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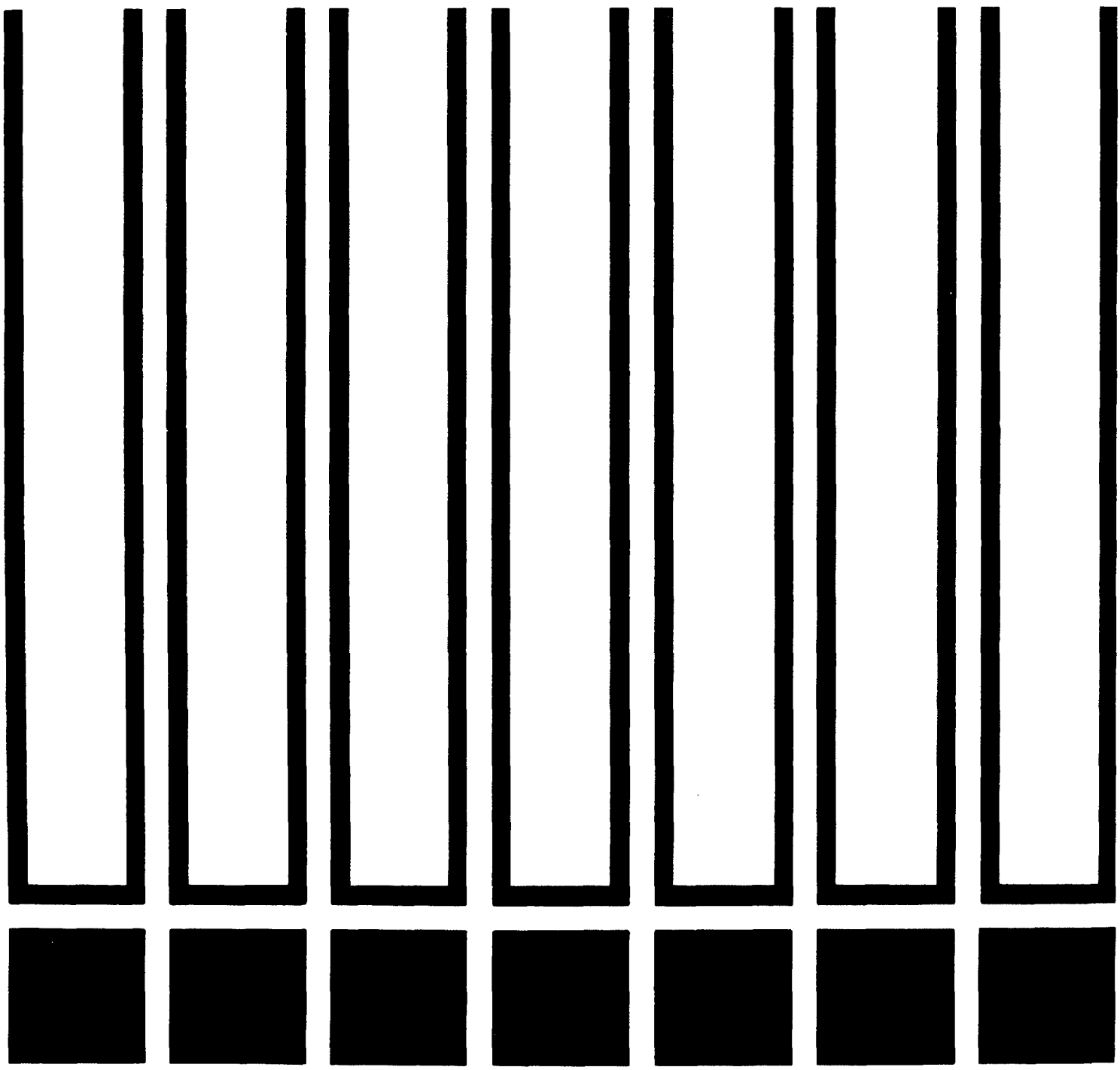

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service Center for Disease Control
National Institute for Occupational Safety and Health

criteria for a recommended standard....

OCCUPATIONAL EXPOSURE TO REFINED PETROLEUM SOLVENTS

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

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

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

I am pleased to acknowledge the contributions to this report on refined petroleum solvents by members of the NIOSH staff and the valuable constructive comments by the Review Consultants on Refined Petroleum Solvents, by the ad hoc committees of the American Conference of Governmental Industrial Hygienists and the Society of Toxicology 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 refined petroleum solvents. 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 standards for refined petroleum solvents. Ludmilla Syrotenko, Ph.D., served as criteria manager and Irwin P. Baumel, Ph.D., had program responsibility. Stanford Research Institute (SRI) developed the basic information for consideration by NIOSH staff and consultants under contract CDC 99-74-31.

The Division review of this document was provided by Keith H. Jacobson, Ph.D. (Chairman), Douglas L. Smith, Ph.D., Frank L. Mitchell, D.O., Paul E. Caplan and Trent M. Lewis, Ph.D. (Division of Biomedical and Behavioral Sciences), with Hervey B. Elkins, Ph.D., and Seymour D. Silver, Ph.D.

The views expressed and conclusions reached in this document, together with the recommendations for a standard, are those of NIOSH. These views and conclusions are not necessarily those of the consultants, other federal agencies or professional societies that reviewed the document, or of the contractor.

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CRITERIA DOCUMENT:
RECOMMENDATIONS FOR AN OCCUPATIONAL
EXPOSURE STANDARD FOR REFINED PETROLEUM SOLVENTS

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I. RECOMMENDATIONS FOR A REFINED PETROLEUM SOLVENTS STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to petroleum ether, rubber solvent, varnish makers' and painters' naphtha, mineral spirits, Stoddard solvents and kerosene in the workplace be controlled by adherence to the following sections. The standards are designed to protect the health and provide for the safety of employees for up to a 10-hour work shift, 40-hour workweek, over a working life. Compliance with all sections of the standards should prevent adverse effects of these chemicals on the health of employees and provide for their safety. Techniques recommended are valid, reproducible, and available to industry and government agencies. Sufficient technology exists to permit compliance with the recommended standards. Although the environmental limits for the workplace are considered to be safe levels based on current information, the employer should regard these as the upper boundary of exposure and every effort should be made to keep the exposure as low as is technically feasible. The criteria and standards will be subject to review and revision as necessary.

