared within 2 weeks after the workers were transferred if no jaundice had yet developed. No cirrhosis developed as a sequela of enlarged livers. The morbidity data for the factory, which included sick leave records, showed that during the year before the screening examinations were started, 21 workers (50%) were absent some time because of ailments related to the liver. In the next 3 years, this percentage was 5.5%, 20%, and 6.3%, respectively.

TABLE III-2

PERCENT OF PENICILLIN FACTORY WORKERS SHOWING SIGNS AND SYMPTOMS DURING PERIODIC EXAMINATIONS

Signs and Symptoms	First Year	Second Year	Third Year
General digestive organ complaints	31	13	2
Enlarged liver	17.8	20	5
Urobilinogenuria	50	24	12
Increased serum bilirubin	20	18.7	7.6

Adapted from Jeney et al [28]

The thymol coagulation test was used during the 3 years [28] to indicate liver dysfuntion. The correlation coefficient between number of workers showing positive results versus employment duration was +0.381 and was significant at the 0.1% level. Other liver function tests such as the Takata-Ucko, gold salt, and Weltmann reactions showed much weaker correlations. The results of the periodic examinations revealed no neurologic disorders, such as paresthesia or loss of reflexes. There was also no correlation found between the duration of employment at this factory and abnormal variations in RBC, hemoglobin content, WBC, and differential WBC.

Signs and symptoms of adverse effects definitely decreased after screening examinations were instituted in July 1953 [28]. The practice of transferring workers as soon as they showed intial signs of liver dysfunction was probably a major factor in this improvement as well as in

the prevention of more advanced liver disease. It is difficult to determine the degree to which the improved conditions, resulting from the different ventilation systems, affected the occurrence of signs and symptoms. Although there was a decrease in concentrations of airborne tetrachloroethane, the wide ranges make it difficult to estimate worker exposure with each ventilation system. Furthermore, it is not possible to accurately correlate the results of the screening examinations with the different conditions because the periods under each ventilation system did not coincide with the yearly intervals for which the signs and symptoms were reported. Even with the periodic examinations and the improved ventilation at the new plant where the concentrations ranged from 1.5 to 36.4 ppm, workers still showed indications of liver dysfunction. At the new plant, the workers were exposed to tetrachloroethane at 15 ppm for most of each work shift and at higher concentrations (up to 36.4 ppm) during the cleaning operations. The authors [28] stated that tetrachloroethane even at these reduced levels caused liver disease. The health effects described in this study were ascribed to tetrachloroethane exposure by the authors. No contaminants that could have contributed to the observed effects were mentioned.

In 1963, Lobo-Mendonca [29] reported the occurrence of nervous and gastrointestinal disorders among workers exposed to tetrachloroethane in India's bangle-manufacturing industry. This survey included 380 of the 474 workers employed in 23 different factories. The manufacturing process included two steps in which the workers had direct dermal contact with liquid tetrachloroethane as well as inhalation exposure to tetrachloroethane vapor. This included 85 cylinder makers who worked with

a 50:50 mixture of tetrachloroethane and acetone and 107 bangle polishers who used undiluted tetrachloroethane. The exposure of the other 188 workers was alleged to be primarily by inhalation of tetrachloroethane at concentrations that varied from one work area to another within a single factory, as well as between the different factories. Air concentrations were measured by the method of Fahy [30], which includes collection on silica gel, extraction with alcohol, hydrolysis with potassium hydroxide, and titration of the liberated chloride against silver nitrate.

Case histories and physical examinations were used in this study [29] to assess the condition of the workers. The number and percent of workers in each job category who showed general, nervous, and gastric effects and the ranges of tetrachloroethane in air concentrations that were measured at the jobsites in several of the factories are listed in Table III-3. These figures are only general indicators of exposure since there was no systematic sampling system or evaluation of skin absorption.

The most common effect [29], fine hand tremors, occurred in 35% of the workers. However, more than 63% of the cylinder makers, one of the two dermally exposed groups, showed this effect. The effect of acetone, which was used in this step, was not considered by the author. In the other dermally exposed group, the bangle polishers, 36% showed fine hand tremors. The author [29] also compared the number of workers showing tremors at four factories having different tetrachloroethane in air concentrations and found a dose-dependent effect. Breathing zone air samples were taken at only two worksites in each factory, and Lobo-Mendonca (written communication, August 1976) stated that the reported concentrations were averages, but he did not specify the number of determinations made for each

TABLE III-3

EFFECTS ON BANGLE FACTORY WORKERS EXPOSED TO TETRACHLOROETHANE

Job Category	Cylinder Making, Turning	Polishing, Separating	Cylinder Cutting	Heating	Packing	Other	Total
Avg Concentrations (ppm)	17, 98	20, 61	14	11	9	No data	-
No. of Workers	85	107	52	50	42	44	383
Effects	Number (%) of Workers Reporting Symptoms						
Tremors	54 (63)	39 (36)	14 (27)	3 (6)	14 (33)	9 (20)	133 (35)
Anemia	33 (39)	45 (42)	12 (23)	9 (18)	15 (36)	14 (32)	128 (34)
Vertigo	33 (39)	43 (40)	6 (12)	22 (44)	7 (17)	5 (11)	116 (31)
Headache	22 (26)	36 (34)	8 (15)	18 (36)	11 (26)	6 (14)	101 (27)
Abdomen pain	14 (16)	36 (34)	11 (21)	16 (32)	6 (14)	7 (16)	90 (24)
Anorexia	22 (26)	28 (26)	14 (27)	11 (22)	8 (19)	3 (7)	86 (23)
Flatus	17 (20)	11 (10)	7 (13)	1 (2)	4 (10)	5 (11)	45 (12)
Vomiting	9 (11)	13 (12)	2 (4)	7 (14)	2 (5)	2 (5)	35 (9)
Fatigue	13 (15)	10 (11)	4 (8)	1 (2)	2 (5)	3 (7)	33 (9)
Nervousness	6 (7)	14 (13)	0 (0)	8 (16)	0 (0)	1 (2)	29 (8)
Constipation	5 (6)	7 (7)	3 (6)	5 (10)	3 (7)	4 (9)	27 (7)
Nausea	1 (1)	10 (11)	1 (2)	11 (22)	0 (0)	1 (2)	24 (6)
Sweating	0 (0)	13 (12)	0 (0)	7 (14)	0 (0)	1 (2)	21 (6)
Numbness	2 (2)	5 (5)	1 (1)	2 (4)	0 (0)	0 (0)	10 (3)
Weight loss	0 (0)	2 (2)	4 (8)	0 (0)	0 (0)	2 (5)	8 (2)

Derived from Lobo-Mendonca [29]

value. In the factory with the highest average tetrachloroethane concentrations (65 and 98 ppm), 50% of the workers exhibited tremors. In the second and third factories, with average concentrations of 50 and 61 ppm, and 40 and 74 ppm, respectively, 41% and 33% of the workers exhibited this effect. Even in the factory with the lowest average concentrations, 9 and 17 ppm, 14% of the workers showed fine tremors of the hand.

Other neurologic complaints reported in this study [29] were headaches in 26.6% and vertigo in 30.5% of the 380 workers surveyed. Gastric symptoms included anorexia (22.6%), abdominal pain (23.7%), and flatus (11.8%). The urine of several workers was analyzed for urobilinogen, but the results were negative. Lobo-Mendonca [29] stated that a 3-month exposure period ensued before the appearance of the various signs and symptoms, which became more pronounced after 6 months. Examinations indicated that 128 workers were anemic but, without a control group, this finding was considered inconclusive because anemia was a common finding in persons of the socioeconomic group from which these workers were drawn.

It appears from this study [29] that hygienic practices were virtually nonexistent in the bangle-manufacturing industry in India. The study was hampered because the workers were transient, only minimal environmental data were presented, and many of the reported signs and symptoms are often associated with common ailments. Nevertheless, Lobo-Mendonca [29] reported that there was an exposure-effect correlation for the most common disorder observed, hand tremors.

In 1964, Horiguchi et al [31] reported tetrachloroethane concentrations measured at three artificial pearl factories (designated A,

B, and C) where tetrachloroethane was used, and the results of clinical examinations of workers in each of them. During the several steps in the pearl-manufacturing process, workers immersed racks of beads into different tanks containing various organic solvents; the first tank contained ethyl acetate and butyl acetate, amyl acetate was in the next tank, and the third tank contained tetrachloroethane. The racks were then put on shelves to dry. The authors [31] reported that tetrachloroethane concentrations in July 1960, during the first of two surveys, ranged from 75 to 224 ppm at the three factories. No information on the sampling and analytical procedures or on whether the values represented single or mean measurements was reported. According to the authors, none of the factories had ventilation equipment, nor did any of the workers use respirators or other protective equipment. A second survey, conducted 16 months later, showed that factories A and C had stopped using tetrachloroethane altogether, while at factory B, the tetrachloroethane in air concentration had been reduced to 20 ppm, primarily by local ventilation (see Table IV-2).

Clinical examinations [31] were performed on 18 male workers during the first survey and on 20 male workers during the second. Most of these workers were examined during both surveys, but neither the number of workers employed at each factory nor the total number of workers exposed to tetrachloroethane at each factory was reported. No control workers were included in this study. Ten different clinical tests were performed in 1960, and 12 tests were done in 1961; however, only 8 of the tests were common to both surveys. Thus, a direct comparison of all of the test results was not possible. The signs which were tested for in both clinical surveys and the criteria used were: lymphocytosis (over 45% of white blood

cells), low whole blood specific gravity (below 1.054), erythropenia (below 4.49 million/cu mm), low white blood cell count (below 4,999/cu mm), reduced hemoglobin content (below 12.9 g/dl), positive urinary urobilinogen and albumin tests, and enlarged liver. A comparison of the percentages of the examined workers having these signs in the two surveys showed a marked reduction in lymphocytosis for workers at factories A and C, down from 50 and 100% to 14 and 20%, respectively; in factory B, the improvement (from 88 to 50%) was less pronounced. The occurrence of abnormal whole blood specific gravity also decreased in workers at factories A and C, from 75 and 83% in the first to 14 and 0% in the second survey, while those workers affected in factory B decreased from 50 to 25%. The occurrence of erythropenia in workers decreased at factories A and C from 50 and 67% to 14 and 20%, respectively, and at factory B from 25 to 13%. The percentage of workers with abnormal white cell counts and urinary urobilinogen showed no definite reductions with decreased tetrachloroethane exposures; the percentage of workers with an enlarged liver increased from 5 to 10% between surveys. No worker had either abnormal hemoglobin content or urinary albumin. An important observation, reported for the first survey only, was that 39% of the workers had abnormal neurologic indications, including tongue spasm, weakened quadricep reflex, headache, and paresthesia.

By comparing the clinical results at the two factories that had discontinued the use of tetrachloroethane totally by the time of the second survey with those at factory B where the exposure level was still 20 ppm, Horiguchi et al [31] inferred a correlation between the tetrachloroethane concentrations and the adverse clinical findings. The absence of

information in several aspects of this report limits the conclusions that can be derived from the study. The exact times of the changes in industrial processes were not reported. It was also unclear whether there was dermal contact in the dipping process or if exposure was limited to inhalation. In addition, the workers were exposed to several other solvents, including ethyl acetate, butyl acetate, and amyl acetate.

Gobbato and Bobbio [32], in 1968, reported on the cardiovascular status of 75 workers employed in the production of tetrachloroethane, trichloroethylene, and tetrachloroethylene in Italy. Observations were made on workers in four different areas: (A) in the plant where tetrachloroethane was produced via chlorination of acetylene; (B) in the plant where trichloroethylene and tetrachloroethylene were produced from tetrachloroethane; (C) in the storage and loading department; and (D) in the quality control laboratories of the two production plants. According to the authors [32], tetrachloroethane exposure was likely to occur in both production plants, which included many different worksites and types of jobs, and in the laboratories, where there was only one type of job in one work area. All worksites at the production plants except the laboratories were outdoors; staff rooms were inside. The 75 workers were 20- to 59-years-old and had worked an average of 7.7 years at the plants. Of the total, 25 worked or had worked in area A, 29 in area B, 7 in area C, 4 in area D, and 10 on the maintenance crew. The authors did not report the age, sex, or number of workers assigned to specific worksites within each production plant. Neither the percentage of the total factory population represented by this study group of 75 workers, nor the basis for their selection was reported.

Gobbato and Bobbio [32] used Truhaut's modification of the Fujiwara method [33]; this is a nonspecific analytical procedure for chlorinated hydrocarbons. All reported worksite concentrations were related to one or a group of compounds and were not assumed to be totally accurate. In production plant A, the minimum tetrachloroethane concentration (average for six determinations) was 0.37 ppm in the staff room, and the maximum average measured concentration was 1.33 ppm in the product recovery zone. An average concentration of 0.79 ppm was reported for the laboratory. The single maximum tetrachloroethane concentration over the five sampling zones in production plant A was 3.20 ppm, measured in the product recovery zone. During maintenance and unusual circumstances, values between 5 and 15 ppm and, occasionally, as high as 40 ppm were measured in the work zone. These routine maintenance operations lasted less than 30 minutes for each work shift; the workers wore filter masks during these operations. The tetrachloroethane concentrations at production plant B could not be estimated because tetrachloroethylene and trichloroethylene were the predominant compounds present. It was noted that concentrations of tetrachloroethylene and trichloroethylene combined did not exceed 10 ppm in the air of production plant B.

The results of clinical examinations of the 75 workers [32] indicated that pulse rates, cardiac capacities, circulatory responses to postural changes, and ECG's were not significantly different from "normal" values the authors chose from the literature. The authors did not report any attempt at considering ages in these comparisons. Eight workers had arterial blood pressure values which were high compared to "normal" values which took age into account; however, the authors [32] minimized the

importance of these cases by noting that five of the eight workers had shown no elevated arterial pressures in previous periodic examinations and the other three workers had either hereditary sclerotic cardiopathy or hypertension. The results from the other cardiovascular function tests did not receive similar critical examination.

Gobbato and Bobbio [32] concluded that the chronic low-level exposures to tetrachloroethane, as well as to trichloroethylene and tetrachloroethylene, in this factory caused no greater occurrence of cardiovascular lesions than that in the general population. However, the exact extent of exposure to tetrachloroethane is uncertain from the data presented in this study. Production plant A was probably the best location for the effects of exposure to tetrachloroethane alone to be investigated, but the clinical test results for workers there were not distinguished from those of the total working group. Furthermore, the authors [32] were inconsistent in their analysis of the data; ages were not considered for those examinations indicating no significant differences from the chosen "normal" values.

Animal Toxicity

In two animal studies, tetrachloroethane has been shown to be readily absorbed through the lungs [34] and through the skin [36]. In 1910, Lehmann and Hasegawa [34] studied the absorption efficiency of inhaled tetrachloroethane in one rabbit exposed at 9.1 mg/liter (1,300 ppm) for 3 hours. The rabbit was tracheotomized for continuous monitoring of expiration volume as well as tetrachloroethane in the expired breath. Tetrachloroethane was determined by absorption and hydrolysis in alkaline

alcohol, in conjunction with the Mohr method [35] of chloride determination. During the first 15-minute exposure period, the rabbit absorbed 44.5% of the inspired tetrachloroethane. Absorption decreased to 34.0% during the second 15 minutes and 21.2% during the third; it fluctuated near this latter figure for the duration of the exposure. During this 3-hour period, the rabbit inspired a calculated total of 883.3 mg of tetrachloroethane and absorbed a total of 258.3 mg. During the 4-hour period following exposure, the rabbit expired only 19.8% of the absorbed tetrachloroethane.

In a 1936 report, Schwander [36] described the application of tetrachloroethane to the shaved abdomens of two rabbits to investigate its dermal absorption. A semispherical glass vessel was attached to the abdomen and sealed with a bandage and a gelatin sealant. Although the amount of tetrachloroethane applied was not given, a 22 sq cm area of skin was in contact with the liquid. An airtight mask was placed over each rabbit's head and the exhaled air was passed through a trap containing alcohol which dissolved any expired tetrachloroethane. A valved duct allowed the rabbits to inspire fresh air. Periodically, a copper wire was dipped in the alcohol and then placed in a Bunsen burner flame. A green-colored flame would indicate that a halogenated compound was being exhaled by the rabbit.

Tetrachloroethane was applied to rabbit A for 3 hours [36], after which the corneal reflex was almost obliterated and "peculiar" actions (motionless periods followed by spontaneous, excited movements) were observed. The flame test was strongly positive after 40 minutes. At the conclusion of the test period, the exposed area of the abdomen was washed

and the rabbit was recaged. The tetrachloroethane odor in the cage several hours later was attributed to its continuing presence in the rabbit's expired air. After an unspecified time, the rabbit was again exposed for 2 hours in the same manner. At the end of this second exposure, the corneal reflex was present but there was mild paralysis of the extremities. The flame reaction after 40 minutes was again strongly positive. The rabbit died 3 days later.

The second rabbit in this study [36] was completely anesthetized after a 6-hour exposure. The animal was flaccid and unresponsive to strong pinching, and its expired breath had the odor of tetrachloroethane. Pulse and respiration were reported to be normal. The flame test at 20 minutes was weakly positive but at 40 minutes was strongly positive. After an unspecified recovery period, the rabbit was exposed a second time for 7 hours. The rabbit, completely anesthetized, was killed by a sharp blow to the head and autopsied. The thoracic cavity had the odor of tetrachloroethane, and microscopic examination showed fatty degeneration of the liver and kidneys. It was further reported that deep anesthesia could be induced within 10-15 minutes if the exposed abdominal area was large enough.

A number of studies [37-39] have been performed which investigated the acute toxicity of tetrachloroethane. Smyth et al [38] reported, in 1969, that three out of six rats died within 14 days after a single 4-hour inhalation exposure to tetrachloroethane at 1,000 ppm. They also reported an oral LD50 for rats of 0.2 ml/kg (0.3 g/kg) and a dermal LD50 for rabbits of 3.99 ml/kg (6.38 g/kg).