Eye, nose, and throat irritation, dermatitis, and effects on the nervous system have been found in workers exposed to some refined petroleum solvents. Benzene, which has been shown to cause blood dyscrasias in humans, is present in small amounts in many refined petroleum solvents. NIOSH has concluded that benzene is leukemogenic. For further information on the hazards of benzene, refer to Appendix I. It is therefore recommended that, when benzene is found to be present in refined petroleum solvents, every effort be made to keep the benzene exposure as low as

possible. The refined petroleum solvents examined in this document are for the most part complex mixtures, and the possibility of synergistic or additive toxic effects of the components of these mixtures should not be overlooked.

These criteria and recommended standards apply to occupational exposure of workers to the following refined petroleum solvents: petroleum ether, rubber solvent, varnish makers' and painters' naphtha, mineral spirits, Stoddard solvents, and kerosene, all included in the term "refined petroleum solvents."

The refined petroleum solvents considered in this document have a total aromatic content of less than 20%. Other hydrocarbon solvents such as thinners, whose total aromatic content may exceed 20%, are not discussed in this document. For the purposes of these recommended standards for refined petroleum solvents, the following definitions will apply to those solvents covered in this document:

"Petroleum ether" is a refined petroleum solvent that has a boiling range of 30-60 C and typically has a chemical composition of 80% pentane and 20% isohexane.

"Rubber solvent" is a refined petroleum solvent with a boiling range of 45-125 C and is composed of organic compounds whose carbon chain lengths range from C5 to C7. The chemical composition of a typical rubber solvent would be: 41.4% paraffins, 53.6% monocycloparaffins, 0.1% monoolefins, 1.5% benzene, and 3.4% alkyl benzene.

"Varnish makers' and painters' naphtha" is a refined petroleum solvent with a boiling range of 95-160 C and is composed of organic compounds whose carbon chain lengths range from C5 to C11. The chemical

composition of a typical varnish makers' and painters' naphtha would be: 55.4% paraffins, 30.3% monocycloparaffins, 2.4% dicycloparaffins, 0.1% benzene, 11.7% alkylbenzenes, 0.1% indans and tetralins.

"Mineral spirits" is a refined petroleum solvent with a boiling range of 150-200 C. A typical chemical composition for mineral spirits would be: 80-86% saturated hydrocarbons, 1% olefins, and 13-19% aromatics.

"Stoddard solvent" is a type of mineral spirits with a boiling range of 160-210 C and is composed of organic compounds whose carbon chain lengths range from C7 to C12. The chemical composition of a typical Stoddard solvent would be: 47.7% paraffins, 26% monocycloparaffins, 11.6% dicycloparaffins, 0.1% benzene, 14.1% alkylbenzenes, 0.5% indans and tetralins.

"140 Flash aliphatic solvent" is a type of Stoddard solvent with a boiling range of 185-207 C and is composed of organic compounds whose carbon chain lengths range from C5 to C12. A typical chemical composition for 140 flash aliphatic solvent would be: 60.8% paraffins, 24.5% monocycloparaffins, 11.2% dicycloparaffins, 0.07% benzene, 3.03% alkyl benzenes, and 0.3% indans and tetralins.

"Kerosene" is a refined petroleum solvent with a boiling range of 175-325 C. A typical chemical composition for kerosene would be: 25% normal paraffins, 11% branched paraffins, 30% monocycloparaffins, 12% dicycloparaffins, 1% tricycloparaffins, 16% mononuclear aromatics, and 5% dinuclear aromatics.

"Deodorized kerosene" is a refined petroleum solvent that has a boiling range of 209-274 C and a typical chemical composition of 55.2% paraffins, 40.9% naphthenes, and 3.9% aromatics.

If exposure to other chemicals also occurs, the employer shall comply also with applicable standards for the other chemicals. In particular, special attention shall be given to the benzene content of the refined petroleum solvents being used.

The "action level" for petroleum ether, rubber solvent, and varnish makers' and painters' naphtha is defined as an airborne time-weighted average (TWA) concentration of 200 milligrams per cubic meter (mg/cu m) of air for up to a 10-hour work shift in a 40-hour workweek. The "action level" for mineral spirits and Stoddard solvent is defined as a TWA concentration of 350 mg/cu m of air for up to a 10-hour work shift in a 40-hour workweek. The "action level" for kerosene is defined as a TWA concentration of 100 mg/cu m of air for up to a 10-hour work shift in a 40-hour workweek. "Occupational exposure" to refined petroleum solvents is defined as exposure above the action level. Exposure to refined petroleum solvents at lower concentrations will not require adherence to the following sections, except for Sections 2(a), 3, 4(a,b), 6(a,c-i), 7, and 8(a).

Section 1 - Environmental (Workplace Air)

(a) Concentration

(1) The employer shall control occupational exposure to airborne concentrations of petroleum ether, rubber solvent, varnish makers' and painters' naphtha, mineral spirits, and Stoddard solvents so that no employee is exposed at a concentration greater than 350 mg/cu m of air, determined as a TWA concentration for up to a 10-hour work shift, 40-hour workweek. In addition, no employee shall be exposed to any of the above

refined petroleum solvents at a ceiling concentration greater than 1,800 mg/cu m as determined by a sampling time of 15 minutes.

(2) The employer shall control occupational exposure to kerosene so that no employee is exposed at a concentration greater than 100 mg/cu m of air determined as a TWA concentration for up to a 10-hour work shift, 40-hour workweek.

(b) Sampling and Analysis

Procedures for the collection and analysis of workroom air samples shall be as provided in Appendices II, III, and IV, or by any methods shown to be at least equivalent in precision and sensitivity to the methods specified.

Section 2 - Medical

Medical surveillance as described below shall be made available to all workers subject to occupational exposure to refined petroleum solvents.

(a) Preplacement examinations shall include at least:

(1) Comprehensive medical and work histories.

(2) Physical examination, giving particular attention to: the skin; appropriate liver function tests such as serum glutamic-oxaloacetic transaminase; complete blood count; urinalysis; and tests of nervous system function.

(3) A judgment of the ability of the worker to use negative or positive pressure respirators.

(b) Periodic examinations shall be made available at least on an annual basis and shall include at least:

[illegible] shall be made available at least on a

(1) Interim medical and work histories.

(2) Physical examination as outlined in (a)(2) above.

(c) During examinations, applicants or employees having medical conditions which would be directly or indirectly aggravated by exposure to these substances, such as chronic dermatitis, shall be counseled on the increased risk of impairment of their health from working or continuing to work with these substances.

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

(e) In an emergency involving these substances, all affected personnel shall be provided with immediate first aid, followed by prompt medical evaluation and care. In the event of eye or skin contact with refined petroleum solvents, contaminated clothing and shoes shall be removed immediately and eyes and skin shall be flushed with copious amounts of water. The medical attendants shall be informed of the possibility of central nervous depression.

(f) Pertinent medical records shall be kept by the employer for all employees occupationally exposed to refined petroleum solvents. Such records shall be kept for at least 30 years after employment has ended. These records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employer, and of the employee or former employee.

Section 3 - Labeling and Posting

All labels and warning signs shall be printed both in English and in the predominant language of non-English-reading employees. Illiterate workers and workers reading languages other than those used on labels and posted signs shall receive information regarding hazardous areas and shall be informed of the instructions printed on labels and signs.

The following warning label and sign shall be affixed in a readily visible location on petroleum ether, rubber solvent, varnish makers' and painters' naphtha, mineral spirits, Stoddard solvents, or kerosene storage tank containers:

NAME OF SOLVENT
(synonym)

WARNING! FLAMMABLE! (or COMBUSTIBLE!)

CAN BE FATAL OR CAUSE SEVERE ILLNESS IF SWALLOWED

Keep away from heat, sparks, and open flame.
No smoking permitted.
Do not take internally.
Keep container closed.
Avoid prolonged or repeated breathing of vapor.
Avoid contact with eyes and skin.
Use with adequate ventilation.

In case of

Fire: Use appropriate foam-type, dry chemical (eg, sodium bicarbonate), or carbon dioxide extinguishers.

Spill: Flush area with adequate amounts of water.

First Aid: In case of eye or skin contact, flush with copious amounts of water while lifting the eyelids. Change clothing if contaminated. In case of accidental swallowing, call a physician. DO NOT INDUCE VOMITING!

Section 4 - Personal Protective Clothing and Equipment

(a) Protective Clothing

(1) Appropriate protective clothing, including gloves, aprons, suits, boots, and face shields (8-inch minimum) with goggles, made of a material resistant to refined petroleum solvents shall be provided for and worn by every employee to limit skin contact. In addition, the protective clothing shall also be fire-resistant. This type of clothing shall be worn by employees removing clothing from drycleaning machines or performing spotting operations. In addition to being solvent-resistant, the gloves used in these operations shall also be of sufficient length to protect the forearms of the employees. Employees performing these operations should keep solvent-saturated materials away from their breathing zones as much as possible.

(2) Unless protective clothing is being worn, the employer shall ensure that a change of clothing is immediately available to and used by any employee whose clothes become wetted with solvents.

(3) Where protective clothing is required, the employer shall provide the employee with separate storage facilities for work clothes and for street clothes, preferably separated by shower facilities.

(4) Safety showers and eyewash fountains shall be provided in appropriate areas. These showers and fountains shall be checked periodically to ensure their proper working condition.

(b) Eye Protection

Chemical safety goggles (splashproof) and face shields (8-inch minimum) meeting the requirements listed in 29 CFR 1910.133 and ANSI Z87.1-1968 shall be provided and worn in any operation in which there is a

reasonable probability of a solvent being splashed into the eyes.

(c) Respiratory Protection

(1) Sparkproof engineering controls, such as local exhaust hoods, fans, or other ventilation systems, shall be used if needed to keep solvent air concentrations below the TWA and ceiling environmental limits. Compliance with the environmental limits may not be achieved by the use of respirators except:

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

(B) For nonroutine operations such as brief exposures at concentrations in excess of the environmental limits resulting from maintenence or repair activities.

(C) During emergencies when air concentrations of the solvent may exceed the environmental limits.

(2) When a respirator is permitted by paragraph (c)(1) of this section, it shall be selected and used pursuant to the following requirements:

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

(B) The employer shall provide respirators in accordance with Tables I-1, I-2, and I-3 depending on the type of solvent used and shall ensure that the employee uses the appropriate respirator when needed. The respiratory protective devices provided in conformance with Tables I-1, I-2, and I-3 shall comply with the standards jointly approved by NIOSH and the Mining Enforcement and Safety Administration (formerly Bureau of Mines) as specified under the provisions of 30 CFR 11.

TABLE I-1

RESPIRATOR SELECTION GUIDE FOR PETROLEUM ETHER, RUBBER SOLVENT, AND VARNISH MAKERS' AND PAINTERS' NAPHTHA

Concentration	Respirator Type Approved under Provisions of 30 CFR 11
Less than or equal to 3,500 mg/cu m	(1) Chemical cartridge respirator with half-mask facepiece and organic vapor cartridge* (2) Supplied-air respirator with half-mask facepiece operated in demand (negative pressure) mode
Less than or equal to 17,500 mg/cu m	(1) Gas mask equipped with full facepiece and organic vapor canister (2) Supplied-air respirator equipped with full facepiece (3) Self-contained breathing apparatus with full facepiece operated in demand mode
Greater than 17,500 mg/cu m	(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 operated in pressure-demand mode, with auxiliary self-contained air supply
Emergency entry (into an area of unknown concentration)	(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 operated in pressure-demand mode, with auxiliary self-contained air supply

*The service life of the organic vapor cartridge should be limited to 1 hour.