In 1934, Barsoum and Saad [37] reported the fatal doses of tetrachloroethane that was administered by three different routes to dogs and rabbits. The following "minimum lethal doses" for tetrachloroethane were reported: oral, 0.7 g/kg within 24 hours (4 dogs); iv, 60 mg/kg within 30 minutes (7 dogs); subcutaneous, 0.5 g/kg within 24 hours (5 rabbits). The possible influence of ether or sodium barbital which were used to anesthetize the dogs prior to administration of the tetrachloroethane was not mentioned.

As part of a screening study reported by the National Research Council [39], a total of 29 adult mice were given single ip doses of tetrachloroethane dissolved in propylene glycol at doses ranging from 500 μl/kg (800 mg/kg) down to 3.8 μl/kg (6.1 mg/kg) and observed for the ensuing 7 days. Deaths occurred in mice injected with doses of 800, 400, 200, and 48 mg/kg; the animals exhibited ataxia, prostration, and dyspnea. No deaths occurred in any of the mice receiving doses of 24.0, 12.0, or 6.1 mg/kg.

Several early studies [26,40-42] demonstrated the anesthetic effectiveness of tetrachloroethane relative to other chlorinated aliphatic hydrocarbons. Lehmann [40] and Lehmann and Schmidt-Kehl [26] performed similar studies of the effects on cats of acute and chronic inhalation of tetrachloroethane at various concentrations. In 1911, Lehmann [40] reported the results of exposing seven cats in a glass chamber ventilated with air mixed with a stream of air bubbled through tetrachloroethane. One cat was used at each of seven test concentrations that were calculated from the weight loss of the liquid divided by the volume of ventilation air. At the lowest experimental concentration, 5.7 mg/liter (830 ppm), the exposed

cat assumed a prone position within 3 hours, reached light narcosis in 4 hours, and attained deep narcosis in 5 hours. The highest tetrachloroethane concentration, 57 mg/liter (8,300 ppm), produced the prone position in 7 minutes, light narcosis in 25 minutes, and deep narcosis in 40 minutes. (Since the air concentration of tetrachloroethane at saturation (21 C) is about 6,600 ppm, the temperature in the exposure chamber had to have been above room temperature to achieve the experimental concentration.) From the seven experimental concentrations employed, consistent dose-dependent effects were demonstrated. Besides showing general signs of irritation, the cats sneezed vigorously both before the onset of, and on slow awakening from, narcosis. Lehmann [40] conducted similar acute experiments with several other chlorinated aliphatic hydrocarbons; tetrachloroethane was reported to be about 9.1 times more toxic than tetrachloromethane (carbon tetrachloride), the least toxic substance according to the criteria of anesthesia selected for this study.

To investigate the effects of chronic exposure, Lehmann [40] exposed two cats and one rabbit to tetrachloroethane at concentrations ranging from 1.1-2.3 mg/liter (160-335 ppm) for 6-7 hours/day, 18 times during 4 weeks. Intervals between exposures were not given. No adverse effects were observed aside from varying degrees of "numbness" and sleep. Body weights dropped by 260-380 g. No autopsies were performed.

Lehmann and Schmidt-Kehl [26], in 1936, exposed cats to tetrachloroethane by inhalation at concentrations ranging from 4.9 mg/liter (710 ppm) to 42 mg/liter (6,100 ppm). The concentrations were calculated as described by Lehmann [40] but, in addition, quantitative measurements were also performed by absorption on calcium oxide, extraction with

alcohol, hydrolysis with alkali, and chloride determination by the Volhard method [27]. Two cats were exposed at each concentration and the time of onset was recorded for each of the predesignated stages of anesthesia from prostration to deep narcosis. The resulting dose-dependent effects were consistent with those observed previously by Lehmann [40]. In the chronic inhalation experiments, two cats and two rabbits were exposed simultaneously at concentrations of 0.8-1.1 mg/liter (116-160 ppm) for 8-9 hours/day, 6 days/week, for 4 weeks. All four animals showed the designated initial stage of prostration, but body weights, behavior, body temperatures, and blood studies did not show any remarkable changes. These results were also consistent with those observed earlier by Lehmann [40]. The animals were killed 7 weeks after the end of the exposure, at which time, gross and microscopic examinations revealed no pathologic changes.

In 1929, Lazarew [42] reported the minimum concentration of tetrachloroethane vapor causing (1) assumption of a lateral (prone) position, (2) loss of reflexes (responses normally displayed when the chamber was tapped), and (3) death, in mice, but gave little detail on the experimental procedures employed. An unspecified number of albino mice was exposed to tetrachloroethane vapor in hermetically sealed glass bottles (10-liter capacity) for a maximum of 2 hours. In comparison with several other chlorinated hydrocarbons, tetrachloroethane ranked most toxic or nearly so according to all three of the stated criteria. Within 2 hours, mice assumed a lateral position when exposed to tetrachloroethane at 7.5-10 mg/liter (1,091-1,455 ppm), lost their reflexes at 10-15 mg/liter (1,455-2,182 ppm), and died at 40 mg/liter (5,820 ppm). No autopsies were performed.

In 1933, Pantelitsch [41] reported the exposure of mice by inhalation to tetrachloroethane at concentrations ranging from 7 mg/liter (1,020 ppm) to 34 mg/liter (4,900 ppm). Results were presented as the recorded times of onset of disturbed equilibrium, prostration, loss of reflexes (determined by slight pressure applied on the paws), and death. The exposure chamber was a 10-liter glass bottle into which tetrachloroethane was discharged from a buret via a small, suspended cup that was lined with filter paper to facilitate evaporation. The concentrations of tetrachloroethane were calculated as well as actually measured, but by unspecified methods. Groups of three mice were exposed at each concentration. A dose-effect relationship was found that was reported to be consistent with the findings of Lazarew [42]. At a concentration of 7 mg/liter (1,020 ppm), the average times for the three mice to reach the sucessive stages of disturbed equilibrium, prostration, and loss of reflexes were 25, 82, and 131 minutes, respectively. After 152 minutes, the experiment was terminated and by the next morning all three mice appeared completely recovered. At 34 mg/liter (4,900 ppm), the average times of onset for each stage were 2, 7, and 7 minutes, respectively, and all three mice died in 100 to 120 minutes.

Horiuchi et al [43], in 1962, reported the results of inhalation exposures of mice, rats, and a monkey to tetrachloroethane at high concentrations. A "dynamic flow" chamber was used in the experiments, but neither the chamber nor the sampling and analytical procedures used were described. Among one group of 10 mice exposed to tetrachloroethane at

5,900 ppm for 3 hours, three died within 1 week. Another group of 10 mice was exposed at 6,600 ppm for the same duration; four of them died within 1 week. In repeated exposure experiments, nine male mice were exposed at an average concentration of 7,000 ppm tetrachloroethane for one 2-hour period/week. Five mice died after the first exposure, three more after the third, and the remaining mouse died soon after the fifth exposure. Six rats were exposed at 9,000 ppm for 2 hours/day, 2 days a week. One rat died after the second exposure, two more rats died after the fourth exposure, and the remaining three rats died after the 11th exposure. The rats lost consciousness within 1-1.5 hours after the beginning of exposure. Blood examinations were performed on three exposed and two control rats prior to and 14 days after the start of the experiment. Two of the three exposed rats had decreased red blood cell counts and hemoglobin levels, but no significant change was found in white blood cell counts of either the exposed or the control groups. Post-mortem microscopic examinations of exposed mice and rats showed "congestion" of tissues and fatty degeneration of the liver. To achieve the reported air concentrations above 6,600 ppm, the temperature in the exposure chamber had to be elevated above room temperature (21 C).

The adult male cynomolgus monkey weighing 7 kg was exposed to tetrachloroethane vapor 2 hours/day, 6 days/week, for 9 months, for a total of 190 exposures [43]. The concentration of tetrachloroethane ranged from 2,000 to 4,000 ppm during the first 20 exposures, from 1,000 to 2,000 ppm for the next 140 exposures, and from 3,000 to 4,000 ppm for the rest of the experiment. The monkey became noticeably weak after about seven exposures and developed diarrhea and anorexia after the 12th exposure. After

recovering from this condition, and beginning with the 15th exposure, it became nearly unconscious 20-60 minutes after the beginning of each exposure. There was a gradual increase in body weight during the 3d through 5th months of exposure and a gradual decrease thereafter. Red blood cell counts and hemoglobin levels decreased during the 3d and 4th months but then increased gradually to preexposure values. White blood cell counts decreased immediately after exposure began, remained low for about 5 months, then tended to increase; however, the recovery was variable for the remaining exposure periods. Urinary albumin and urobilinogen did not change appreciably. The monkey was exsanguinated at the end of the 9-month experiment. Histologic examination showed no definitive changes in tissues of the heart, lungs, kidneys, pancreas, and testes; however, the central zone of the liver had marked vacuolation of the cytoplasm as noted with hematoxylin-eosin staining.

In this same study [43], a second adult male monkey (4.5 kg) was injected subcutaneously with tetrachloroethane in 50% v/v olive oil solution. The dosage was 5 ml on day 1, 2 ml on day 4, 1 ml on day 19, 2 ml on day 20, and 4 ml on day 29. Thus, a total of 7 ml of tetrachloroethane in five applications was given over a 29-day period. The monkey showed signs of CNS depression after the first administration and thereafter, periods of unconsciousness and recovery occurred after subsequent injections of tetrachloroethane. The monkey was comatose after the last injection and died 2 days later. Its body weight had decreased from 4.5 to 3.3 kg at death. Red blood cell count and hemoglobin level increased slightly during the experiment; there were no remarkable changes in the total white blood cell count, but the differential count showed

lymphopenia and neutrophilocytosis. There were no appreciable changes in urinary albumin and urobilinogen, but urinary coproporphyrin increased toward the end of the experiment. Histologic examination of the heart, lungs, liver, and kidneys showed no remarkable changes apart from "congestion."

The findings reported by Horiuchi et al [43] are of limited value, primarily because of the high doses employed. The indication of fatty degeneration of liver in rats is consistent with reports of other investigators [36,44,45]. Although only two monkeys were studied, the lack of pronounced liver involvement in the 9-month inhalation study and the total absence of liver effects in the injection experiment, both at exposure levels sufficient to maintain profound CNS depression, is noteworthy.

Fiessinger et al [45], in 1922, reported the effects in mice of repeated inhalation exposure to tetrachloroethane. Groups of four mice were placed in a 17-liter chamber with a Petri dish containing 10-20 ml of tetrachloroethane. The mice were left in the chamber for 1-1.5 hours; the evaporation never exceeded 1.5 ml for each exposure. Some of the mice were comatose by the end of an exposure period. They exhibited convulsive movements and staggering of the hindquarters. After the eighth exposure, or a total of 10 hours, the mice had "bristly hair," had lost weight, and were anorexic. There was no mention of the interval between exposures. The urines contained bile pigment and the feces were discolored; autopsies indicated the peritoneum to be slightly yellowish and the liver nutmeg in color. Between the 8th and 28th exposures, hepatic lesions developed, the liver became yellowish, and histologic examination revealed signs of

centrilobular parenchymal degeneration with some fatty infiltration.

In 1931, Bollman and Mann [46] reported that repeated administration of 150 1-ml doses of tetrachloroethane to a dog over a 1-year period produced a condition typical of portal cirrhosis of the liver. Neither the route of administration nor the specifics of the experimental procedures were stated. Early symptoms consisted of gastrointestinal upsets, diarrhea, and intestinal hemorrhage, followed by jaundice and marked ascites with continued administration. The liver which was hypertrophic after 1 year, returned to normal size within 3 months after the exposures were discontinued.

In 1932, Muller [44] detailed the effects of tetrachloroethane administered by various routes to mice, guinea pigs, and one rabbit. An unspecified number of mice was placed in a 0.5-cu m chamber in which tetrachloroethane was evaporated to an initial concentration of 80 mg/liter (11,400 ppm). After 6 hours, the deeply anesthetized mice were removed and they recovered rapidly in fresh air. This procedure was repeated the next day with the same mice. After a second apparent recovery, all the mice had convulsions and died within a few hours. Autopsies showed fatty degeneration of the liver, particularly in the peripheral lobes and also focal fatty degeneration of the renal tubular cells. The stated concentration of tetrachloroethane in the inhalation chamber was only the initial, calculated concentration and there were no indications of what concentrations existed as the exposure progressed.

When tetrachloroethane was injected iv, ip, or subcutaneously into an unspecified number of guinea pigs and mice by the same author [44], no notable species or injection-mode differences were found. The animals died

in convulsions shortly after being injected with doses of 0.2 ml. No other test doses were reported. Autopsies revealed no morphologic changes. In an attempt to simulate chronic poisonings, Muller [44] injected mixtures of tetrachloroethane in olive oil, glycerin, or paraffin subcutaneously into an unspecified number of guinea pigs. The mixtures of tetrachloroethane in olive oil or glycerin (liquids at animal body temperature) produced effects similar to those reported (above) in mice injected with unmixed tetrachloroethane at a dose of 0.2 ml; the guinea pigs died within a few hours in convulsions, and no morphologic changes were apparent at autopsy. Tetrachloroethane mixed with paraffin (semisolid at animal body temperature) increased the lethal dose of tetrachloroethane to 0.7 ml administered in five injections over 14 days. Details on the schedule of individual injections were not given. Other than body weight losses, the guinea pigs showed no clinical symptoms preceding death. Autopsies revealed liver and kidney effects similar to those noted above in Muller's inhalation studies in mice [44].

An iv dose 0.2 g tetrachloroethane was also administered to a rabbit [44]. The animal went into immediate narcosis, apparently recovered after about 15 minutes, but died after 30 hours. Autopsy indicated liver enlargement with pasty, fine yellow fields. Microscopic examination showed severe coarse- and fine-droplet fatty degeneration of the parenchymal cells corresponding to the yellow fields, especially in the periphery of the lobes.

In 1972, Deguchi [47] reported the effect of tetrachloroethane on the activities of serum transaminases in male Wistar Daikoku rats exposed at 10, 100, and 1,000 ppm by inhalation for 6 hours. Six mature (200 g) rats

were exposed at each concentration and 20 rats served as controls. A stream of air was passed over saturated wicks immersed in flasks of tetrachloroethane and directed into a 66-liter exposure chamber. The measured tetrachloroethane concentration fluctuated by ± 20% of the nominal concentration. The techniques used for air analysis were not reported. The rats were killed prior to serum transaminase determinations. At 24 hours after the single inhalation exposures at 10 and 100 ppm, the average serum glutamic oxaloacetic transaminase (SGOT) values were 144 and 206 units, respectively, while the control rats showed an average value of 110 units. The corresponding average serum glutamic pyruvic transaminase (SGPT) values were 51 and 53 units, respectively, for the exposed groups and 41 units for the control group. Four of the six rats exposed at 1,000 ppm for 6 hours died within 24 hours after the start of the exposure. Serum transaminase values for the two surviving rats were lower than control levels. Transaminase activities for rats exposed at 10 ppm were monitored further at 48, 72, 96, and 120 hours after exposure; three values were reported for each period. The mean SGOT values of 214, 245, 160, and 140 units, respectively, increased gradually up to 72 hours and then decreased. The respective mean SGPT values of 45, 55, 46, and 48 units showed no significant trends over the observation period. Histologic examinations performed at necropsy after 24 and 120 hours of recovery by the 10-, 100-, and 1,000-ppm groups showed no definite changes in the liver, heart, kidney, spleen, brain, or bone marrow.

In 1969, Tomokuni [48] reported the development of fatty livers in 18 female Cb mice exposed to tetrachloroethane at 600 ppm for 3 hours. The exposure chamber was supplied with a constant flow of air bubbled through a

tetrachloroethane vaporization unit. The tetrachloroethane concentration was determined by gas chromatography every 30 minutes during the exposure period. Groups of six mice were killed at 0, 4, and 8 hours after termination of exposure; their livers were removed, weighed, and analyzed for adenosine triphosphate (ATP), total lipids, and triglyceride content. Eight female mice were used as controls. The author [48] concluded that tetrachloroethane inhalation caused fatty liver by increasing the total liver lipid and triglyceride contents during, and up to 8 hours after, exposure. Compared with the controls, total liver lipids increased to 115, 155, and 216% of control values at 0, 4, and 8 hours, respectively; triglyceride content increased to 163, 288, and 518%, respectively; and hepatic ATP content decreased to 75, 59, and 46% of the control values, respectively.

In a subsequent study, Tomokuni [49] exposed 35 female mice to tetrachloroethane at 800 ppm for 3 hours. The triglyceride and phospholipid contents of the liver and plasma were measured in five mice each at 5, 20, 25, 30, 45, 70, and 90 hours postexposure. Eight female mice were used as controls. The hepatic triglyceride content increased after exposure, reached a maximum of 50.4 mg/g liver at 20 hours, then decreased to near the control level of 8.4 mg/g by 90 hours. The hepatic phospholipid content decreased after exposure, reached a minimum of 16.7 mg/g at 25 hours, and then slowly increased to near the control level of 23.2 mg/g by 90 hours. Both plasma triglycerides and phospholipids decreased until 25 hours after exposure. Triglyceride content decreased from 0.98 mg/ml to 0.39 mg/ml plasma, and phospholipids decreased from 0.84 mg/ml to 0.54 mg/ml. Both then gradually increased, the phospholipids to

the control level and the triglycerides to above the control level, between 70 and 90 hours after exposure. Judging from the increase in hepatic triglyceride levels, the author [49] concluded that the development of fatty liver reached a peak in the period between 20 and 25 hours postexposure. The decreased values observed for both liver and plasma phospholipids were not adequately explained.