TABLE I-2

RESPIRATOR SELECTION GUIDE FOR STODDARD SOLVENTS AND MINERAL SPIRITS

Concentration	Respirator Type Approved under Provisions of 30 CFR 11
Less than or equal to 3,500 mg/cu m	(1) Chemical cartridge respirator with half-mask facepiece and organic vapor cartridge* (2) Supplied-air respirator with half-mask facepiece operated in demand (negative pressure) mode
Less than or equal to 17,500 mg/cu m	(1) Gas mask equipped with full facepiece and organic vapor canister (2) Supplied-air respirator equipped with full facepiece (3) Self-contained breathing apparatus with full facepiece operated in demand mode
Less than or equal to 30,000 mg/cu m	Supplied-air respirator equipped with full facepiece, hood, helmet, or suit in continuous-flow or other positive pressure mode
Greater than 30,000 mg/cu m	(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 operated in pressure-demand mode, with auxiliary self-contained air supply
Emergency entry (into an area of unknown concentration)	(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 operated in pressure-demand mode, with auxiliary self-contained air supply

*The service life of the organic vapor cartridge should be limited to 1 hour.

TABLE I-3

RESPIRATOR SELECTION GUIDE FOR KEROSENE

Concentration	Respirator Type Approved under Provisions of 30 CFR 11
Less than or equal to 1,000 mg/cu m	(1) Chemical cartridge respirator with half-mask facepiece and organic vapor cartridge* (2) Supplied-air respirator with half-mask facepiece operated in demand (negative pressure) mode
Less than or equal to 5,000 mg/cu m	(1) Gas mask equipped with full facepiece and organic canister (2) Supplied-air respirator equipped with full facepiece (3) Self-contained breathing apparatus with full facepiece operated in demand mode
Greater than 5,000 mg/cu m	(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 operated in pressure-demand mode, with auxiliary self-contained air supply
Emergency entry (into an area of unknown concentration)	(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 operated in pressure-demand mode, with auxiliary self-contained air supply

*The service life of the organic vapor cartridge should be limited to 1 hour.

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

(D) The employer shall ensure that no employee is being exposed to solvent air concentrations in excess of the environmental limits because of improper respirator selection, fit, use, or maintenance.

(E) The employer shall ensure that respirators are adequately cleaned and maintained and that employees are instructed in the proper use and in testing for leakage of respirators assigned to them.

(F) Respirators shall be easily accessible in work areas and employees shall be informed of their location.

Section 5 - Informing Employees of Hazards from Refined Petroleum Solvents

(a) The employer shall institute a continuing education program, conducted by persons qualified by experience or training, to ensure that employees have current knowledge of job hazards, of proper maintenance and cleanup methods, and of proper respirator use. The instructional program shall also include a description of the general nature of the medical surveillance procedures and of the advantages to the employee of undergoing these examinations. Educational programs for employees engaged in maintenance and repair shall include instruction on those work situations in which they may be occupationally exposed to refined petroleum solvents.

(b) Training program material in written or published form shall be kept on file at each establishment or department and shall be readily

be kept on file at each establishment or department and shall be readily

accessible to all employees occupationally exposed to refined petroleum solvents.

The specific information required by the US Department of Labor form OSHA-20 "Material Safety Data Sheet," shown in Appendix V, or on a similar form approved by the Occupational Safety and Health Administration, US Department of Labor, shall also be kept on file, and be accessible to the employees. The employees shall be informed, and reinformed at least annually, as to the availability and location of the above files.

Section 6 - Work Practices

(a) Emergency Procedures

For all work areas in which there is potential for emergencies involving refined petroleum solvents, the employer shall take necessary steps to ensure that employees are instructed in and follow the procedures specified below and any other appropriate procedures specific to the type of operation or process in a particular workplace.

(1) Procedures shall include prearranged plans for obtaining first-aid and emergency medical care and for transportation of injured workers.

(2) Firefighting procedures shall be established and implemented. The refined petroleum solvent sources shall be clearly marked, and workers and emergency personnel shall be instructed in proper shutoff procedures. The instructions shall include procedures for emergencies involving the release of solvent vapor. In case of fire, solvent sources shall be shut off or removed. Containers shall be removed or cooled with water. Chemical foam, carbon dioxide, or dry chemicals

shall be used for fighting solvent fires, and proper respiratory protection and protective clothing shall be worn.

(3) Approved eye, skin, and respiratory protection, as specified in Section 4, shall be used by personnel essential to emergency operations.

(4) Nonessential employees shall be evacuated from exposure areas during emergencies. During an emergency, perimeters of hazardous areas shall be roped off, posted, and secured.

(5) Personnel who may be required to shut off sources of solvent, clean up spills, and repair leaks shall be properly trained in the appropriate procedures.

(6) Warning or alarm systems should be considered to alert workers to possible hazardous exposures to refined petroleum solvents during emergencies involving the release of refined petroleum solvent liquid or vapors.

(b) Exhaust Systems

Engineering control systems shall be used when needed to reduce exposure of employees to refined petroleum solvents to recommended limits. When a local exhaust ventilation system is used, it shall be designed and maintained to prevent the accumulation or recirculation of solvent vapor in the workroom. Drycleaning apparatus shall be operated under negative pressure so that, when the loading door is opened, air from the workroom will be drawn into the apparatus, thus preventing the escape of solvent vapors into the workroom. Exhaust systems discharging into outside air must conform with applicable local, state, and federal air pollution regulations. When mechanical ventilation is used to control exposure,

measurements which demonstrate system efficiency, eg, air velocity, static pressure, or air volume, shall be made at least every 3 months, or more frequently if required for the safe and efficient operation of a particular system. Measurements of system efficiency shall also be made as soon as possible but not later than 5 workdays after any change in production, process, or control that might result in an increase in air concentrations. When a fan is located in duct work and where a flammable solvent is likely to be present at concentrations at or above one-fourth the lower flammable limit, the fan rotating element shall be of nonsparking material or the casting shall be coated with or consist of a nonsparking material. The ventilation system shall contain devices along the length of the exhaust system intended to prevent the occurrence and propagation of flashbacks.

(c) Loading and Unloading

The handling and storage of refined petroleum solvents shall comply with NFPA Article 30 for flammable or combustible liquids.