Navrotskiy et al [50] tested the chronic inhalation toxicity of several chlorinated hydrocarbons including tetrachloroethane in 350 rats and rabbits. It was the authors' intent to show that upon continual exposure to low concentrations of an environmental contaminant, the "blood chemistry" of the tested species would be altered. Tetrachloroethane at 2, 10, or 100 mg/cu m (0.3, 1.46, or 14.6 ppm) was administered 3-4 hours "daily" for 7-11 months. No further details of the experimental and analytical procedures were reported. At 100 mg/cu m (14.6 ppm), hemagglutinin (antibody that agglutinates erythrocytes) production was progressively suppressed with continued exposure; phagocytic activity was increased 15-30% at 1-1.5 months, and suppressed (amount not specified) at 2-3 months after exposure. During the first 2-4 months of exposure at this concentration, the rabbits excreted 30-40% more 17-ketosteroids than they had excreted initially; after further exposure, there was a reduction to 10-20% below the initial rate. Other findings at the 14.6-ppm concentration were increased total serum proteins, moderate hyperurobilinogen, phasic fluctuations in acetylcholine content and cholinesterase activity in the blood, decreased hemoglobin content, and reduced erythrocyte counts. At autopsy, rabbits exposed to tetrachloroethane at 14.6 ppm showed signs of incipient liver and kidney

degeneration, but no further details were provided. The only effects specifically reported at 1.46 ppm were suppression of hemagglutinin production and phasic fluctuations in the whole blood acetylcholine content and cholinesterase activity. No effects were reported in rabbits exposed to tetrachloroethane at 0.3 ppm.

Insufficient information on the experimental procedures as well as on the test results was the major limitation of this 1971 paper [50]. Although it is difficult to thoroughly evaluate the authors' conclusions, the reported structural changes in the liver and kidneys of rabbits exposed chronically at 14.6 ppm are noteworthy, as are the apparent dose-effect relationships in the blood and urine parameters checked. Deviations from normal values at 14.6 ppm, for example, were greater than at 1.46 ppm, and no effects were reported at 0.3 ppm.

In 1972, Schmidt et al [51] described the toxic effects of low concentrations of tetrachloroethane to which rats were exposed by inhalation, with and without ethanol treatment. A total of 294 male rats (60 days old) weighing 210-270 g were used, 84 in a subacute experiment, and 210 in a chronic experiment. The animals were exposed in 200-liter chambers to a continuous flow of a tetrachloroethane-air mixture. Airborne concentrations of tetrachloroethane were determined both colorimetrically [52] and by calculation of the ratio of the weight of tetrachloroethane volatilized to the total air volume. The average tetrachloroethane concentration determined in both the subacute and chronic experiments was 13.3 ± 0.24 mg/cu m (1.94 ppm).

In the subacute study [51], 42 rats were exposed to tetrachloroethane at the test concentration for 4 hours/day on 8 of 10 days. Another group

of 42 rats was similarly exposed to air only. To study the effects of ethanol on tetrachloroethane-induced toxicity, the authors gave ethanol (4 g/kg, with an equal volume of isotonic saline) by intubation to 21 of the tetrachloroethane-exposed rats and to 21 of the controls. Seven rats each were intubated after their first, third, or seventh exposure. The other 42 rats were given saline only. The rats were thus subdivided into four groups of 21 animals each: those exposed to tetrachloroethane alone, those exposed to ethanol alone, those exposed to tetrachloroethane plus ethanol, and those exposed to air alone. Measurements performed in each group after the second, fourth, or eighth exposure indicated no significant differences among the groups in body weight, white blood cell counts, SGOT and SGPT activities, BSP excretion test values, and total fat content of the liver. Although significant fluctuations were noted in serum proteins and adrenocorticotropic hormone (ACTH) in the pituitary gland, the results were inconclusive because no consistent pattern or relationship could be established from the data.

In the 9-month chronic exposure experiments, Schmidt et al [51] exposed 105 rats each to tetrachloroethane and to air alone "daily" for 4 hours/day. The exposure chambers and the tetrachloroethane concentration (1.94 ppm) were identical to those of the subacute study, but no ethanol was used. Groups of seven each of experimental and control rats were examined after 110 and 265 days of exposure. At the end of 110 days, the exposed rats weighed significantly less than the controls (415 ± 5.3 g versus 435 ± 4.9 g), while their white blood cell counts averaged 90% higher than the control values. After 265 days, there was wide variation in group body weights and differences were no longer significant. No white

blood cell count data were given. The ACTH content of the hypophysis was significantly increased in the exposed rats at both intervals, and the total fat content of the liver was about 34% higher in the exposed than in control rats after 265 days. There were no significant differences between exposed and control mortality rates.

Schmidt et al [51] also investigated the effect of chronic exposure to tetrachloroethane on the reproductive capacity of male rats. One week prior to the end of the 9-month chronic exposure, seven control and seven exposed male rats were each mated with five unexposed, virgin female rats. The 1.94-ppm exposure of the male rats was continued during the mating period. Gross examinations of the F1 generation were carried out for 12 weeks. No differences of note were found in percentage of females littering and litter size, average weight, male-to-female sex ratios, growth rates, and percent mortality in the young.

Tetrachloroethane was one of several chlorinated hydrocarbons tested by Plaa and Larson [53] for potential kidney toxicity in mice following ip injection. Indicator paper dipped in the urine and compared to standard color charts was used to quantitate glucose and protein contents. Ten mice were injected ip every other day for 6 days with tetrachloroethane-corn oil solutions equivalent to doses of either 0.5 or 1.0 ml/kg (0.8 or 1.6 g/kg) tetrachloroethane. A group of 60 mice was used as a control. At 0.8 g/kg, all 10 mice survived, but 2 of them had a significant urinary protein increase (over 100 mg%), although none showed significant urinary glucose (over 250 mg%). At 1.6 g/kg, only one of the 10 mice survived, and it had significant increases in both urinary protein and glucose. No evidence of kidney necrosis or swelling in the proximal convoluted tubules was noted in

the five mice receiving 0.8 g/kg that were examined. No details were given on kidney effects for the group receiving 1.6 g/kg. The authors [53] classified tetrachloroethane as a weaker nephrotoxin in mice than either chloroform or carbon tetrachloride.

There have been several reports [24,54,55] describing the metabolism and excretion of tetrachloroethane in animals. In 1939, Barrett et al [24] reported the results of administering tetrachloroethane, either by inhalation or by subcutaneous injection, to unspecified numbers of dogs, rats, guinea pigs, and rabbits. The dogs were exposed at an unspecified concentration in an enclosed chamber for 1 hour, the period necessary to produce narcosis, for 20 successive days. The rats, rabbits, and guinea pigs were administered tetrachloroethane by subcutaneous injection; again, however, the dose was not stated. Concentrations of chlorinated hydrocarbons in the urine were determined by the Fujiwara reaction [52]. Not more than 0.5 mg/liter of chlorinated hydrocarbons was detected in dog urine; similar results were obtained in the other species. This amount was about 0.1% of that reported after similar experiments with trichloroethylene by the same authors [24].

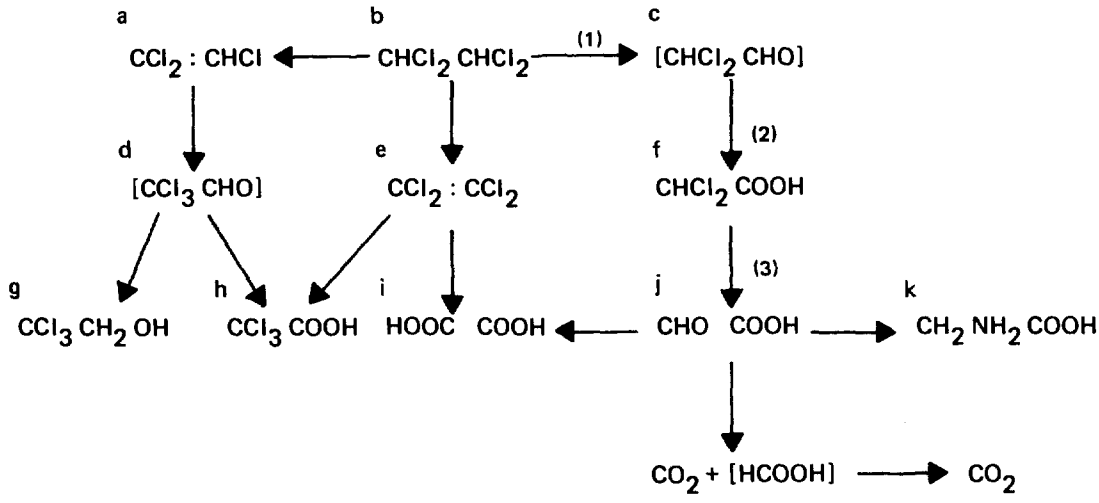
In 1971, Yllner [55] reported experiments in which 0.21-0.32 g/kg of 14C-labeled tetrachloroethane was injected ip into an unspecified number of female albino mice after which the elimination of radioactivity was monitored for 3 days. Of the total radioactivity measured, about 50% (range 45-61%) was accounted for in the expired carbon dioxide, about 28% (range 23-34%) was excreted in the urine, about 16% (range 11-19%) remained in the animal, and less than 4% was expired as tetrachloroethane. Dichloroacetic acid, trichloroacetic acid (TCA), trichloroethanol (TCE),

oxalic acid, and small quantities of glyoxalic acid and urea were identified in the urine by paper chromatographic and isotope dilution techniques. Half of the activity in the urine could not be identified. From these studies, a metabolic scheme for tetrachloroethane was developed; it is presented in Figure III-1. The primary pathway (1, 2, 3) was proposed to consist of a stepwise hydrolytic cleavage of the chlorine-carbon bonds yielding glyoxalic acid and then carbon dioxide. A nonenzymatic oxidation of tetrachloroethane produced a small amount of tetrachloroethylene. It was also demonstrated in vitro that tetrachloroethane could be dehydrochlorinated to form small amounts of trichloroethylene. The trichloroethylene was suggested as the precursor to the TCA and TCE found in the urine. Glycine production was indicated by the significant amounts of labeled hippuric acid excreted after a simultaneous injection of 14C-labeled tetrachloroethane and sodium benzoate [55].

In 1972, Ikeda and Ohtsuji [54] reported that rats exposed to tetrachloroethane excreted very small amounts of TCA and TCE in their urine. Eight groups of six immature Wistar rats (50 g) each were exposed to tetrachloroethane at 200 ppm for 8 hours. Urine samples were collected and pooled for each group for 48 hours after exposure and analyzed by a modification of the Fujiwara reaction [52]. Results indicated an average of 8.2 ± 3.0 mg/kg total trichlorocompounds, 1.7 ± 0.9 mg/kg TCA, and 6.5 ± 2.7 mg/kg TCE. These values were less than 1/20 of those observed for rats exposed to the isomer, 1,1,1,2-tetrachloroethane. Another eight groups of five Wistar rats each were injected ip with 2.78 mmole/kg (467 mg/kg) of

FIGURE III-1

PROPOSED TETRACHLOROETHANE METABOLIC SCHEME IN MICE



a) Trichloroethylene
b) Tetrachloroethane
c) Dichloroacetaldehyde
d) Trichloroacetaldehyde
e) Tetrachloroethylene
f) Dichloroacetic acid
g) Trichloroethanol
h) Trichloroacetic acid
i) Oxalic acid
j) Glyoxalic acid
k) Glycine

Derived from Yllner [55]

the tetrachloroethane isomers diluted with soybean oil (total dose of 1 ml/kg body weight). Urine samples were collected for two successive 48-hour periods and analyzed as before. Results were consistent with the inhalation experiment that showed much lower total trichlorocompounds, TCA, and TCE values for rats administered 1,1,2,2-tetrachloroethane than for those administered 1,1,1,2-tetrachloroethane. It was postulated that the rate and means of excretion are determined largely by the ease of biotransformation. A simple hydrolytic dehalogenation is required by 1,1,1,2-tetrachloroethane, while the symmetrical isomer requires a chlorine atom shift. The slow elimination of 1,1,2,2-tetrachloroethane from the body may be a definite factor in its high toxicity. Volatile compounds can also be exchanged into the lungs and expired effectively, but the authors [54] pointed out that elimination through the breath is low for these two isomers because of their relatively low vapor pressures.

Reported data on the possible carcinogenicity or teratogenicity of tetrachloroethane have not been found. The National Cancer Institute is conducting a study of the carcinogenic potential of tetrachloroethane, the results of which will be evaluated by NIOSH when they become available. Brem et al [56] used two different bacterial assay techniques to investigate the mutagenic potential of several haloalkanes, including tetrachloroethane. With one assay method, the growth inhibition by haloalkanes of a strain of E. coli lacking DNA polymerase I was compared with that of an E. coli strain having the enzyme. The two strains of E. coli (pol A+ and pol A-) were grown on separate agar plates. A sterile paper disc was laid on each plate and 10 μl of the haloalkane were placed on the disc. The plates were incubated at 37 C for 8 hours, after which

the zones of inhibition around the discs were measured. This was done in duplicate at least three different times for each test chemical. The ratio of the diameters of inhibition zones (pol A-/pol A+) was 1.00 for a control using 30 μg chloramphenicol. Ratios of the diameters of the zones in excess of 1.00 were considered indicative of some preferential inhibition of the pol A- strain. DNA polymerase I was claimed to play an important role in DNA repair. The polymerase-deficient strain (pol A-) was more sensitive than the parent strain (pol A+) to the inhibitory or toxic action of the haloalkanes. The degree of preferential inhibition was considered an indicator of the mutagenic potential of the test chemicals. The tetrachloroethane ratio of 1.88 indicated moderate mutagenic activity in E. coli relative to the other test chemicals. Ratios for the two most active haloalkanes tested were 3.39 for 1,1,2,2-tetrabromethane and 2.70 for 1,1-dibromoethane.

In a second mutagenesis study [56], three strains of Salmonella typhimurium were used. Strains TA 1530 and TA 1535 each had a base substitution in the histidine G gene, while strain TA 1538 had a single base deletion in the histidine D gene. Each of the three strains was inoculated on separate minimal agar plates containing only trace amounts of histidine. A paper disc impregnated with 10 μmol of test substance was deposited on the surface of each plate. Water (10 μl) and chloramphenicol (30 μg) were used as control substances. The plates were then incubated in darkness at 37 C for 54 hours and the histidine-independent colonies (mutants) were then counted. The use of duplicate plates could not be determined for this part of the study. In the presence of tetrachloroethane, mutant colonies totaled 77, 49, and 28 in strains TA

1530, TA 1535, and TA 1538, respectively; on control plates, they numbered 23, 26, and 19 for water and 20, 31, and 14 for chloramphenicol. The results indicated that tetrachloroethane was more active in inducing mutations of the base-substitution than of the frame-shift type in these bacterial test systems.

In these two assays [56], tetrachloroethane was more active than the controls and it was intermediate in effect among the other test substances--1,2-dibromoethane, 1,2-dichloroethane, 1-bromo-2-chloroethane, 1,1,2,2-tetrabromoethane, etc. Additional mammalian mutagenicity experiments in vitro and in vivo should be performed before a definite conclusion is reached concerning the mutagenic potential of tetrachloroethane in mammals.

Correlation of Exposure and Effect

The pronounced anesthetic properties of tetrachloroethane have been shown in both human and animal studies [26,40-43]. In humans, the effects of acute exposures to tetrachloroethane have been mainly observed in several reports of nonoccupational poisonings by ingestion. Rapid loss of consciousness, progressive CNS depression, and death within 20 hours after consumption of unknown amounts of tetrachloroethane were reported in five suicide cases [15-19]. Sherman [20] and Ward [21] reported two incidents in which 3 ml of tetrachloroethane were mistakenly given orally to each of 10 adults. Within 2 hours, five of the subjects became comatose while the other five lapsed into various degrees of semiconsciousness. All recovered and no aftereffects were reported. Ward [21] also mentioned a young girl

who ingested 2 ml of tetrachloroethane without adverse effects.

The report of Lehmann and Schmidt-Kehl [26] in 1936 described human experiments on the effects of tetrachloroethane after short-term inhalation exposures. Two men were exposed simultaneously by inhalation to the chemical at concentrations ranging from 2.9 to 335 ppm. At 2.9 ppm both men detected tetrachloroethane by its odor. Exposure at 116 ppm for 20 minutes produced dizziness and mild vomiting; at 146 ppm, both subjects experienced dizziness after 10 minutes, mucosal irritation at 12 minutes, and fatigue at 20 minutes. At concentrations of 262 and 335 ppm, these same symptoms were reported after progressively shorter exposure periods. Olfactory fatigue, which became apparent at the higher concentrations, indicated that odor is not a reliable indicator of the presence of tetrachloroethane.

Inhalation experiments on cats [26,40], rabbits [26,36], and mice [41,42] have confirmed the anesthetic effectiveness of tetrachloroethane. Lehmann [40] reported a dose-dependent anesthetic effect in one cat exposed to tetrachloroethane at each of seven test concentrations ranging from 830 to 8,300 ppm. At the lowest concentration, salivation, sneezing, and licking were observed after 17 minutes; prostration was evident after 3 hours, as was light narcosis after 4 hours, and deep narcosis was seen after 5 hours. Exposure times necessary for the onset of anesthesia decreased with each incremental increase in concentration; at 8,300 ppm, the cat salivated after 5 minutes, was prostrate after 7 minutes, was narcotized lightly after 25 minutes, and was narcotized deeply after 40 minutes. Lehmann [40] also exposed two cats and one rabbit to tetrachloroethane at 160-335 ppm for 6-7 hours/day on 18 of 28 days. The

animals exhibited varying degrees of "numbness" and sleep during the experiment.