(1) Fire extinguishers approved for Class IB fires, such as dry chemical extinguishers, shall be available in loading and unloading areas. Fire extinguishers shall be inspected annually and recharged or replaced if necessary.

(2) Safety showers and eyewash fountains shall be installed near loading and unloading areas and maintained in proper working order.

(3) The equipment required by paragraph (c)(1) and (c)(2) of this section shall be inspected regularly to ensure that it is in proper working order. The employer shall ensure that such inspection is performed by a qualified person.

(4) In case of a leak, loading or unloading operations should continue, as rapidly as possible (if safe) to drain the tank or make necessary repairs. Operations should cease in the event of a severe leak causing unsafe conditions, and emergency procedures should be instituted.

(5) Bonding facilities for protection against static sparks during the loading of tank vehicles shall be provided as required in 29 CFR 1910.106(f)(3)(iv).

(d) Solvent Carloading and Truckloading Procedures

(1) Smoking, matches, or lighters shall be strictly prohibited in car- and truckloading areas.

(2) Safety showers, eyewash fountains, and fire extinguishers containing chemicals approved for Class IB fires shall be installed and maintained in proper working order.

(3) A wheel chock, a car-loading sign, and a derail shall be placed in position and ground cables attached before any lines are connected to a tank car containing solvents.

(4) Wheel chocks, ground cables, and loading sign shall be in place before any lines are connected to a trailer containing solvents.

(5) Ground cables shall be removed only after loading or unloading lines have been removed and the dome covers have been secured.

(6) Rubber gloves and chemical safety goggles (splashproof) shall be used where the possibility of solvent splashes exists. Breathing of solvent vapor should be avoided.

(7) Any part of the body on which solvent has been spilled should be washed immediately with water and soap. Eyes should be flushed immediately with copious amounts of water while lifting the eyelids, and

the incident should be reported immediately to the appropriate health unit.

(e) Storage

Storage of bulk amounts shall meet the requirements for Class IB flammable liquid storage as specified in 29 CFR 1910.106(b).

(f) Waste Disposal

Spills of large amounts of solvents should be washed with water into an appropriate drainage system where it may be safely stored and either recovered or discarded. Discarding of waste shall be in compliance with applicable Environmental Protection Agency (EPA) standards. When it is not possible to wash a spill with water, the area should be cordoned off until cleanup operations have been completed. If a vacuum truck is used to remove the solvents, there should be no sources of ignition in the vicinity and sufficient flashback devices should be provided.

(g) Vessel Entry

Entry into confined spaces, such as tanks, pits, tank cars, and process vessels, which have contained refined petroleum solvents shall be controlled by a permit system. Permits shall be signed by an authorized employer representative, certifying that preparation of the confined space, precautionary measures, and personal protective equipment are adequate, and that the prescribed procedure will be followed.

(1) All lines shall be disconnected or blocked while the vessel is being cleaned. All valves or pumps leading to and from the vessel shall be locked out or tagged out.

(2) The vessel shall be washed with water and purged with air, or first with nitrogen and then with air.

(3) A calibrated combustible gas meter shall be used to check for explosion hazard. The test shall be performed by a person trained in the use of the combustible gas meter. Where it is possible that refined petroleum solvent vapors could increase in concentration within the confined space, this test shall be repeated every 30 minutes.

(4) The vessel shall then be checked for airborne solvent level, possible oxygen deficiency, and concentrations of other likely contaminants. A positive pressure respirator shall be used during this checking procedure.

(5) If a respirator is necessary, an appropriate type shall be provided to the employee. Section 4(c) of this chapter describes the types of respirators which are suitable under various conditions.

(6) Each employee entering the vessel shall be equipped with appropriate respiratory protection, a harness, and a lifeline. At least two other persons equipped with appropriate respiratory protection (one of which is a positive pressure type), harnesses, and lifelines shall watch at all times from the outside. At least one more person should be available to assist in an emergency.

(h) General Housekeeping

Employers shall ensure that proper maintenance of equipment is provided to minimize the accidental escape of refined petroleum liquid solvent or vapor. Cleanup of spills and repair of equipment and leaks shall be performed as soon as practical.

(i) Specific Operations

For specific information concerning operations such as spray finishing, dip tank procedures and the design of open surface tank ventilation, appropriate regulations, such as 29 CFR 1910.94(c)(d), 29 CFR 1910.107, and 29 CFR 1910.108, shall be followed.

Section 7 - Sanitation Practices

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

(b) Food or beverage preparation, storage, dispensing (including vending machines), and consumption shall be prohibited in work areas where any refined petroleum solvents are present.

(c) Smoking shall be prohibited in areas where refined petroleum solvents are used, transferred, stored, or manufactured.

(d) Adequate facilities with soap and water for handwashing shall be made available. If soap and water are inadequate, the employer shall provide appropriate substitutes. Skin cleansing with refined petroleum solvents shall be prohibited.

Section 8 - Monitoring and Recordkeeping

(a) Survey Requirements

Workers are not considered to have occupational exposure to refined petroleum solvents if environmental concentrations, as determined on the basis of an industrial hygiene survey, do not exceed the action level. Surveys shall be repeated at least once a year and within 30 days after any process change likely to result in increases of airborne refined petroleum

solvent concentrations. Records of these surveys, including the basis for concluding that concentrations of airborne refined petroleum solvents are at or below the action level, shall be maintained. If there is occupational exposure to refined petroleum solvents, then the following requirements shall apply:

(b) Personal Monitoring

(1) A program of personal monitoring shall be instituted to identify and measure, or permit calculation of, the exposures of all employees who are occupationally exposed to refined petroleum solvents. Monitoring of employee exposures to airborne refined petroleum solvents shall be conducted at least every 6 months. If monitoring of an employee's exposure to a refined petroleum solvent reveals that this employee is exposed at concentrations in excess of the appropriate recommended environmental limit(s), control measures shall be initiated, the employee shall be notified of the exposure and of the control measures being implemented to correct the situation; the exposure of that employee shall be measured at least once every 30 days. Such monitoring shall continue until two consecutive samplings, at least a week apart, indicate that the employee's exposure no longer exceeds the environmental limits stated in Section 1(a). Semiannual monitoring may then be resumed.