Besides the anesthetic effects, tetrachloroethane has been reported to cause other neurologic effects in occupationally exposed workers. Grimm et al [12] reported a number of poisonings in German aircraft factory workers who experienced tremors, headaches, pains in the limbs, "numbness," sensation of pins and needles in the extremities, knee-jerk areflexia, and excessive sweating after long-term exposures to tetrachloroethane. Leri and Breitel [13] described the poisoning of two young women who worked in an artificial pearl factory where tetrachloroethane was used. Both experienced paralysis of the interosseous muscles of their feet and hands, obliteration of their ocular and pharyngeal reflexes, and paralysis of their jaw and ocular muscles. Poisonings of this type have not usually been fatal; however, the victims were seriously incapacitated, and they continued to experience effects long after their exposure to tetrachloroethane ended.

Lobo-Mendonca [29] found that a high percentage of workers in India's bangle industry had neurologic and gastrointestinal signs and symptoms; the measured concentrations of tetrachloroethane in air ranged from 9 to 98 ppm. There was considerable dermal contact with the liquid in at least two of the manufacturing processes and there was possible mixed exposure to acetone as well. The most frequently reported symptoms were hand tremors (35%), vertigo (30.5%), headache (26.6%), abdominal pain (23.7%), and anorexia (22.6%). In a four-factory comparison in which he related measured tetrachloroethane in air concentrations (values represented averages of unspecified numbers of samples) and the percentage of workers

having hand tremors, Lobo-Mendonca [29] reported hand tremors in 50% of the workers at the factory with the highest measured concentrations (65 and 98 ppm) of tetrachloroethane, compared with 40% at the factory with measured concentrations of 50 and 61 ppm, 33% at the third factory (40 and 74 ppm), and 14% at the factory with the lowest measured concentrations (9 and 17 ppm).

The main concern with occupational exposure to tetrachloroethane results from the numerous reported poisonings [7,8,12,57] due mainly to chronic inhalation exposures which resulted in liver damage and gastrointestinal disturbances. Most of these occupational case reports described a consistent clinical picture including initial symptoms of general malaise, anorexia, exhaustion, headache, and nausea. After continued exposure, jaundice was observed, frequently accompanied by vomiting, pale stools, and bile-stained urine. Finally "jaundice with toxemia" was seen including intensified jaundice, delirium, convulsions, coma, and death [9]. Unfortunately, the sparse occupational exposure data which were presented in these reports permitted little correlation of gastrointestinal and hepatic effects with tetrachloroethane exposure. Descriptions of the work operations [8,12] indicated the probability of dermal contact in addition to respiratory exposure in some of these poisonings.

The potent liver toxicity of tetrachloroethane has been also documented in numerous studies in rabbits [36,44,50], rats [43,47,51], mice [43-45,48,49], and guinea pigs [44]. Several of these studies were of short exposures at high concentrations. Horiuchi et al [43] exposed 20 male mice, 10 at 5,900 ppm and 10 at 6,600 ppm, to tetrachloroethane for a

single 3-hour period. After 1 week, three and four deaths had occurred, respectively, in the two groups. At autopsy, fatty degeneration of the liver along with "tissue congestion" was consistently evident. The same investigators [43] exposed six rats at 9,000 ppm for 2 hours/day, twice a week. One rat died after 2 exposures, 2 more died after 4 exposures, and the remaining 3 rats died after 11 exposures. Microscopic examination again showed fatty degeneration of the liver and generalized "tissue congestion."

Concentrations of airborne tetrachloroethane ranging from 1.5 to 247 ppm were measured in a penicillin-manufacturing plant [28] where there was an outbreak among the workers of signs and symptoms indicative of liver dysfunction. This 3-year study demonstrated the effectiveness of bimonthly medical screening examinations and improved ventilation; however, the author stated that some workers exposed to tetrachloroethane at concentrations ranging from 15 to 34.6 ppm still suffered liver damage. Effects seen at these concentrations included enlarged liver, urobilinogenuria, increased serum bilirubin, and general and digestive organ complaints.

Five of the more recent animal studies [47-51] have reported toxic liver effects after exposures at concentrations from 800 to as low as 1.94 ppm of airborne tetrachloroethane. Tomokuni [48,49] found fatty liver changes in mice exposed by inhalation to tetrachloroethane at 800 and 600 ppm for 3 hours. At 600 ppm, liver triglycerides increased almost linearly from the beginning of exposure until 8 hours postexposure. At 800 ppm, liver triglycerides increased for up to 20-25 hours after exposure, while at the same time there was a decrease in plasma triglycerides; although

they later decreased, liver triglyceride levels did not return to preexposure values even 90 hours after exposure.

Rats were found to have elevated SGOT values 24 hours after exposure to tetrachloroethane at 10 or at 100 ppm for 6 hours, and four of six rats exposed at 1,000 ppm for 6 hours died within 18 hours after the end of exposure [47]. The average SGOT values for the rats exposed at 10 ppm increased from a control value of 110 units to 144, 214, 245, 160, and 140 units at 24, 48, 72, 96, and 120 hours after exposure, respectively. The average SGPT values increased only minimally after exposure.

Navrotskiy et al [50] reported that rabbits exposed to tetrachloroethane at 14.6 ppm, 3-4 hours/day, for 7-11 months had signs of incipient liver and kidney degeneration at autopsy. There were also alterations in the rabbits' immunoresponse system as indicated by abnormal variations in blood and urine parameters at 14.6 ppm and, to a lesser extent, at 1.46 ppm.

Chronic inhalation exposure of male rats to tetrachloroethane at 1.94 ppm, 4 hours/day for 265 days resulted in significant increases in total liver fat content (34% more than controls) [51]. Body weights were lower, white blood cell counts higher, and pituitary ACTH greater in exposed than in control rats. No effects on the reproduction or mortality rates were observed. This long-term inhalation study is important in that 1.94 ppm is the lowest tetrachloroethane exposure concentration at which liver effects have been found in animals.

Carcinogenicity, Mutagenicity, and Teratogenicity

No data were found in the available literature which address the question of whether tetrachloroethane is carcinogenic or teratogenic. The mutagenic potential of tetrachloroethane was tested in two different bacterial assay systems by Brem et al [56]. Tetrachloroethane was more active than the controls (water, chloramphenicol) in both assays and intermediate in effect among the other haloalkanes tested. While the observations of small increases of point mutation frequency in bacteria are cause for concern, they are insufficient to establish the existence of any significant risk of genetic hazards to the human population exposed to tetrachloroethane.

Summary Tables of Exposure and Effect

Summaries of the human and animal data correlating tetrachloroethane exposure and effect are given in Tables III-4 through III-6.

TABLE III-4

SUMMARY OF EFFECTS OF OCCUPATIONAL EXPOSURE TO TETRACHLOROETHANE

Route of Exposure	Subjects	Exposure Concentration and Duration	Effects	Reference
Respiratory	18 men	75 - 224 ppm	Lymphocytosis, erythropenia, reduced whole blood specific gravity	31
"	34 - 75 men	15 - 36.4 ppm	Gastrointestinal disorders, enlarged liver, urobilinogenuria, increased serum bilirubin	28
"	75	0.37*- 1.33* ppm 7.7 yr, av time worked	No cardiovascular effects	32
Respiratory and dermal	380	9* - 98* ppm	Gastrointestinal and neurologic disorders (mixed exposure to acetone in some cases); dose-dependent occurrence of hand tremors	29

*Average values

TABLE III-5

SUMMARY OF EFFECTS OF INHALED TETRACHLOROETHANE
ON TWO MEN EXPOSED EXPERIMENTALLY

Exposure Concentration	Duration	Effects
335 ppm	10 min	Dizziness at 3 min; fatigue, mucosal irritation at 10 min; odor not discernable after 3 min
262 ppm	"	Dizziness, mucosal irritation at 5 min; odor not discernable after 5 min
146 ppm	30 min	Dizziness at 10 min, mucosal irritation at 12 min, fatigue at 20 min
131 ppm	10 min	Dizziness at 10 minutes (exposure terminated)
116 ppm	20 min	Dizziness, mild vomiting; odor not discernable after 10 min
2.9 - 13 ppm	-	Detection of odor, no complaints

From Lehmann and Schmidt-Kehl [26]

TABLE III-6

SUMMARY OF EFFECTS OF TETRACHLOROETHANE EXPOSURE ON ANIMALS

Route of Exposure	Species	No.	Exposure Concentration and Duration	Effects	Reference
Respiratory	Mouse	-	11,400 ppm 6 hr x 2 d	Deep anesthesia with rapid recovery after 1st exposure, death after 2d; fatty degeneration of liver and kidney	44
"	Rat	6	9,000 ppm 2 hr twice/wk	Unconsciousness within 1-1.5 hr; death of 1 after 2d exposure, 2 after 4th, 3 after 11th; fatty degeneration of liver, decreased RBC and Hgb content	43
"	"	9	7,000 ppm 2 hr	Death of 5 after 1st exposure, 3 after 3rd, 1 after 5th; fatty degeneration of liver	43
"	Mouse	10	6,600 ppm 3 hr	Death of 4 within 1 wk, fatty degeneration of liver, tissue congestion	43
"	"	10	5,900 ppm 3 hr	Death of 3 within 1 wk, fatty degeneration of liver, tissue congestion	43
"	Monkey	1	1,000-4,000 ppm 2 hr/d 6 d/wk 190 total in 9 mo	Weakness after 7th exposure, diarrhea and anorexia after 12th, anesthesia after 15th; fluctuations in RBC, WBC, and Hgb content; marked vacuolation of liver	43
"	Rat	6	1,000 ppm 6 hr	Death of 4 within 24 hr; no histologic changes in remaining 2 after 24 or 120 hr	47

TABLE III-6 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHANE EXPOSURE ON ANIMALS

Route of Exposure	Species	No.	Exposure Concentration and Duration	Effects	Reference
Respiratory	Rat	6	1,000 ppm 4 hr	Death of 3 within 14 d	38
"	Mouse	35 F	800 ppm 3 hr	Increased hepatic and decreased plasma triglycerides	49
"	"	18 F	600 ppm 3 hr	Increased hepatic triglycerides and total lipids, decreased hepatic ATP content	48
"	Rat	6 M	100 ppm 6 hr	Increased SGOT levels 24-96 hr postexposure; no histologic changes	47
"	Rabbit	-	14.6 ppm 3 - 4 hr/d 7 - 11 mo	Suppressed hemagglutinin production and phagocytosis, altered blood chemistry, signs of liver and kidney degeneration	50
"	Rat	6 M	10 ppm 6 hr	Increased SGOT levels 24 hr postexposure; no histologic changes	47
"	"	105 M	1.94 ppm 4 hr/d 110 or 265 d	Increased WBC, pituitary ACTH, total fat content of liver; decreased body weight	
"	Rabbit	-	1.46 ppm 3 - 4 hr/d 7 - 11 mo	Suppressed hemagglutinin production, decreased RBC and Hgb content, fluctuating blood chemistry	50
"	"	-	0.3 ppm 3 - 4 hr/d 7 - 11 mo	None reported	50

TABLE III-6 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHANE EXPOSURE ON ANIMALS

Route of Exposure	Species	No.	Exposure Concentration and Duration	Effects	Reference
Dermal	Rabbit	1	Liquid of unknown dose to shaved abdomen (22 sq cm) 13 hr total	Complete anesthesia after both a 6-hr and an added 7-hr exposure, fatty degeneration of liver and kidneys	36
"	"	1	Liquid of unknown dose to shaved abdomen (22 sq cm) 5 hr total	Obliterated corneal reflex and excitability after the 3-hr exposure, mild paralysis after the added 2-hr exposure, death in 3 d	36
"	"	-	-	LD50 = 6.38 g/kg	38
Oral	Dog	4	0.70 g/kg (in acaia gum)	Minimum lethal dose	37
"	Rat	-	-	LD50 = 0.3 g/kg	38
iv, ip, or sub-cutaneous	Guinea pig	-	0.7 ml total (in paraffin) in 5 doses over 14 d	Weight loss, convulsions, death, histologic changes similar to effects in mice inhalation study	44
"	"	-	0.2 ml	Convulsions and death	44
iv	Rabbit	1	0.2 g	Immediate narcosis with recovery in 15 min, death in 30 hr, enlarged liver with fatty degeneration	44
"	Dog	7	60 mg/kg (in olive oil)	Minimum lethal dose	37
Sub-cutaneous	Rabbit	5	0.5 g/kg	"	43

TABLE III-6 (CONTINUED)

SUMMARY OF EFFECTS OF TETRACHLOROETHANE EXPOSURE ON ANIMALS

Route of Exposure	Species	No.	Exposure Concentration and Duration	Effects	Reference
Subcutaneous	Monkey	1	1 - 5 ml (in olive oil) x 5 in 29 d	Minimum lethal dose	43
ip	Mouse	10	1.6 g/kg (in corn oil) on 3 alterate d	Death of 9, increased urinary protein and glucose in survivor	53
"	"	10	0.8 g/kg (in corn oil) on 3 alternate d	Increased urinary protein in 2	53
"	"	5	800 mg/kg*	Ataxia, prostration, dyspnea; death within 1 d	39
"	"	3	400 mg/kg*	Ataxia; death within 3 d	39
"	"	3	200 mg/kg*	Ataxia; death within 7 d	39
"	"	3	100 mg/kg*	Death of 1 within 2 d	39
"	"	3	48 mg/kg*	Death of 2 within 3-4 d	39
"	"	3	24 mg/kg*	No deaths	39
-	Dog	1	1 ml x 150 in 1 yr	Diarrhea, intestinal hemorrhage, jaundice, marked ascites; after 1 yr, liver hypertrophy but returned to normal after 3 mo	46

*Dissolved in propylene glycol

IV. ENVIRONMENTAL DATA AND ENGINEERING CONTROLS

Sampling and Analytical Methods

Most of the sampling methods for tetrachloroethane are dependent on its effective and reproducible uptake by various collection media. Collected air samples are usually transported to a laboratory, then desorbed or chemically treated, and finally analyzed quantitatively.

Elkins et al [58] used amyl acetate in a sampling train to collect tetrachloroethane from sampled air. Midget impingers containing m-xylene have been used for collection in conjunction with gas chromatographic analysis [59]. Bubbler bottles containing pyridine have been used for collection of tetrachloroethane in conjunction with colorimetric analysis [52]. The use of liquid in impingers and bubblers poses problems in field measurements because breathing-zone samples are difficult to collect and to transport without liquid spillage.

Williams and Umstead [60] reported the use of porous polymer beads as a collection medium. With this method, the same column was used for sample collection and gas chromatographic analysis. The advantage of this method is that it consolidates collection and analysis into one operation. However, only one analysis can be performed on each sample, and the method has not been adapted to field use.

Silica gel has been widely used as a collection medium for organic vapors [61-64]. Silica gel is a polar adsorbent and shows pronounced selectivity in adsorbing polar molecules, particularly water. Hence, during sampling of large volumes, atmospheric moisture may compete for the adsorption sites and displace tetrachloroethane [61,65].

Activated charcoal is another popular solid adsorbent for organic vapors [62], and its use in conjunction with gas chromatography has been well documented [66-68]. Activated charcoal is nonpolar and will generally adsorb organic vapors in preference to water vapor; this results in less interference from atmospheric moisture than is the case with silica gel [65]. Activated charcoal has been specifically shown to be an effective adsorbent for tetrachloroethane [69].

When a solid collection medium is used, it is necessary to desorb the tetrachloroethane from the medium prior to analysis. The choice of desorbing agent depends on its desorption efficiency for tetrachloroethane and, if gas chromatography is the chosen analytic method, on the comparative retention times for the desorber and for tetrachloroethane. Carbon disulfide has been shown to be a highly efficient desorber of numerous organic solvents from activated charcoal [66,70]. In a report [69] on tetrachloroethane sampling and analysis, it was shown that carbon disulfide efficiently desorbed tetrachloroethane from activated charcoal and did not interfere with tetrachloroethane in gas chromatographic analysis. Petroleum-based charcoal was preferred over coconut-based charcoal in this study [69] because tetrachloroethane was more efficiently desorbed from the petroleum-based charcoal. Adsorption and desorption efficiencies may vary with different batches of charcoal. It is, therefore, necessary to determine the desorption efficiency for each batch of charcoal. The recommended air sampling method using activated charcoal tubes and the recommended desorption method using carbon disulfide, as well as an equation for the desorption efficiency calculation, are presented in Appendices I and II.

Other sampling methods have included grab samples taken directly from tetrachloroethane-contaminated atmospheres with a variety of containers ranging from plastic bags to hypodermic syringes [66,71,72]. Although no specific data have been found on collection of tetrachloroethane in plastic bags, several types have been shown to have good retention times for other chlorinated hydrocarbon solvents such as dichloromethane (greater than 98% after 120 hours) [71] and trichloroethylene (90% after 90 hours) [72]. The advantages of using plastic sampling bags are that they are resistant to chemicals and that it is possible to collect unknown gaseous contaminant mixtures for subsequent quantitative and qualitative analysis. Also, the samples can be injected directly from the bag into a gas chromatograph. A disadvantage is that the shorter sampling duration and smaller sample volume available with this method would not accurately represent the atmosphere in a plant location during a work shift.

The numerous analytical methods for quantifying tetrachloroethane in air samples can be divided into two broad categories: methods based on chemical reactions and methods based on physical and chemical properties and analytical instrumentation.

The three most extensively used chemical methods are dechlorination with strong alkali followed by gravimetric or volumetric chloride determinations; colorimetric measurement of the reaction products of tetrachloroethane and pyridine heated in alkali solution (Fujiwara reaction [52]); and direct-reading with colorimetric indicators.

The dechlorination method requires collection of the tetrachloroethane-contaminated air by a suitable collection medium such as silica gel [30] followed by alkaline hydrolysis in isopropyl alcohol. The

liberated chloride may be determined gravimetrically when silver nitrate is added to the solution (which has been slightly acidified with nitric acid) to produce silver chloride, a curdy, white precipitate. The precipitate is washed, carefully dried, and weighed [73]. The chloride ion may be determined volumetrically by the Volhard method [27], by the Mohr method [35], or with adsorption indicators [74,75]. Each of these involves the direct or indirect titration of the liberated chloride with silver nitrate. The chloride ion has also been measured by potentiometric methods [76]. Two disadvantages of the alkaline hydrolysis method are that the dechlorination step is nonquantitative, ie, the amount of chloride liberated depends on the reaction duration, and that the method is not specific for tetrachloroethane in the presence of other halogenated compounds.

In the colorimetric analytical method based on the Fujiwara reaction, a stream of air containing tetrachloroethane is passed through a wash bottle containing pyridine [52]. Then methylethyl ketone (MEK) and NaOH are added to an aliquot of the sample solution in pyridine, and this mixture, together with an aliquot of the MEK and NaOH solution (blank), is heated in a boiling water bath and cooled for a specific time period. The sample and blank absorption coefficients are then determined with a suitable spectrophotometer. This method requires less time than the dechlorination method, but the problem of specificity with mixtures of chlorinated hydrocarbons remains.

The third chemical method utilizes direct-reading detector tubes [77]. Glass tubes are packed with solid chemicals that change color when a measured and controlled flow of air containing tetrachloroethane is passed

through the packed material. The test vapor may be drawn directly through the tube and compared with a calibration chart, or it may be drawn into a pyrolyzer and then through the packed tube [77]. In either case, the method is not specific for tetrachloroethane since the stain to be read is produced by the liberated halogen ion, and any halogen or halogenated compound will interfere. Although widely used for other chlorinated hydrocarbons, detector tubes have not been recommended for measuring tetrachloroethane because of their lack of sensitivity in the critical, low-ppm range necessary for tetrachloroethane (5-ppm TLV).

The analytical methods based on the physical and chemical properties of tetrachloroethane include those using infrared spectrometry [78], photodetector analyzers (halide meters) [79], and gas chromatography [66].

An infrared spectrophotometer in conjunction with a suitable recorder can be used to indicate concentrations instantaneously. With this method, concentrations are measured directly, and it is not necessary to collect individual samples and transport them to a laboratory for analysis. Infrared has been used for continuous monitoring of industrial operations for chlorinated hydrocarbons [78]; however, complicated instrumentation is necessary to draw the samples and continuously record the data. It is also important that the atmosphere of relevant working stations is sampled and that such samples correspond to the breathing zones of workers at their assigned stations [78]. Infrared analysis is subject to interferences from other air contaminants. Substantial knowledge of infrared spectrophotometry is needed if one is to easily detect and resolve such interferences with assurance.

Halide meters detect the increased brightness of an a-c arc (metal electrode) when it is enveloped by an atmosphere contaminated with halogenated hydrocarbons [79]. These instruments are sensitive to all halogens and halogenated compounds, and consequently they are not specific for tetrachloroethane. Halide meters seem suitable for continuous monitoring if tetrachloroethane is known to be the only halogenated air contaminant.

Gas chromatography provides a specific quantitative analytical method for tetrachloroethane when appropriate column conditions are provided [80]. The sensitivity of the flame ionization detector is more than adequate to allow quantitation of tetrachloroethane in the low-ppm range. However, the possibility exists that several compounds found in an occupational environment may have similar column retention times. Resolution of interferences can be overcome by changing the stationary phase of the gas chromatography column or by changing the column temperature or other chromatographic conditions. Two separatory columns with different stationary phases can be used for more positive identification of compounds.

Also, mass spectrometry can be used with gas chromatography to identify more positively the substances present. Cooper et al [81] reported the use of a capillary charcoal tube to trap and transfer the material associated with a gas chromatogram peak to a mass spectrometer for qualitative identification. There are gas chromatography-mass spectrometry instruments available that do not require the intermediate transfer step [82].

Of the analytical methods reviewed, gas chromatography is recommended as the method of analysis for samples of tetrachloroethane collected from the workplace environment in tubes containing activated charcoal. Carbon disulfide is the preferred desorbent. The recommended sampling method has the advantage of using a small, portable collecting device which requires no liquid; this is convenient for sampling employees' breathing zones. The gas chromatograph possesses adequate sensitivity, and it is capable of separating and quantitating organic compounds in a mixture. Gas chromatographic procedures which are specific for tetrachloroethane are available [69]. The recommended sampling and analytical methods are described in detail in Appendices I and II.

Environmental Levels

In 1957, airborne concentrations of tetrachloroethane ranging from 1.5 to 247 ppm were reported by Jeney et al [28] from 170 area samples taken in a penicillin-manufacturing plant in Czechoslovakia. Air samples were collected in bubblers containing amyl alcohol and analyzed according to the method described by Lehmann and Hasegawa [34]. This involved the addition of sodium to the sample solution, refluxing for 8 hours, and titration of the liberated chloride with silver nitrate. Tetrachloroethane was used to extract the penicillin from the fermentation liquid. Because of the nature of the process, "separators," which were used to break the emulsions, had to be routinely dismantled and cleaned by rinsing the parts. The extraction and especially the cleaning processes introduced airborne tetrachloroethane into the 900-cu m workroom. During the course of the 3-year study, the ventilation system was improved once at the original plant,

and then the whole extraction process was moved to another building, where initially the ventilation was worse but was greatly improved later. Airborne levels of tetrachloroethane during the three different ventilation conditions are shown in Table III-1. The greatest reduction in airborne tetrachloroethane levels occurred in the sludging process (part of the cleaning process) where maximum concentrations were reduced from 247 to 36.4 ppm. Jeney et al [28] stated that, at the new plant, airborne tetrachloroethane concentrations during normal operations were about 15 ppm and increased to no more than 36.4 ppm during the cleaning operations. The extent of dermal contact with tetrachloroethane by the workers, if any, was not mentioned.

In 1963, Lobo-Mendonca [29] reported concentrations of tetrachloroethane in air ranging from 9 to 98 ppm in India's bangle-manufacturing industry. Tetrachloroethane, an efficient solvent for cellulose acetate, was used during several manufacturing stages, including the initial cylinder making (precut bangles) and the polishing of the individual bracelets. Breathing-zone air samples were taken at one to three worksites at seven different factories. Tetrachloroethane was collected on silica gel, extracted with alcohol, hydrolyzed with potassium hydroxide, and the chloride was titrated against silver nitrate [30]. The reported concentrations of tetrachloroethane in the air at the different worksites within the seven factories are given in Table IV-1. In a written communication (LR Lobo-Mendonca, September 1976), it was stated that these were averages, but the number of determinations made for each value was not reported.

TABLE IV-1

TETRACHLOROETHANE IN AIR CONCENTRATIONS AT SEVEN BANGLE FACTORIES

Factory Number	Sampling Site	Concentration (ppm)	Remarks
1	Near cylinder making; at breathing zone of 2 workers	39.3	Cylinder makers on platform between door and windows
	"	74.1	Poorly ventilated platform between 2 windows
2	Packing, near cylinder making	9.1	Well ventilated room with several windows and doors
	Cylinder making	17.4	"
3	Heating; between workers	10.59	25 ft from polishing; shed with 3 walls, 1 side open
	Cylinder cutting	14.00	15 ft from polishing; shed with walls on 2 sides
4	Cylinder making	98.00	Platform in small room with 1 window; no ventilation
	"	65.00	Center of large room
5	"	29.00	Open shed
6	"	60.56	Corner of room
	Polishing; at breathing zone	40.58	Workers squatting on floor near doors
7	Polishing	61.48	Workers beside table
	Near polishing; at floor level	50.00	3 ft from polishing table
	Near polishing; at breathing zone	20.49	Amylacetate area 10 ft from polishing table

Derived from Lobo-Mendonca [29]

Horiguchi et al [31] measured concentrations of tetrachloroethane in the air at three Japanese artificial pearl factories where individual beads were strung on racks and immersed in tanks of tetrachloroethane to produce a clear surface membrane. Two surveys were conducted 16 months apart in 1960 and 1961. The first survey revealed concentrations of tetrachloroethane in air ranging from 70 to 224 ppm in the three factories. By the time of the second survey, two of the factories had replaced tetrachloroethane in their processes and had no detectable airborne tetrachloroethane. The third factory had instituted local ventilation, and the second survey showed that the tetrachloroethane had been reduced to 20 ppm there. No details about the type of local ventilation were given. Horiguchi et al [31] also did not describe their sampling schedule, sampling locations, or analytical methods. The reported values of the two surveys are given in Table IV-2.

In 1968, Gobbato and Bobbio [32] reported the results of a survey of tetrachloroethane concentrations present during normal operations, as well as during maintenance periods, in a plant manufacturing tetrachloroethane in Italy. The process involved the chlorination of acetylene. The tetrachloroethane produced was converted to trichloroethylene and tetrachloroethylene. The proximity of the areas where these two operations were performed was not clearly stated in the report, but they were designated as being at separate locations. Samples of airborne tetrachloroethane were taken at five different manufacturing plant locations. Except for the laboratory and staff room, the sampling sites were outdoors. Bubblers containing absolute ethanol were used to collect tetrachloroethane, and a modification of the Fujiwara reaction [33] was

TABLE IV-2

TETRACHLOROETHANE IN AIR CONCENTRATIONS AT THREE ARTIFICIAL PEARL FACTORIES*

Factory	Tetrachloroethane (ppm)	
	July 1960	Nov 1961
A	139.8 86.8	0
B	111.9 88.5 74.6	19.8
C	223.7 113.7 70.0	0 0

*Work areas not specified

Derived from Horiguchi et al [31]

used for analysis. The disadvantage of this method was that it is not specific for tetrachloroethane, and interference by other chlorinated compounds was possible. All values were therefore based on the assumption that tetrachloroethane was the predominant chlorinated compound being sampled. Six determinations were made at each of the five worksites. Table IV-3 shows the mean as well as the maximum and minimum values found at each location. The location with the highest mean concentration of tetrachloroethane in air, 1.33 ppm, was the product-recovery zone. Higher concentrations were reported during maintenance periods: 5-15 ppm in the staff room and the reaction zone, and 40 ppm in the actual zone of maintenance work. These unspecified maintenance activities usually lasted

TABLE IV-3

TETRACHLOROETHANE IN AIR CONCENTRATIONS
AT A TETRACHLOROETHANE PRODUCTION PLANT

	Tetrachloroethane (ppm)		
Work Area	Mean	Maximum	Minimum
Staff room	0.37	0.51	0.00
Tower reaction zone	1.12	3.10	0.46
Product recovery zone	1.33	3.20	0.31
Water tank ejector zone	0.94	1.65	0.50
Laboratory	0.79	2.00	0.30

Derived from Gobbato and Bobbio [32]

less than 30 minutes. At tank and tank-truck loading openings, tetrachloroethane concentrations between 10 and 20 ppm were measured; however, these operations were of very short duration.

Engineering Controls

Engineering design for working safely with tetrachloroethane should be such as to reduce the concentration of airborne tetrachloroethane. Closed systems under negative pressure, properly operated and maintained, should be used in all cases where practicable. Frequent tests must be conducted for leaks in closed systems. Where closed systems are not feasible, well-designed local exhaust ventilation systems must be provided.

Guidance for design can be found in Industrial Ventilation--A Manual of Recommended Practice [83], or more recent revisions, and in Fundamentals Governing the Design and Operation of Local Exhaust Systems, ANSI Z9.2-1971 [84]. In operations where tetrachloroethane is transferred, charged, or discharged into otherwise normally closed systems, continuous local exhaust should be provided at the transfer point. Sufficient ventilation with clean air should be maintained in the area to prevent recirculation of contaminated air into the workplace.

Respiratory protective equipment is not an acceptable substitute for proper engineering controls, but it should be available in emergencies and for nonroutine maintenance and repair work.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

Regulation of the industrial use of tetrachloroethane occurred during World War I when the toxicity of this solvent became apparent in the aircraft industries of Europe and the United States. In November 1915 [85], toxic jaundice, caused by tetrachloroethane in a factory or workshop, was added to the list of diseases in section 73 of England's Factory and Workshop Act of 1901. This Act stipulated that such cases be reported by the employer or medical practitioner to the Chief Inspector of Factories and Workshops. Before the end of World War I, Germany, France, Holland, and England banned the use of tetrachloroethane in their airplane industries [5] because of its high toxicity.

In the United States, Bowditch et al [86] recommended a "maximum concentration" of 10 ppm for tetrachloroethane in their 1940 "Code for Safe Concentrations of Certain Common Toxic Substances Used in Industry." They stated that this exposure limit did not guarantee prevention of ill health, nor did it mean that medical controls could be neglected. They did not report the bases for the recommended levels.

A list of maximum allowable concentrations (MAC's) of industrial atmospheric contaminants compiled by Cook [87] in 1945 included the tetrachloroethane standards set by the federal government and five states. A 10-ppm MAC was recommended by the US Public Health Service and by the following state agencies: California Industrial Accident Commission, New York State Department of Labor, Oregon State Board of Health, and Utah

Department of Health. The Massachusetts Department of Labor and Industries recommended a 5-ppm MAC. These concentrations were specified generally as allowable for prolonged exposures, presuming a 40-hour workweek [87].

Cook [87] also stated that 10 ppm was a tentatively acceptable concentration for tetrachloroethane. In deriving this level he considered the severe poisonings in industry, many of them fatal, together with animal experiments that indicated tetrachloroethane was more potent than carbon tetrachloride in inducing anesthesia. Cook [87] cited specific human case studies reported by Hamilton [10] and Coyer [57]. In addition, he urged that workers who were exposed under industrial conditions to tetrachloroethane at known concentrations be observed to verify this tentative MAC.

The American Conference of Governmental Industrial Hygienists (ACGIH) adopted a list entitled "Maximum Allowable Concentrations of Air Contaminants for 1946" which was prepared by its Subcommittee on Threshold Limits [88] and included the 10-ppm MAC for tetrachloroethane recommended by Cook [87].

The ACGIH [89] recommended an MAC of 5 ppm for tetrachloroethane in 1947; no justification for the reduction was reported at that time. In 1948, the designation of the limit was changed from "MAC" to "Threshold Limit Value (TLV)," but the level remained at 5 ppm. In 1953, the ACGIH [90] defined threshold limit values (TLV's) as the "maximum average atmospheric concentration of contaminants to which workers may be exposed for an 8-hour working day without injury to health." In 1958, the preface of the TLV list [91] included the statement that TLV's "represent conditions under which it is believed that nearly all workers may be

repeatedly exposed, day after day, without adverse effect." In 1962, the ACGIH [92] added the "Skin" notation to the tetrachloroethane TLV and thus indicated that there was a potential for exposure to airborne and liquid tetrachloroethane.

The 1971 ACGIH Documentation of TLV's [93] gave the basis for the recommended TLV of 5 ppm for tetrachloroethane. It contained references to Von Oettingen [94], Coyer [57], and Wilson and Brumley [95] who had detailed fatal poisonings attributed to tetrachloroethane, as well as the neurologic and gastrointestinal symptoms and the liver injuries associated with these poisonings. A report by Lobo-Mendonca [29] describing the general, neurologic, and gastrointestinal effects noted from occupational exposure to airborne tetrachloroethane at concentrations between 9 and 98 ppm, mostly between 20 and 65 ppm, was cited. There was also a reference to Elkins [62] who cited unpublished information from an unavailable personal communication indicating that adverse human effects had occurred at levels below 10 ppm. The 5-ppm TLV was recommended by the ACGIH [93] with the statement that it would probably prevent serious health effects and minimize, if not totally eliminate, the neurologic and gastrointestinal symptoms.

In addition to the existing TLV-TWA, in 1976, the ACGIH [96] proposed a Threshold Limit Value-Short Term Exposure Level (TLV-STEL) for tetrachloroethane of 10 ppm. They defined this as the "maximal concentration to which workers can be exposed for a period up to 15 minutes continuously without suffering from 1) intolerable irritation, 2) chronic or irreversible tissue change, or 3) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work

efficiency, provided that no more than four excursions per day are permitted, with at least 60 minutes between exposure periods, and provided that the daily TLV-TWA also is not exceeded."

According to a 1968 joint report of the International Labour Office and the World Health Organization [97], tetrachloroethane standards, each as an "MAC," for six countries were as follows: Finland, 5 ppm; Germany (Federal Republic), 1 ppm; Japan, 5 ppm; Rumania, 1.5 ppm; USSR, 0.7 ppm; and Yugoslavia, 1 ppm. The USSR standard is an absolute limit never to be exceeded. According to the publication, it was set at a concentration expected to produce neither disease nor other detectable deviations from normal in any exposed person.

The current federal standard for worker exposure to tetrachloroethane is 5 ppm (35 mg/cu m) as a TWA concentration limit with a "Skin" notation (29 CFR 1910.1000). This was based on the 1968 ACGIH recommendation for a TLV, which was documented in 1971 [93].

Basis for the Recommended Standard

Effects on the nervous system, the gastrointestinal tract, and the liver from occupational exposures to tetrachloroethane have been documented in numerous reports [5,7,8,10-13,28,29,98] since the beginning of World War I. The reduction in industrial use of tetrachloroethane and in poisonings resulting from it since 1945 may account for the paucity of recent industrial exposure data that can be used in arriving at an environmental limit. Therefore, much of the information correlating exposure and effect has been obtained through experiments on humans [26] and animals [26,40,47-51].

The early case studies did show that two different groups of symptoms, sometimes overlapping in part, were produced by chronic tetrachloroethane exposure. The more common clinical picture was characterized by gastrointestinal and hepatic symptoms [5,7,8,10,12,28,98]. These symptoms included anorexia, exhaustion, nausea, and vomiting followed by jaundice and sometimes liver enlargement. Jaundice increased with the progression of the disease and was often accompanied by delirium, convulsions, coma, and finally death. Autopsies generally revealed fatty degeneration and cirrhosis of the liver.

Other cases [11,13] were characterized by signs and symptoms of the nervous system. Usually the first signs and symptoms were numbness of the toes and fingers, paresthesia, hand tremors, and plantar pain. Although fatalities were rare, the advanced effects were incapacitating and persisted for long periods, even in the absence of continued exposure.