(2) In all personal monitoring, samples of airborne refined petroleum solvents shall be collected that, when analyzed, will provide an accurate representation of the concentration of the refined petroleum solvent or solvents in the air breathed by the worker. Procedures for sampling and analysis of refined petroleum solvents shall be as provided in Appendices III and IV, or by any method shown to be at least equivalent in

precision and sensitivity to the methods specified.

(3) For each TWA determination, a sufficiently large number of samples shall be taken and analyzed to permit construction of valid estimates of TWA and ceiling concentration exposures of employees during each work shift. Variations in work and production schedules shall be considered in deciding when and how many samples are to be collected. The number of representative TWA and ceiling concentration determinations for an operation or process shall be based on such factors as variations in location and job functions of employees in that operation or process.

(c) Recordkeeping

Records of environmental monitoring shall be kept by the employer for at least 30 years. These records shall include the dates of measurements, job function and location of the employees at the worksite, sampling and analytical methods used, number, duration, and results of the samples taken, TWA and ceiling concentrations estimated from these samples, type of personal protective equipment used, and exposed employees' names. Each employee shall have access to information on his or her own environmental exposures. Environmental records shall be made available to designated representatives of the Secretary of Labor and of the Secretary of Health, Education, and Welfare. Pertinent medical records shall be retained by the employer for 30 years after employment has ended. 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 from workplace exposure to refined petroleum solvents. 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 upon which standards can be established to protect the health and to provide for the safety of employees exposed to hazardous chemical and physical agents. The criteria and recommended standard should enable management and labor to develop better engineering controls and more healthful work practices and should not be used as a final goal.

These criteria for a standard for refined petroleum solvents are part of a continuing series of documents developed by NIOSH. The recommended standard applies to workplace exposure to petroleum solvents arising from the processing, manufacture, use, and handling of solvents 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 general

occupational exposures is not warranted. It is intended to (1) prevent injury from refined petroleum solvents, (2) be measurable by techniques that are valid, reproducible, and available to industry and official agencies, and (3) be attainable with existing technology.

Since petroleum ether, rubber solvent, and varnish makers' and painters' naphtha contain substantial amounts of C5-C8 alkanes, the possibility that exposure to these solvents could cause polyneuropathy must be recognized. Therefore, the recommended standards for these solvents reflect data and recommendations cited in the NIOSH document entitled Criteria for a Recommended Standard....Occupational Exposure to Alkanes.

The analytical method for refined petroleum solvents is recommended in Appendix IV. Additional suggestions have been made that may be helpful in adapting this method for specific analyses. It is nearly impossible, however, to prescribe gas-chromatographic conditions that will result in adequate analytical determinations in all cases. The success of the method will ultimately depend on how well the analyst adapts the chromatographic conditions to suit the analysis of the particular refined petroleum solvent that is being tested.

Although many reports were found and reviewed on "solvent" toxicity, many investigations failed to chemically describe the type of solvent used in their studies. In future experiments, it is important for the physical and chemical characteristics of a solvent, such as boiling range, flashpoint, and total aromatic as well as benzene content, to be given so that the solvent can be adequately defined. Additional toxicologic experiments are necessary for all the solvents examined in this document, and they should include studies on the effects of solvent vapor inhalation

on both animals and humans. Possible teratogenic, mutagenic, and carcinogenic potential of these solvents also need to be assessed. In addition, long-term epidemiologic studies should be undertaken to evaluate solvent toxicity and to correlate the observed effects with the data on the concentrations of the solvents to which workers are exposed during normal working conditions. More specific and efficient sampling devices should be designed and new and improved analytical procedures need to be developed for personal, automatic, and continuous monitoring systems.

III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

(a) Petroleum Ether

Petroleum ether is a mixture of volatile aliphatic hydrocarbons with a boiling range of about 30-60 C (86-140 F) [1-4]. Petroleum ether is sometimes referred to as benzin, benzine, petroleum benzin, canadol, light ligroin, and Skellysolve [2-5]. Reference is sometimes made to high-boiling petroleum ether. This terminology is essentially synonymous with ligroin or varnish makers' and painters' naphtha [3].

Physically, petroleum ether is a clear, colorless, nonfluorescent, volatile liquid [3]. It has a characteristic odor and is highly flammable [4]. Its flashpoint is about -46 to -57 C (-50 to -70 F) [6-8] and it has a specific gravity of about 0.64. Chemically, petroleum ether consists primarily of pentane and isohexane [3,4]. It typically contains no aromatics [6]. It is a low boiling fraction obtained from the fractional distillation of petroleum [1]. Additional physical and chemical properties are given in Table XIV-1.

Petroleum ether is used as a solvent for oils, fats, and waxes; a detergent; a fuel; in paints and varnishes; an insecticide; and in photography [2-4].

(b) Rubber Solvent

Rubber solvent is a mixture of hydrocarbons that boils in the range of 45-125 C (113-257 F) [1,2,9]. This solvent is sometimes referred to as benzine and lacquer diluent [4,10].

Physically, rubber solvent is usually a clear, colorless liquid with a specific gravity of about 0.74 [1,9]. It has a Kauri-Butanol value (the measurement of milliliters of solvent needed to cause cloudiness in a solution of Kauri gum and butyl alcohol; indicates aromatic content of the solvent) of 30-33 and therefore has a relatively low solvent power [2]. It is less volatile than petroleum ether [3]. Rubber solvent is primarily a mixture of paraffins (chiefly C5-C8) and aromatics [4,9]. The actual composition will vary depending on the boiling range, the refinery stocks from which the solvent is produced, and the method of preparation. In general, rubber solvent has 70-90% paraffins, 11-22% naphthenes, and 9-22% aromatics [11-14]. A sample of rubber solvent analyzed by Carpenter et al [9] showed 41.4% paraffins, 53.6% monocycloparaffins, 0.1% monoolefins, 1.5% benzene, and 3.4% alkyl benzenes. Additional physical and chemical properties are given in Table XIV-1.