Some early reports suggested that tetrachloroethane affected the kidneys [8,12,98], the cardiovascular system [8,12,98], and the lungs [98]. However, when found, these less common effects always occurred in conjunction with severe hepatic injury.

In one of the few studies providing occupational exposure data, Lobo-Mendonca [29] reported hand tremors in a high percentage (14%) of a transient working population at a factory where average airborne tetrachloroethane concentrations of 9 and 17 ppm were measured. The author stated that only those workers present at the time of the survey, and not those who had left work because of illness, were included. Because this factory had a very limited sampling schedule and several processes involved dermal contact, the reported airborne concentrations of tetrachloroethane

are viewed only as approximations of the actual worker exposure.

Occupational exposure to airborne tetrachloroethane at concentrations ranging from 1.5 to 247 ppm was shown by Jeney et al [28] to produce signs of liver damage, such as enlarged liver, urobilinogenuria, and increased serum bilirubin, in factory workers. These signs were still reported after improved ventilation in the work area had decreased the concentration of tetrachloroethane in the air to 15 ppm during normal operations and to no more than 36.4 ppm during the cleaning process. Screening examinations of workers in alternate months helped to prevent serious liver disease at this factory; those workers showing signs and symptoms of incipient liver dysfunction were transferred to other work areas.

Until recently, most of the studies of the hepatotoxicity of tetrachloroethane in animals consisted of short-term exposures at high concentrations. These experiments showed fatty degeneration of the liver in rabbits, guinea pigs, rats, and mice [43-45]. Since 1969, five reports [47-51] of effects in animals exposed to tetrachloroethane at lower concentrations have confirmed a direct dose-effect relationship. Increased hepatic triglycerides with decreased serum triglycerides in mice exposed at 800 ppm for 6 hours were reported by Tomokuni [49], who also observed increased hepatic triglycerides in mice exposed at 600 ppm for 6 hours [48]. The activity of SGOT, a cellular enzyme released when cells are damaged, is measured as an index of liver cell destruction. Deguchi [47] reported increased SGOT activity in rats 24 hours after a 6-hour exposure at 100 ppm; in rats exposed for 6 hours at 10 ppm, increased SGOT activity, which peaked 72 hours postexposure, was noted. Navrotskiy et al [50] reported morphologic changes in the liver and kidneys of rabbits exposed

repeatedly to tetrachloroethane vapor at 14.6 ppm. Several changes associated with suppression of the immunoresponse system of the rabbits were also noted at this concentration. Evidently this important homeostatic process was altered at this exposure concentration. Increased total fat content of the liver was reported by Schmidt et al [51] after 265 days in rats chronically exposed to tetrachloroethane at 1.94 ppm for 4 hours/day. They also reported decreased body weights, increased white blood cell counts, and increased pituitary ACTH in rats at different times during the experiment. Navrotskiy et al [50] reported minimal effects in blood studies and no morphologic changes in rabbits repeatedly exposed to tetrachloroethane at 1.46 ppm; no effects were seen at 0.3 ppm.

A comparison of available data suggests that hepatotoxic effects from inhalation exposure to other chlorinated hydrocarbons are produced at similar concentrations in animals and in humans. Carbon tetrachloride has been shown to cause adverse liver effects, such as increased liver weights in guinea pigs exposed at 5 ppm for 7 hours/day, 5 days/week, for 184 days [99] and enlarged livers with liver fatty infiltration in monkeys, rats, guinea pigs, and rabbits exposed continuously at 10 ppm for 90 days [100]. Available occupational data show that carbon tetrachloride at concentrations in air of 6.3-9.5 ppm caused liver effects, including increased serum iron and serum glutamic dehydrogenase, in workers exposed 2 or 3 times/year, 14 workdays each time, for 5 years [101]. At 100-200 ppm, tetrachloroethylene has been shown to cause increased liver weights and fatty liver degeneration in guinea pigs exposed for 7 hours/day, 5 days/week, for 132 exposures [102]. Workers exposed to tetrachloroethylene

at concentrations of 232-385 ppm for 8 hours, twice a week, for at least 2 years had increased BSP retention, liver cirrhosis, and urobilinogen in the urine [103]. One worker exposed at 50-250 ppm for 4 months died; liver cell necrosis was observed during autopsy [104]. No such information on other chlorinated hydrocarbon solvents was found, so similar comparisons cannot be made for them. However, the data indicate that hepatic effects from exposure to carbon tetrachloride and tetrachloroethylene were produced at similar air concentrations in humans and in animals.

The major concern in occupational exposure to tetrachloroethane is the hepatotoxic effect. In a factory where the air concentrations of tetrachloroethane had been reduced to 15-35 ppm, adverse liver effects were still seen in the workers [28]. No other data were found that would indicate exposure levels at which tetrachloroethane initiates liver damage in humans. Tetrachloroethane at an exposure concentration of 15 ppm administered repeatedly by inhalation to rabbits caused liver morphologic changes [50]. This concentration is within the range that caused liver effects in humans [28]. In view of the comparison showing similar liver effect levels in humans and animals from exposure to carbon tetrachloride, tetrachlorethylene, and tetrachloroethane, the animal data on tetrachloroethane cannot be ignored in recommending an environmental limit that will protect the health and safety of exposed workers. Consistent with these observations, the data showing biochemical indications of liver effects in rats at tetrachloroethane concentrations as low as 2 ppm [51] suggest that the current TLV of 5 ppm is too high to protect employees chronically exposed to tetrachloroethane for up to 10 hours/day, 40 hours/week, over a working lifetime. NIOSH therefore recommends that the

current federal standard of 5 ppm for tetrachloroethane be reduced to a TWA exposure limit not to exceed 1 ppm.

In addition, because tetrachloroethane is structurally similar to other hepatotoxic chlorinated hydrocarbons, some of which NIOSH has recognized as potential human carcinogens, the possibility for tetrachloroethane to have similar carcinogenic potential can not be disregarded. This lends further support for recommending a low exposure limit. Tetrachloroethane is currently being tested by the National Cancer Institute in its Carcinogenesis Bioassay Program.

It has been shown that hepatic and neurologic effects are of primary concern in occupational exposure to tetrachloroethane. Thus, a medical surveillance program should include preplacement and periodic medical examinations that give attention to liver function tests, such as serum transaminase determinations, and screening tests for neurologic function. The preplacment examination may identify workers that are susceptible to tetrachloroethane exposure at concentrations below the recommended environmental limit and will provide baseline data that can be used to evaluate the health of workers after varying lengths of exposure. The annual examination will provide the opportunity for early detection of effects on the health of the workers, as well as provide information for evaluating the effectiveness of the recommended environmental limit.

For the medical program to be effective, it is important that workers recognize the signs and symptoms of overexposure and the hazards of working with tetrachloroethane. A physician should be consulted immediately if specific symptoms attributable to exposure occur. Thus, NIOSH recommends that employees be informed of health hazards and that warning signs be

posted in appropriate locations in plants where tetrachloroethane is manufactured, used, or stored. Further information should be transmitted through a continuing education program instituted by the employer.

Absorption of liquid tetrachloroethane through the skin has been shown in rabbits [36], and one human fatality was attributed primarily to skin absorption [57]. Because of this, care must be exercised to ensure adequate protection against contact with tetrachloroethane. Personal protective clothing and respiratory protective equipment should be available and worn where indicated. Work practices that prevent skin and eye contact must be followed. Showers and eye wash fountains must be available for immediate use if accidental contact occurs.

Engineering controls must be used whenever feasible to control concentrations of airborne tetrachloroethane within the recommended limit. When tetrachloroethane is present, a closed system of control should be used. During the time required to install adequate controls and equipment, to make process changes, to perform routine maintenance operations, or to make repairs, overexposure to tetrachloroethane can be prevented by the use of respirators and protective clothing.

Medical and other pertinent records, which are important in assessing an employee's exposure, must be maintained for the duration of employment plus 30 years. This will allow enough time for future detection of chronic sequelae which may be related to the employee's known occupational exposure.

It is recommended that airborne tetrachloroethane be collected with charcoal tubes, desorbed with carbon disulfide, and analyzed by gas chromatography [69]. The basis for this recommendation is discussed in

Chapter IV and in Appendices I and II. These methods have been chosen because of their specificity, the availability of the necessary components, and their relative convenience.

Concern for worker health requires that protective measures be instituted below the enforceable environmental limit to ensure that exposures stay below that limit. An action level is set as a TWA concentration of one-half the environmental limit. It has been chosen on the basis of professional judgment rather than on the basis of any quantitative data that delineate nonhazardous areas from areas in which hazards may exist. However, in the case of tetrachloroethane it is also recognized that employees work with the liquid form of the substance in situations where there may be skin contact with it, resulting in dermal or systemic effects. Consequently, appropriate work practices, training, and other protective measures should be required regardless of concentrations of tetrachloroethane in air. Therefore, occupational exposure to tetrachloroethane has been defined as work in an area where tetrachloroethane is stored, produced, or otherwise used. Under these conditions, all provisions of this recommended standard except environmental monitoring and associated recordkeeping should be complied with; in work areas where the action level is exceeded, this latter requirement (Section 8) should also be complied with.

VI. WORK PRACTICES

Strict adherence to detailed work practices is mandatory if unhealthful occupational exposures to tetrachloroethane are to be prevented. The characteristics of tetrachloroethane which determine the nature and extent of the prescribed work practices are: (a) its rapid absorption following respiratory and dermal exposures; (b) its anesthetic properties and the associated acute effects; (c) its ability at low concentrations to cause severe chronic effects; and (d) its odor properties which are not sufficient to provide adequate exposure warning. The work practices specified in this document are derived from the tetrachloroethane manufacturer's literature [6 (pp 9-11)], the Manufacturing Chemists' Association's Chemical Safety Data Sheet SD-34 [2], plant visit observations [6], and, where pertinent, from established work practices for other chlorinated hydrocarbon solvents.

Tetrachloroethane is manufactured by the chlorination of acetylene [6 (p 4)]; in the United States, tetrachloroethane is used mainly as an intermediate in the manufacture of trichloroethylene and tetrachloroethylene [6 (p 4)]. Information is available on the safe handling of chlorine, acetylene, trichloroethylene, and tetrachloroethylene in their respective chemical safety data sheets issued by the Manufacturing Chemists' Association [105-108].

Storage, Handling, and Use

Tetrachloroethane should be stored in cool, dry places in tightly closed containers made of galvanized iron, black iron, or steel. Dehydrochlorination of tetrachloroethane, with the formation of trichloroethylene and traces of phosgene [3], occurs slowly in the presence of air. Although nonflammable and nonexplosive, tetrachloroethane may decompose pyrolytically to toxic and corrosive substances such as hydrogen chloride and chlorine [3]. Proximity to open flames and hot surfaces therefore should be avoided in the storage, handling, and use of this substance. Contact of tetrachloroethane with sodium, potassium, and other chemically active metals such as hot iron, aluminum, and zinc also should be avoided [1,3]. The vapor density of tetrachloroethane is 5.79 times greater than that of air. Tetrachloroethane, therefore, should not be stored in pits, depressions, basements, or unventilated areas. Because of its toxicity, processes in which large quantities of tetrachloroethane are used should be carried out in closed systems. Well designed hoods and ventilation systems can be used to maintain exposures at or below the concentration limit specified in this standard. Further measures should include the use of personal protective equipment and clothing.

Equipment Maintenance

All equipment used for handling tetrachloroethane must be emptied and purged prior to disassembly or entry. Pipelines should be disconnected and capped. Under conditions necessitating tank entry or work with tetrachloroethane-contaminated equipment, maintenance personnel must use either an impervious protective suit and a self-contained, pressure-demand

mode breathing apparatus or a combination supplied-air suit with an auxiliary self-contained air supply. Safety precautions for emergency rescue require that all maintenance personnel be informed of the toxic properties of tetrachloroethane and of the need to wear personal protective equipment [2]. Anyone entering an empty tank should be observed constantly by a properly equipped standby worker familiar with emergency procedures, in case rescue work is necessary.

Emergencies

In areas where tetrachloroethane is handled, safety showers and eyewash fountains are necessary to minimize the effects of accidental skin and eye exposure.

Spills of tetrachloroethane must be anticipated. Storage tanks and drum storage areas should be diked to contain the contents. In addition, it is advisable to have facilities for pumping diked spills to other tanks, as well as, for transferring the contents of leaking tanks to other suitable containers. Normal work should be discontinued in spill areas until the environmental concentration of tetrachloroethane has been reduced to within the limit prescribed by this standard. A warning system, including appropriate postings, should be instituted to keep unauthorized personnel out of such areas until the hazard no longer exists. Disposal of tetrachloroethane or tetrachloroethane-contaminated materials should be carried out in compliance with local, state, and federal regulations.

Skin and Eye Protection

Tetrachloroethane is readily absorbed through the skin [36,57] and thus can cause systemic poisoning by this route. For this reason, gloves and other protective clothing impervious to tetrachloroethane should be worn by workers who handle the liquid. There are commercially available gloves coated with polyvinyl alcohol that are very resistent to chlorinated solvents [109]. This type is recommended for duties involving the handling of liquid tetrachloroethane. However, polyvinyl alcohol is water soluble, and this type of glove is therefore impractical for general work activities.

The eyes of workers should be protected against possible contact with tetrachloroethane from either liquid splash or high vapor concentrations. Contact can cause lacrimation, burning, and other symptoms of inflammation; serious eye damage may result if immediate care is neglected. Protection should be provided with chemical safety goggles and face shields, which are especially appropriate when liquid tetrachloroethane is handled. Because of the added potential for eye irritation and damage, it is advisable that contact lenses not be worn by those working with tetrachloroethane [110].

Sanitation

Good sanitation and personal hygiene practices should minimize the risk of exposure to tetrachloroethane, especially by ingestion. As little as 3 ml of tetrachloroethane taken orally have been shown to cause loss of consciousness in humans [20,21]. Because of this, food and beverage consumption should not be allowed in any tetrachloroethane work or storage area. An eating area that is clean and removed from the general work

location should be designated. It is also recommended that smoking be prohibited in areas where liquid tetrachloroethane is handled. Before drinking, eating, or smoking in the properly designated areas, employees should thoroughly wash their hands.

Respiratory Protection

Adequate respiratory protection against tetrachloroethane under the various conditions which may be encountered in individual operations can be provided by many types of approved respirators. Each has particular applications and limitations from the standpoint of protection, as well as advantages and disadvantages from the standpoint of operational procedures and maintenance. Detailed information on the selection and use of respirators can be obtained from the Respiratory Protective Devices Manual [111] published by the AIHA and the ACGIH in 1963. The American National Standards Practices for Respiratory Protection, ANSI Z88.2-1969 [112], also classifies, describes, and states the limitations of respirators.

There are three categories of respirators: atmosphere-supplying, air-purifying, and those that are both atmosphere-supplying and air-purifying.

One factor affecting 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 negative pressure. To provide uniform regulations that take into account the variations in the sizes and shapes of American workers' faces, NIOSH recommends that respirators with half-mask or quarter-mask facepieces, operated with negative pressure, be used only for protection at

levels below 10 times the TWA. On the same basis, NIOSH recommends that the full facepiece, operated under negative pressure, be used at up to 50 times the TWA limit.

NIOSH periodically issues lists of approved or certified respiratory protective devices. All devices approved by the Mining Enforcement and Safety Administration are listed in Information Circular 8559 and its supplements. All types of devices certified by the NIOSH Testing and Certification Laboratory are listed in a separate publication available from the Testing and Certification Laboratory, NIOSH, Morgantown, West Virginia 26505.

VII. RESEARCH NEEDS

Epidemiologic studies of worker populations exposed to tetrachloroethane at or below the recommended environmental limit are needed. The gastrointestinal, hepatic, and neurologic effects that have already been documented in the work environment should be investigated in such studies, since the insufficiency of the available environmental exposure data have made it difficult to correlate tetrachloroethane exposure and effects. The only reports found of effects from long-term exposure to tetrachloroethane on organs other than the liver were those in which such effects were secondarily associated with severe hepatic poisoning. The effects of extended exposure on the renal, cardiovascular, pulmonary, and other organ systems, as well as possible carcinogenic effects of tetrachloroethane, also should be considered in epidemiologic studies. Variations in blood cell counts, hemoglobin content, and other blood tests have been described in the human case reports and in animal studies involving tetrachloroethane, but the accumulated data are inadequate and inconclusive. Further research in this area may result in the development of a biologic monitoring system that could be used to indicate worker overexposure to tetrachloroethane before the appearance of clinical signs or symptoms.

Alcohol has been either suggested or demonstrated to be a potentiator of the effects of several chlorinated hydrocarbons, such as carbon tetrachloride, chloroform, and trichloroethylene. Animal studies should be conducted to determine what interaction, if any, exists between alcohol and tetrachloroethane. Furthermore, since tetrachloroethane is used as a

starting material in the manufacture of both trichloroethylene and tetrachloroethylene, the possibility of mixed exposures to these three haloalkanes exists. Research is needed to determine if there are additive, synergistic, or inhibitory effects of tetrachloroethane in combination with these chlorinated hydrocarbons.

A study by Yllner [55] on mice is the only detailed study found on the metabolic pathways for tetrachloroethane. Experiments on other species are needed to further elucidate the distribution, metabolism, and excretion of tetrachloroethane after it is inhaled, ingested, or absorbed through the skin.

Information is needed on the possible carcinogenic or teratogenic effects of tetrachloroethane; the results of the National Cancer Institute's Carcinogenesis Bioassay study will be evaluated as soon as they are made available to NIOSH. The only identified mutagencity study [56] of tetrachloroethane involved two bacterial assay systems; the results were inconclusive. Studies are now being conducted by NIOSH to investigate any mutagenic potential of tetrachloroethane. Experiments involving mammalian species are essential if information on carcinogenicity, mutagenicity, and teratogenicity relevant to human occupational exposures to tetrachloroethane is to be obtained.