Rubber solvent can be produced from a straight-run petroleum distillate of paraffin base crude [2]. It is used as a rubber cement diluent and as an agent in rubber dope mixing and rubber spreading [2,10].

The United States in 1965 produced 28,857,000 barrels (1 barrel = 159 liters or 42 gallons) of what was described as special naphthas (including rubber solvent and varnish makers' and painters' naphtha), which represented 0.7% of the total production of petroleum products [2]. In 1973, 33,083,000 barrels of special naphthas were produced, 0.7% of the total production of petroleum derivatives [15], in 1974, 33,537,000 barrels or 0.8% of the total production, and, in 1975, 27,325,000 barrels of naphthas [16].

NIOSH estimates that about 600,000 workers in the United States are potentially exposed to all "specialized" naphthas.

(c) Varnish Makers' and Painters' Naphtha

Varnish makers' and painters' (VM and P) naphtha is a mixture of hydrocarbons that has a boiling range of approximately 95-160 C (203-320 F) [1,10,17,18]. It is sometimes known as benzine, Naphtha 76, ligroin, or high boiling petroleum ether [10,18].

Physically, VM and P naphtha is a colorless to yellow liquid that has an aromatic odor [18]. It has a flashpoint (closed cup) of -7 to 13 C (20-55 F) and is classified as a type I B flammable liquid [18]. Its mean molecular weight ranges from 87 to 114 and it is composed of about 45-60% paraffins, 30-45% naphthenes, and 5-13% aromatics [11-14]. A sample of VM and P naphtha analyzed by Carpenter et al [17] showed 55% paraffins, 30% monocycloparaffins, 2% dicycloparaffins, and 12% alkylbenzenes. The hydrocarbon chain ranges chiefly from C7 to C11 [4]. Additional physical and chemical properties are given in Table XIV-1.

VM and P naphtha can be produced from a straight run distillate of paraffinic or mixed base crude [2]. It is used as a quick-evaporating paint thinner of moderate solvent power [2].

NIOSH estimates that about 600,000 workers in the United States are potentially exposed to all "specialized" naphthas.

(d) Mineral Spirits

Mineral spirits are a mixture of hydrocarbons that have a boiling range of 150-200 C (302-392 F) [1,19]. These compounds have also been termed white spirits, petroleum spirits, and light petrol [5,19,20].

Stoddard solvent is considered by some investigators to be synonymous with mineral spirits [19,21].

Mineral spirits are clear, colorless liquids with a "pleasant, sweetish odor," and are very slightly soluble in water [5]. They do not blacken or corrode a clean metallic copper strip in 30 minutes at the boiling point of the mineral spirits [22]. The solvent contains about 30-65% paraffins, 15-55% naphthenes, and 10-30% aromatic hydrocarbons [11-14]. Additional chemical and physical properties are given in Table XIV-1.

This solvent is produced from straight-run naphtha derived from a paraffin-base or mixed-base crude [2]. Mineral spirits are used as a general-purpose thinner, a solvent for paint and varnish industries, and a drycleaning agent [2,5,20].

NIOSH estimates that 61,000 workers in the United States are potentially exposed to mineral spirits.

(e) Stoddard Solvent

Stoddard solvent is a mixture of hydrocarbons, predominantly C9 to C11, that has a boiling range between 160 and 210 C (320-410 F) [1,21,23]. It is a clear, colorless liquid and has a minimum flashpoint of 38 C (100 F) [19,24]. The dry point ranges from 166 to 210 C (330-410 F). Its Kauri-Butanol value ranges from 27 to 45. It is insoluble in water but readily soluble in most organic solvents [19]. Stoddard solvent must be negative on a specific test for mercaptans, and the copper strip corrosion test (ability to blacken or corrode a strip of polished copper placed in the solution) for 3 hours at 100 C (212 F) must be negative [25]. Chemically, Stoddard solvent is a mixture of 30-50% straight and branched chain paraffins, 30-40% naphthenes, and 10-20% aromatic hydrocarbons

[11,14,19,23]. Additional chemical and physical properties are given in Table XIV-1.

While Stoddard solvent and mineral spirits are not always considered the same petroleum products and are used differently for different purposes in industry, their boiling ranges (Stoddard solvent, 160-210 C; mineral spirits, 150-200 C) [1] are almost identical and therefore their chemical compositions are similar. In fact, many investigators use the terms mineral spirits and Stoddard solvent interchangeably, and some consider Stoddard solvent to be a specific type of mineral spirits [3,4,18,19,21].

There are currently four classes of Stoddard solvent: regular Stoddard solvent, 140 flash solvent, odorless solvent, and low end point solvent [24]. The flashpoint, dry-point test (evaporation rate), and odor are used to classify the types of Stoddard solvent [24]. The flashpoint, Kauri-Butanol value, and dry point of four classes of Stoddard solvent are listed in Table III-1.

Stoddard solvent, used primarily as a drycleaning agent [25], can be produced from a straight-run distillate of paraffinic or mixed base crude [2]. It was reported in 1964 that industry uses 150 million gallons Stoddard solvent a year [25]. One gallon of Stoddard solvent will clean about 25-35 pounds of clothes [25]. It was estimated in 1964 that 55% of the volume of drycleaning in the United States is carried out in Stoddard solvent [25].

NIOSH estimates that 75,000 workers in the United States are potentially exposed to Stoddard solvent.

TABLE III-1

CHARACTERISTICS OF THE FOUR CLASSES OF STODDARD SOLVENT

Solvents	Properties					
	Flashpoint (C)		Dry Point (C)		Kauri-Butanol Value (KBV)	
	Average	Range	Average	Range	Average	Range
Regular Stoddard	43	39-51	195	187-209	36.8	30.7-44.5
140 flash	60	59-60	201	189-210	33.0	30.1-35.6
Odorless	52	49-54	198	191-207	27.6	27.2-28.7
Low end point	39	38-42	174	166-183	35.0	28.7-39.0

Adapted from reference 24

Flashpoint values have been used to classify all solvents used in the drycleaning industry and accordingly there are four classes of solvents used in the industry [26]. Class I solvents are flammable liquids having a flashpoint below 38 C (100 F). Class II solvents are flammable liquids with flashpoints at or above 38 C (100 F) but below 60 C (140 F). Class IIIA solvents are combustible liquids with flashpoints at or above 60 C (140 F) and below 93 C (200 F). Class IIIB solvents are combustible liquids with flashpoints at or above 93 C (200 F). Class IV solvents are classified as nonflammable.