VIII. REFERENCES

1. Sax NI: Acetylene tetrachloride, in Dangerous Properties of Industrial Materials, ed 3. New York, Van Nostrand Reinhold Co, 1968, pp 373-74

2. Tetrachloroethane, Chemical Safety Data Sheet SD-34. Washington, DC, Manufacturing Chemists' Association Inc, 1949, 14 pp

3. Hardie DWF: 1,1,2,2-Tetrachloroethane, in Kirk-Othmer Encyclopedia of Chemical Technology, ed 2 rev. New York, Interscience Publishers, 1964, vol 5, pp 159-64

4. Weast RC (ed): Handbook of Chemistry and Physics--A Ready-Reference Book of Chemical and Physical Data, ed 55. Cleveland, CRC Press Inc, 1974, p C-287

5. Zollinger F: [The importance of tetrachloroethane in occupational pathology.] Arch Gewerbepathol Gewerbehyg 2:298-325, 1931 (Ger)

6. Summary plant observation report and evaluation. Menlo Park, Calif, Stanford Research Institute, 1976 (Submitted to NIOSH under Contract No. CDC-99-74-31)

7. Heffter, K: [Industrial poisoning by tetrachloroethane.] Vierteljahresschr Gerichtl Med Oeff Sanitaetswes 48:109-114, 1914 (Ger)

8. Willcox WH, Spilsbury BH, Legge TM: An outbreak of toxic jaundice of a new type amongst aeroplane workers--Its clinical and toxicological aspect. Trans Med Soc London 38:129-56, 1915

9. Browning E: Toxicity and Metabolism of Industrial Solvents. New York, Elsevier Publishing Co, 1965, pp 220-29,263-75

10. Hamilton A: Industrial poisoning in aircraft manufacture. JAMA 69:2037-39, 1917

11. Schultze E: [Encephalo-myelomalacia after an accident of occupational poisoning (tetrachloroethane ?).] Berl Klin Wochenschr 57:941-45, 1920 (Ger)

12. Grimm V, Heffter A, Joachimoglu G: [Industrial intoxication in airplane manufacturing.] Vierteljahresschr Gerichtl Med Oeff Sanitaetswes 48:161-204, 1914 (Ger)

13. Leri A, Breitel: [Chronic polyneuritis--Tetrachloroethane induced polyneuritis in pearl workers.] Bull Mem Soc Med Hosp Paris 46:1406-12, 1922 (Fre)

14. Fiessinger N, Wolf M: [Jaundice among workers manufacturing simulated pearls--Hepatitis caused by tetrachloroethane.] Ann Med Paris 12:269-95, 1922 (Fre)

15. Hepple RA: An unusual case of poisoning. J Army Med Corps 49:442-45, 1927

16. Elliott JM: Report of a fatal case of poisoning by tetrachloroethane. J Army Med Corps 60:373-74, 1933

17. Forbes G: Tetrachloroethane poisoning. Br Med J 1:348-50, 1943

18. Lilliman B: Suggested mechanism of poisoning by liquid tetrachloroethane. Analyst 74:510-11, 1949

19. Lynch PG: Acute tetrachloroethane poisoning--A report on a fatal case. J Forensic Med 14:118-20, 1967

20. Sherman JB: Eight cases of acute tetrachloroethane poisoning. J Trop Med Hyg 56:139-40, 1953

21. Ward JM: Accidental poisoning with tetrachloroethane. Br Med J 1:1136, 1955

22. Morgan A, Black A, Belcher DR: The excretion in breath of some aliphatic halogenated hydrocarbons following administration by inhalation. Ann Occup Hyg 13:219-33, 1970

23. Morgan A, Black A, Belcher DR: Studies on the absorption of halogenated hydrocarbons and their excretion in breath using 38Cl tracer techniques. Ann Occup Hyg 15:273-82, 1972

24. Barrett HM, Cunningham JG, Johnston JH: A study of the fate in the organism of some chlorinated hydrocarbons. J Ind Hyg Toxicol 21:479-90, 1939

25. Fujiwara K: [A new, highly sensitive reaction for the detection of chloroform.] Sitzungsber Abh Naturforisch Ges 6:33-43, 1914 (Ger)

26. Lehmann KB, Schmidt-Kehl L: [Study of the 13 most important chlorohydrocarbons from the standpoint of industrial hygienics.] Arch Hyg 116:132-268, 1936 (Ger)

27. Caldwell JR, Moyer HV: Determination of chloride--A modification of the Volhard method. Ind Eng Chem (Anal Ed) 7:38-9, 1935

28. Jeney E, Bartha F, Kondor L, Szendrei S: [Prevention of industrial tetrachloroethane intoxication--Part III.] Egeszsegtudomany 1:155-64, 1957 (Hun)

29. Lobo-Mendonca R: Tetrachloroethane--A survey. Br J Ind Med 20:50-56, 1963

30. Fahy JP: Determination of chlorinated hydrocarbons in air. J Ind Hyg Toxicol 30:205-07, 1948

31. Horiguchi S, Morioka S, Utsunomiya T, Shinagawa K, Korenari T: [A survey of the actual conditions of artificial pearl factories with special reference to the work using tetrachloroethane.] Jpn J Ind Health 6:251-56, 1964 (Jap)

32. Gobbato F, Bobbio G: [Investigation of the cardiovascular function in 75 industrial workers employed in the production of tetrachloroethane, trichloroethylene and perchloroethylene.] Securitias 53:43-63, 1968 (Ita)

33. Truhaut R: [Contribution to the study of trichloroethylene toxicology--Establishment of a titration method applicable to air and biological media.] Ann Pharm Fr 9:175-87, 1951 (Fre)

34. Lehmann KB, Hasegawa: [Absorption on chlorinated hydrocarbon compounds from air in animals and man--Chloroform, carbon tetrachloride, tetrachloroethane.] Arch Hyg 72:327-42, 1910 (Ger)

35. Matsuyama G: Indicators for precipitation and complex-formation reactions, in Kirk-Othmer Encyclopedia of Chemical Technology, ed 2 rev. New York, Interscience Publishers, 1966, vol 11, pp 558-61

36. Schwander P: [Diffusion through the skin of halogenated hydrocarbon compounds.] Arch Gewerbepathol Gewerbehyg 7:106-16, 1936 (Ger)

37. Barsoum GS, Saad K: Relative toxicity of certain chlorine derivatives of the aliphatic series. Q J Pharm Pharmacol 7:205-14, 1934

38. Smyth HF Jr, Carpenter CP, Weil CS, Pozzani UC, Striegel JA, Nycum JS: Range-finding toxicity data--List VII. Am Ind Hyg Assoc J 30:470-76, 1969

39. Table V--Toxicity tests, in Summary Table of Biological Tests. Washington, DC, National Research Council, Chemical Biological Coordination Center, vol 4, 1952, p 378

40. Lehmann KB: [Experimental studies on the influence of technologically and hygienically important gases and vapors on the organism (XVI-XXIII)--Chlorinated aliphatic hydrocarbons and considerations on the one-stage and two-stage toxicity of volatile products.] Arch Hyg 74:1-3,24-28,46-60, 1911 (Ger)

41. Pantelitsch M: [Experiments concerning the effect of chlorinated methane and ethane on mice--The relative sensitivity of mice and cats

to poisons.] Inaugural Dissertation, Hygienischen Institut der Universitat Wurzburg, pp 1-13, 1933 (Ger)

42. Lazarew NW: [Narcotic effectiveness of vapors of the chlorine derivatives of methane, ethane and ethylene.] Arch Exp Pathol Pharmakol 141:19-24, 1929 (Ger)

43. Horiuchi K, Horiguchi S, Hashimoto K, Kadowaki K, Aratake K: Studies on the industrial tetrachloroethane poisoning (2). Osaka City Med J 8:29-38, 1962

44. Muller L: [Experimental contribution to tetrachloroethane poisoning.] Arch Gewerbepathol Gewerbehyg 2:326-29, 1932 (Ger)

45. Fiessinger N, Wolf M, Blum G: [Experimentally induced hepatitis in mice following inhalation of ethane tetrachloride.] C R Soc Biol Ses Filia 87:19-20, 1922 (Fre)

46. Bollman JL, Mann FC: Experimentally produced lesions of the liver. Ann Intern Med 5:699-712, 1931

47. Deguchi T: [A fundamental study of the threshold limit values for solvent mixtures in the air--Effects of single and mixed chlorinated hydrocarbons upon the level of serum transaminases in rats.] Osaka City Med J 21:187-209, 1972 (Jap)

48. Tomokuni K: Studies on hepatotoxicity induced by chlorinated hydrocarbons--Lipid and ATP metabolisms in the liver of mice exposed to 1,1,2,2-tetrachloroethane. Acta Med Okayama 23:273-82, 1969

49. Tomokuni K: Studies on hepatotoxicity induced by chlorinated hydrocarbons--II. Lipid metabolism and absorption spectrum of microsomal lipid in the mice exposed to 1,1,2,2-tetrachloroethane. Acta Med Okayama 24:315-22, 1970

50. Navrotskiy VK, Kashin LM, Kulinskaya IL, Mikhaylorskaya LF, Shmuter LM, Burlaka-Vovk ZN, Zadorozhniy BV: [Comparative assessment of the toxicity of a number of industrial poisons when inhaled in low concentrations for prolonged periods.] Trudy S'ezda Gigenistov Ukranisoi 8:224-26, 1971 (Rus)

51. Schmidt P, Binnewies S, Gohlke R, Rothe R: [Subacute action of low concentrations of chlorinated ethanes on rats with and without additional ethanol treatment-- 1. Biochemical and toxico-metric aspects, especially results in subacute and chronic toxicity studies with 1,1,2,2-tetrachloroethane.] Int Arch Arbeitsmed 30:283-98, 1972 (Ger)

52. Lugg GA: Fujiwara reaction and determination of carbon tetrachloride, chloroform, tetrachloroethane, and trichloroethylene in air. Anal Chem 38:1532-36, 1966

53. Plaa GL, Larson RE: Relative nephrotoxic properties of chlorinated methane, ethane, and ethylene derivatives in mice. Toxicol Appl Pharmacol 7:37-44, 1965

54. Ikeda M, Ohtsuji H: A comparative study of the excretion of Fujiwara reaction-positive substances in urine of humans and rodents given trichloro- or tetrachloro-derivatives of ethane and ethylene. Br J Ind Med 29:99-104, 1972

55. Yllner S: Metabolism of 1,1,2,2-tetrachloroethane-14C in the mouse. Acta Pharmacol Toxicol 29:499-512, 1971

56. Brem H, Stein AB, Rosenkranz HS: The mutagenicity and DNA-modifying effect of haloalkanes. Cancer Res 34:2576-79, 1974

57. Coyer HA: Tetrachloroethane poisoning--Seven cases: Review of several treated. Ind Med 13:230-33, 1944

58. Elkins HB, Hobby AK, Fuller JE: The determination of atmospheric contaminants--I. Organic halogen compounds. J Ind Hyg Toxicol 9:474-85, 1937

59. Levadie B, Harwood JF: An application of gas chromatography to analysis of solvent vapors in industrial air. Am Ind Hyg Assoc J 21:20-24, 1960

60. Williams FW, Umstead ME: Determination of trace contaminants in air by concentrating on porous polymer beads. Anal Chem 40:2232-34, 1968

61. Campbell EE, Ide HM: Air sampling and analysis with microcolumns of silica gel. Am Ind Hyg Assoc J 27:323-31, 1966

62. Elkins HB: The Chemistry of Industrial Toxicology. New York, John Wiley and Sons Inc, 1950, pp 138-39,266-67

63. Cralley LV, Shea TE, Cralley LJ: A modification of the silica gel method for the determination of atmospheric organic solvent vapors. J Ind Hyg Toxicol 25:172-74, 1943

64. Feldstein M, Balestrieri S, Levaggi DA: The use of silica gel in source testing. Am Ind Hyg Assoc J 28:381-85, 1967

65. Cropper FR, Kaminsky S: Determination of toxic organic compounds in admixture in the atmosphere by gas chromatography. Anal Chem 35:735-43, 1963

66. Otterson EJ, Guy CU: A method of atmospheric solvent vapor sampling on activated charcoal in connection with gas chromatography, in Transactions of the 26th Annual Meeting, American Conference of Governmental Industrial Hygienists. Philadelphia, ACGIH, 1964, pp 37-46

67. White LD, Taylor DG, Mauer PA, Kupel RE: A convenient optimized method for the analysis of selected solvent vapors in the industrial atmosphere. Am Ind Hyg Assoc J 31:225-32, 1970

68. Fraust CL, Hermann ER: Charcoal sampling tubes for organic vapor analysis by gas chromatography. Am Ind Hyg Assoc J 27:68-74, 1966

69. NIOSH Analytical Methods for Set I. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service Center for Disease Control, National Institute for Occupational Safety and Health, Division of Laboratories and Criteria Development, 1975, pp S124-1 to S124-8

70. Collaborative Testing of Activated Charcoal Sampling Tubes for Seven Organic Solvents. HEW publication No. (NIOSH) 75-184. Cincinnati, US Dept of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Division of Laboratories and Criteria Development, 1975, 219 pp

71. Smith BS, Pierce JO: The use of plastic bags for industrial air sampling. Am Ind Hyg Assoc J 31:343-48, 1970

72. Apol AG, Cook WA, Lawrence EF: Plastic bags for calibration of air sampling devices--Determination of preceision of method. Am Ind Hyg Assoc J 27:149-53, 1966

73. Nicholson DG: Chlorine--Analysis, in Kirk-Othmer Encyclopedia of Chemical Technology, ed 2 rev. New York, Interscience Publishers, 1966, vol 5, pp 5-6

74. Kolthoff IM: Adsorption indicators. Chem Rev 16:87-98, 1935

75. Mehrotra RC, Tandon KN: Adsorption indicators in precipitation titrations. Talanta Review 11:1093-1111, 1964

76. Pungor E, Szepesvary E, Szepesvary P: Voltammetric determination of the chlorine content of aqueous solutions using a silicone-rubber based graphite electrode. Talanta 17:334-38, 1970

77. Saltzman B: Direct reading colorimetric indicators, in American Conference of Governmental Industrial Hygienists: Air Sampling Instruments for Evaluation of Atmospheric Contaminants, ed 4. Cincinnati, 1972, pp S1-S10,S28

78. Barretta ED. Stewart RD, Mutchler JE: Monitoring exposures to vinyl chloride vapor--Breath analysis and continuous air sampling. Am Ind Hyg Assoc J 30:537-44, 1969

79. Nelson GO, Shapiro EG: A field instrument for detecting airborne halogen compounds. Am Ind Hyg Assoc J 32:757-65, 1971

80. Rushing DE: Gas chromatography in industrial hygiene and air pollution problems. Am Ind Hyg Assoc J 19:238-45, 1958

81. Cooper CV, White LD, Kupel RE: Qualitative detection limits for specific compounds utilizing gas chromatographic fractions, activated charcoal and a mass spectrometer. Am Ind Hyg Assoc J 32:383-86, 1971

82. Tyson BJ: Chlorinated hydrocarbons in the atmosphere--Analysis at the parts-per-trillion level by GC-MS (gas chromatography-mass spectrometry). Anal Letter 8:807-13, 1975

83. American Conference of Governmental Industrial Hygienists, Committee on Industrial Ventilation: Industrial Ventilation--A Manual of Recommended Practice, ed 14. Lansing, Mich, ACGIH, 1976

84. American National Standards Institute--Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2. New York, American National Standards Institute Inc, 1971

85. Durrans TH: Sym-tetrachloroethane CHC12-CHC12, in Solvents, ed 6. London, Chapman and Hall, 1950, pp 192-93

86. Bowditch M, Drinker CK, Drinker P, Haggard HH, Hamilton A: Code for safe concentrations of certain common toxic substances used in industry. J Ind Hyg 22:251, 1940

87. Cook WA: Maximum allowable concentrations of industrial atmospheric contaminants. Ind Med 14:936-46, 1945

88. Report of the Sub Committee on Threshold Limits, in Proceedings of the Eighth Annual Meeting of the American Conference of Governmental Industrial Hygienists, Chicago, April 7-13, 1946, pp 54-55

89. 1947 M.A.C. Values, in Proceedings of the Ninth Annual Meeting of the American Conference of Governmental Industrial Hygienists, Buffalo, April 26-29, 1947, p 15

90. Threshold limit values for 1953. Ind Hyg Occup Med, 1953, pp 296-98

91. Threshold limit values for 1958. Arch Ind Health 18:178-82, 1958

92. Threshold Limit Values for 1962--Adopted at the 24th Annual Meeting of the American Conference of Governmental Industrial Hygienists, Washington, DC, May 13-15, 1962. Cincinnati, ACGIH, 1962, 12 pp

93. American Conference of Governmental Industrial Hygienists, Committee on Threshold Limit Values: Documentation of the Threshold Limit Values for Substances in Workroom Air, ed 3, 1971. Cincinnati, ACGIH, 2nd printing, 1974, pp 249-50

94. Von Oettingen WF: The Halogenated Hydrocarbons, Their Toxicity and Potential Dangers, PHS publication No. 414. US Dept of Health, Education, and Welfare, Public Health Service, 1955, pp 158-64

95. Wilson RH, Brumley DR: Health hazards--In the use of tetrachloroethane. Ind Med 13:233-34, 1944

96. American Conference of Governmental Industrial Hygienists: TLVs--Threshold Limit Values for Chemical Substances in Workroom Air Adopted by ACGIH for 1976. Cincinnati, ACGIH for 1976. Cincinnati, ACGIH, 1976, p 28

97. Permissible Levels of Toxic Substances in the Working Environment--6th Session of the Joint ILO/WHO Committee on Occupational Health, Geneva, June 4-10, 1968, Occupational Safety and Health Series No. 20, Geneva, International Labour Office, 1970, pp 204,210,219,239,337,353

98. Lee WE: A fatal case of dope poisoning. Lancet 1:24, 1916

99. Adams EM, Spencer HC, Rowe VK, McCollister DD, Irish DD: Vapor toxicity of carbon tetrachloride determined by experiments on laboratory animals. Arch Ind Hyg Occup Med 6:50-66, 1952

100. Prendergast JA, Jones RA, Jenkins LJ, Siegel J: Effects on experimental animals of long-term inhalation of trichloroethylene, carbon tetrachloride, 1,1,1-trichloroethane, dichlorodifluoromethane, and 1,1-dichloroethylene. Toxicol Appl Pharmacol 10:270-89, 1967

101. Rabes U: [Results of occupational medical examinations of workers exposed for many years to carbon tetrachloride.] Wiss Z Univ Halle 21:73-80, 1972 (Ger)

102. Rowe VK, McCollister DD, Spencer HC, Adams EM, Irish DD: Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects. Arch Ind Hyg Occup Med 5:566-79, 1952

103. Coler HR, Rossmiller HR: Tetrachloroethylene exposure in a small industry. Arch Ind Hyg Occup Med 8:227-33, 1953

104. Trense E, Zimmermann H: [Lethal inhalation poisoning due to the chronic effects of tetrachloroethylene vapors.] Zentralbl Arbeitsmed Arbeitschutz 19:131-37, 1969 (Ger)

105. Chlorine, Chemical Safety Data Sheet SD-80. Washington, DC, Manufacturing Chemists' Association Inc, 1970, 32 pp

106. Properties and Essential Information for Safe Handling and Use of Acetylene, Chemical Safety Data Sheet SD-7, rev. Washington DC, Manufacturing Chemists' Association Inc, 1957, 11 pp

107. Trichloroethylene, Chemical Safety Data Sheet SD-14. Washington, DC. Manufacturing Chemists' Association Inc, 1956, 16 pp

108. Properties and Essential Information for Safe Handling and Use of Perchloroethylene, Chemical Safety Data Sheet SD-24, rev. Washington, DC, Manufacturing Chemists' Association Inc, 1971, 15 pp

109. Job-fitted Gloves--General Prupose Liquidproof Product Protection, MFGR's Code 7514. Coshocton, Ohio, Edmont-Wilson, 1975, pp 12-13, 1975

110. NIOSH/OSHA Draft Technical Standards for Set I (Part 2 of 2) as of September 17, 1975. Occupational Safety and Health Administration, Office of Standards, 1975, pp 36-54

111. Joint AIHA-ACGIH Respiratory Protective Devices Committee (EC Hyatt, Chmn): Respiratory Protective Devices Manual. Cincinnati, American Industrial Hygiene Association and American Conference of Governmental Industrial Hygienists, 1963, 162 pp

112. American National Standard: Practices for Respiratory Protection, Z88.2-1969. New York, American National Standards Institute Inc, 1969, 31 pp

IX. APPENDIX I

METHOD FOR SAMPLING 1,1,2,2-TETRACHLOROETHANE IN AIR

The sampling and analytical methods described here and in Appendix II are based on those described in Method No. S124 of NIOSH Analytical Methods [69].

General Requirements

(a) Collect air samples from within the breathing zones of workers to characterize the exposure from each job or specific operation in each work area.

(b) Collect samples representative of exposures of individual workers.

(c) Record the following:

(1) Date and time of sample collection.

(2) Sampling rate and duration and total sample volume.

(3) Location of sampling.

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

(5) Other pertinent information.

Sampling

(a) Collect samples in the breathing zones of workers without interfering with their freedom of movement.

(b) Collect samples to permit determination of TWA workday exposures for every job involving exposure to tetrachloroethane in sufficient numbers to express the variability of the exposures for the work situation.

(c) Apparatus for Charcoal-Tube Sampling

(1) Battery-operated sampling pump and a clip for attachment to workers' clothing: Airflow through the pump shall be within 5% of the desired rate.

(2) Charcoal tubes: Glass tubes with both ends flame-sealed, 7 cm long with a 6-mm outer diameter and a 4-mm inside diameter, and containing two sections of 20/40 mesh activated charcoal separated by a 2-mm portion of urethane foam. The adsorbing section contains 100 mg of charcoal; the backup section has 50 mg. A 3-mm portion of urethane foam is inserted between the outlet end of the tube and the backup section, and a plug of silylated 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 flow rate of 1 liter/minute.

(d) Calibration of Sampling Instruments

(1) Calibrate air sampling instruments with a representative charcoal tube in line over a normal range of flowrates (50-1,000 ml/minute). Establish calibration curves for each sampling pump and use them in adjusting the pump prior to and during each field use. Establish new calibration curves for each sampling pump any time repairs are made or when the sampling system is modified.

(2) Spot check the volumetric flow rate through the sampling system and make the proper adjustments before and during each study to ensure that accurate airflow data are obtained.

(e) Collection and Handling of Samples

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

(2) Position the smaller, backup section of the charcoal tube nearest the sampling pump. Tubing may be used to connect the back of the tube to the pump, but air being sampled should not pass through any hose or tubing before the charcoal tube.

(3) Place the charcoal tube in a vertical position with the inlet face down during sampling.

(4) To determine a TWA concentration, take two 4-hour samples, each at a flow rate of 100 ml/minute, to give a total volume of 24 liters/4-hour sample.

(5) Cap the charcoal tubes with inert plastic caps immediately after sampling. Under no circumstances should rubber caps be used.

(6) Handle (break, seal, transport) one charcoal tube, which will be an analytical blank, in the same manner as the sample tubes but draw no air through it.

X. APPENDIX II

ANALYTICAL METHOD FOR 1,1,2,2-TETRACHLOROETHANE

Principle of the Method

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

(b) The tetrachloroethane 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 sampling and analytical method is intended to provide a measure of airborne tetrachloroethane in the range of 0.5-15 ppm. This method has been validated for a 10-liter sample only over the range of 2.3-10 ppm; however, it was stated in the validation report [69] that the method is useful over the extended range (0.5-15 ppm) necessary for the recommended standard.

(b) The lower limit of this method is determined by the efficiency with which small amounts of tetrachloroethane can be desorbed from the charcoal. Desorption efficiency must be determined over the range used.

(c) The upper limit of the range of the method is dependent on the adsorptive capacity of the charcoal tube. This capacity varies with the concentrations of tetrachloroethane and other substances in the air. When a test atmosphere containing 14.4 ppm of tetrachloroethane was sampled at 0.185 liter/minute for 4 hours, the first section of the charcoal tube held at least 4.5 mg of tetrachloroethane. During the sampling, the concentration of tetrachloroethane in the effluent was less than 5% of that in the influent, thus indicating that no breakthrough had occurred. If it is suspected that a particular atmosphere contains a large amount of contaminant, a smaller volume of sample should be collected.

Interferences

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

(b) When compounds other than tetrachloroethane are known or thought to be present in the air, such information, including their suspected identities, should be transmitted with the sample.

(c) Any compound which has the same retention time as tetrachloroethane at the gas chromatographic conditions described in this method will interfere with the analysis. This type of interference may be eliminated by using a different column packing.

Precision and Accuracy

(a) The coefficient of variation for the total analytical and sampling method in the range of 16-70 mg/cu m (2.3-10 ppm) was 0.057 [69]. This value corresponds to a 2-mg/cu m (0.3-ppm) standard deviation at a level of 35 mg/cu m (5 ppm).

(b) On the average, the concentration values obtained at the 35-mg/cu m (5 ppm) level with the overall sampling and analytical method were 5.6% higher than the "true" concentrations for a limited number of laboratory experiments [69]. Any difference between the "found" and "true" concentrations may not represent a bias in the sampling and analytical method, but rather a random variation from the experimentally determined "true" concentrations. Therefore, no recovery correction should be applied to the final result.

Advantages of the Method

(a) The analytical 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 can be accomplished rapidly.

Disadvantages of the Method

(a) The amount of sample which can be taken is limited by the capacity of the charcoal tube before overloading. When the sample value obtained for the backup section of charcoal exceeds 25% of that for the front section, the possibility of appreciable sample loss exists.

(b) The precision of the method is limited by the reproducibility of the pressure drop across the tubes. Because the pump is usually calibrated for only one tube, variability in this drop will effect flow rate and will cause the sample volume to be in error.

Apparatus

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

(b) Stainless steel column (10 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 areas.

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

(e) Microliter syringes: 10-μl and other convenient capacities for making standards and sample injections.

(f) Pipets: 1.0-ml delivery pipets.

(g) Volumetric flasks: 10-ml or other convenient capacities for making standard solutions.

Reagents

(a) "Spectroquality" carbon disulfide.

(b) Tetrachloroethane, preferably "spectroquality."

(c) Purified nitrogen.

(d) Prepurified hydrogen.

(e) Filtered compressed air.

Analysis of Samples

(a) Wash all equipment used for the analysis in detergent, followed by appropriate tap and distilled water rinses.

(b) Preparation of samples: With a file, score each charcoal tube in front of the first section of charcoal, and break it open. Remove and discard the glass wool. Transfer the charcoal in the first (larger) section to a small stoppered test tube. Remove and discard the separating foam. Transfer the second section of charcoal to another, similar test tube. Analyze these two sections separately.

(c) Desorption of samples: Prior to analysis, pipet 1.0 ml of carbon disulfide into each test tube to desorb tetrachloroethane from the charcoal. Desorption should be done for 30 minutes. Tests indicate that this is adequate if the sample is agitated occasionally during this period.

BE EXTREMELY CAUTIOUS AT ALL TIMES WHEN USING CARBON DISULFIDE BECAUSE IT IS HIGHLY TOXIC, FLAMMABLE, AND EXPLOSIVE. IT CAN BE IGNITED BY HOT STEAM PIPES. PERFORM ALL WORK WITH CARBON DISULFIDE UNDER AN EXHAUST HOOD.

(d) Typical chromatographic operating conditions:

(1) 50 ml/minute (60 psig) nitrogen carrier gas flow.

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

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

(4) 175 C injector temperature.

(5) 230 C manifold temperature (detector).

(6) 160 C isothermal oven or column temperature.

(e) 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 and to increase accuracy and reproducibility of the sample volume injected, use the solvent-flush injection technique. First, flush the 10-μl syringe with carbon disulfide several times to wet the barrel and plunger. Draw 3 μl of carbon disulfide into the syringe. Remove the needle from the carbon disulfide solvent, and pull the plunger back about 0.2 μl to separate the solvent flush from the sample with an air pocket which will serve as a marker. Immerse the needle in the sample and withdraw a 5-μl aliquot, taking into consideration the volume of the needle, since the sample in the needle will be completely injected. After removing the needle and prior to injecting the sample, pull the plunger back a short distance to minimize evaporation of the sample from the tip of the needle. Make duplicate injections of each sample and standard. No more than a 3% difference in peak area is to be expected.

(f) Measurement of area: Determine the area of the sample peak and read preliminary sample results from a standard curve prepared as discussed below.

Determination of Desorption Efficiency

It is necessary to determine the percentage of tetrachloroethane that is removed from the charcoal in the desorption process. This desorption efficiency is determined at least once for a given compound for each batch of charcoal used.

Place 100 mg of charcoal, equivalent to the amount in the first section of a sampling tube, in a 2-inch-long tube with an inside diameter of 4 mm and flame-sealed at one end. This charcoal must be from the same batch as that used in collecting the samples and can be obtained from unused sampling tubes. Cap the open end with an inert plastic film. Inject a known amount of tetrachloroethane through the plastic cap directly into the charcoal with a microliter syringe, and recap the tube with inert plastic film. The amounts of tetrachloroethane injected should be in the expected concentration range of that found in the samples.

Prepare at least five tubes for each concentration in this manner and let them stand for at least 12 hours to ensure complete adsorption of tetrachloroethane onto the charcoal. These five tubes are the "desorption samples." Treat a parallel blank tube in the same manner except add no tetrachloroethane to it. Desorb and analyze the desorption samples and blanks in exactly the same manner as previously described.

Prepare two or three desorption standards for analysis by injecting the same volume of tetrachloroethane into 1.0 ml of carbon disulfide with the same syringe used in the preparation of the desorption samples. Analyze these 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

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

The desorption efficiency is dependent on the amount of tetrachloroethane recovered from the charcoal. Plot the desorption

efficiency versus weight of tetrachloroethane found. This curve is used in Calculations, subsection (e), to correct for adsorption losses when sample concentrations are calculated.

Calibration and Standards

It is convenient to express the concentrations of standards in terms of mg tetrachloroethane/1.0 ml of carbon disulfide because samples are desorbed in this amount of carbon disulfide. To minimize error, inject 10 times the desired weight of tetrachloroethane into 10 times the desired volume of carbon disulfide. For example, to prepare a 0.3 mg/1.0 ml standard, inject 3.0 mg (1.88 μl) of tetrachloroethane into a glass-stoppered flask containing exactly 10 ml of carbon disulfide. Use the density of tetrachloroethane (1.60 g/ml) to convert 3.0 mg into microliters that are easily measured with a microliter syringe. Prepare a series of standards varying in concentration over the appropriate range, and analyze under the same gas chromatographic conditions and at the same time as the unknown samples. To establish standard curves, plot concentration in mg/1.0 ml versus average peak area.

Calculations

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

(b) Subtract the weight of tetrachloroethane present in the front section of the blank charcoal tube from the weight of tetrachloroethane in the front section of the sample charcoal tube to give a corrected weight for the front section.

(c) Subtract the weight of tetrachloroethane present in the backup section of the blank charcoal tube from the weight of that in the backup section of the sample charcoal tube to give a corrected weight for the backup section.

(d) Add the corrected amounts of tetrachloroethane present in the front and backup sections of the sample tube to determine the total measured tetrachloroethane in the sample.

(e) Read the desorption efficiency (DE) from the curve (see Determination of Desorption Efficiency) for the amount found in the front section. Divide the total weight by this desorption efficiency to obtain the corrected mg/sample.

$$\text{corrected mg/sample} = \frac{\text{total weight}}{\text{DE}}$$

(f) The concentration of tetrachloroetane in the air sampled can be expressed in mg/cu m.

$$\text{mg/cu m} = \frac{\text{corrected mg} \times 1000 \text{ (liters/cu m)}}{\text{air volume sampled (liters)}}$$

(g) Concentration may also be expressed in ppm.

$$\text{ppm} = \text{mg/cu m} \times \frac{24.45}{168} \times \frac{760}{P} \times \frac{t + 273}{298}$$

where:

P = pressure (mmHg) of air sampled

t = temperature (C) of air sampled

24.45 = molar volume (liter/mole) at 25 C and 760 mmHg

168 = formula weight (g/mole) of tetrachloroethane

760 = standard pressure (mmHg)

298 = average room temperature (K)

X. APPENDIX III

MATERIAL SAFETY DATA SHEET

The following items of information which are applicable to a specific product or material shall be provided in the appropriate block of the Material Safety Data Sheet (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 rules 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, eg, "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. Flashpoint, shock sensitivity

or similar descriptive data may be used to indicate flammability, reactivity, or similar hazardous properties of the material.

(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 (mmHg); 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 flashpoint 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 TWA concentration, as a permissible exposure, or by some other indication of an acceptable standard. 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, possibly mild irritation.
>
> 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 employees.

(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 employees 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 antipollution ordinances" are proper but not sufficient. Specific procedures shall 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. Respirators shall be specified as to type and NIOSH or US Bureau of Mines approval class, ie, "Supplied air," "Organic vapor canister," etc. Protective equipment must be specified as to type and materials of construction.

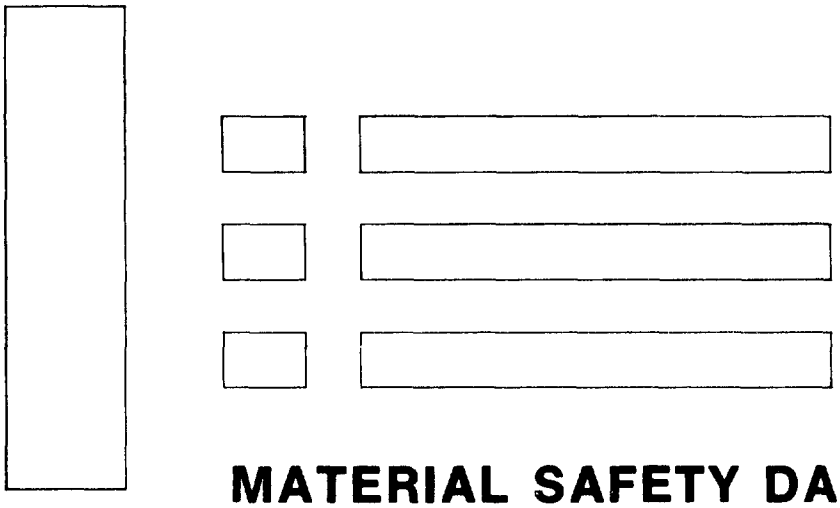
(i) Section IX. Special Precautions

"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 employees exposed to the hazardous substance. 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 in 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. APPENDIX IV

PHYSICAL AND CHEMICAL PROPERTIES OF 1,1,2,2-TETRACHLOROETHANE

Molecular formula	$CHCl_2 - CHCl_2$
Formula weight	167.9
Boiling point at 760 mmHg	146.3 C
Melting point	-36 C
Vapor pressure	5 mmHg at 21 C; 10 mmHg at 32 C
Specific gravity at 20 C (water = 1.000 at 4 C)	1.596
Solubility	0.29 g/100 g water at 25 C; miscible with most organic solvents
Explosive limit	None
Flashpoint	None
Vapor density (air = 1)	5.79
Conversion factors (760 mmHg and 25 C)	1 mg/l = 145.5 ppm 1 mg/cu m = 0.146 ppm 1 ppm = 6.87 μg/l 1 ppm = 6.87 mg/cu m

Adapted from 2-4

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