Drycleaning plants or systems are classified into five categories according to the solvent used [26]. For example, a class I drycleaning plant would use a class I solvent such as 50 flashpoint naphtha, a class II drycleaning plant would use a class II solvent such as Stoddard solvent, a class IIIA drycleaning plant would use a class IIIA solvent such as 140 flash aliphatic solvent, and class IV and V drycleaning plants or systems would use a class IV solvent such a perchloroethylene. Class I drycleaning plants or systems are prohibited, and class IV and I drycleaning plants or systems do not use the solvents covered in this document.

(f) Kerosene

Kerosene is a mixture of petroleum hydrocarbons, with carbon chain lengths that range from C9 to C16 carbon atoms per molecule and distills between 175 and 325 C (347-617 F) [18,27]. Synonyms for kerosene include astral oil, coal oil, and No. 1 fuel oil [5].

Physically, kerosene is usually a pale yellow or water-white, mobile, low volatile, oily liquid that has a flashpoint (closed cup) of about 38-74 C (100-165 F) and is therefore considered a combustible compound [18]. The composition of kerosene varies depending on the source of crude oil and the method of refining. Kerosene is a complex mixture of aliphatic, naphthenic, and alkylated aromatic hydrocarbons. A typical analysis of kerosene indicates that there are about 25% normal paraffins, 12% branched paraffins, 30% monocycloparaffins, 12% dicycloparaffins, 1% tricycloparaffins, 16% mononuclear aromatics, and 5% dinuclear aromatics [28]. The aromatic content of kerosene ranges from 5 to 20% [27]. The predominant aromatic molecular types include indenes, diphenyls, methylnaphthalenes, and tetralins [27]. Additional chemical and physical

properties of kerosene are given in Table XIV-1.

Kerosene can be produced in a refinery using a straight-run treated distillate from paraffinic or mixed crude, a solvent-treated distillate from paraffinic or mixed crude, or a solvent-treated distillate from aromatic crude [2]. Deodorized kerosene (washed with fuming sulfuric acid, followed by a sodium plumbite solution and sulfur) is a highly refined product of low aromatic content [4], often used in insect sprays [27].

Kerosene is used as a fuel, as a carrier for pesticides, as a weed killer, as a mold release agent in the ceramic and pottery industry, as a cleaning solvent, and in asphalt coatings, enamels, paints, thinners and varnishes [18,27].

The United States in 1965 produced 94,455,000 barrels of kerosene (including range oil) which represented 2.5% of the total production of petroleum derivatives [2]. In 1973, production was 80,126,000 barrels of kerosene, 1.7% of the total production of petroleum derivatives [15]. In 1974, kerosene production declined to 56,891,000 barrels, 1.3% of the total petroleum derivatives [15], and in 1975, 55,673,000 barrels of kerosene were produced [16].

NIOSH estimates that 310,000 workers in the United States are potentially exposed to kerosene.

A number of occupations where a potential for solvent exposure exists are listed in Table XIV-2 [1,2,5,10,19,29-31].

Historical Reports

There have been several instances in which workers cleaning equipment in rubber factories were overcome by solvent vapors [32-34]. Lawrence [33]

suggested that workers might have been intoxicated by solvent fumes if they worked over large tanks of rubber dissolved in naphtha and when room temperature was kept above 32 C (90 F) to aid the evaporation. Kulkow [34], in 1926, described numerous cases of poisoning after a 45-minute breakdown of the ventilation system in a factory which manufactured rubber galoshes, thus causing increased, but unmeasured, concentrations of petroleum naphtha and benzene. Ninety workers were affected and 30 required medical treatment. The type or extent of medical treatment was not reported.

In 1936, Hayhurst [35] reported several incidents of poisoning by petroleum distillates. Four men, 27-49 years old, brushed or submerged wood shingles by hand into a tank containing a solvent composed of one part petroleum naphtha and two parts kerosene (plus 4% creosote) and were exposed to the solvent vapors at an unknown concentration. The only ventilation in the room was from open windows and a door on one side of the room. One worker lost weight, became weak, and developed diarrhea, numbness, vertigo, and gastric disturbances after 11 months of exposure. Two months later, a physical examination showed undescribed cardiac disturbances, neurasthenia, paresthesia, increased respiration rate, and syncopal attacks following all work efforts. The second worker was exposed for 8 months and developed rashes and nervousness. Subsequently, he developed pruritus and low macular-type dermatitis on his arms. The third worker had been exposed to the solvent for 18 months when he showed signs of insomnia, nervousness, itching, and paresthesia. After a 1-year job transfer, the worker returned to the shingle-staining plant. He eventually developed sleeplessness, chronic headache, pain in the eyes, anorexia,

constipation, and nervousness. The fourth worker, who primarily inhaled solvent fumes, had been exposed to the solvent for 2 years before he developed weakness, gastric cramps, constant headache, anorexia, and nervousness. Subsequently, his reflexes became moderately exaggerated, and he developed diarrhea and lost weight. All of these workers were removed from exposure for periods in excess of 1 year. No followup studies of the solvent exposure were reported.

One man, 48 years old, was employed as a painter in an automobile assembly plant where he used mineral spirits as a degreaser and paint thinner [35]. The worker placed his hands in the solvent several times a minute during the working day. The normal workday was 8 hours, but he often worked up to 12 hours/day, 6 days/week. A mechanical ventilation system was in operation, but the solvent odor was still apparent. After about 3 years of steady employment, he quit his job because of ill health. He developed, during the course of his employment, a burning sensation in his nose and throat, "smarting" and watery eyes, headache, dizziness, anorexia, nausea, occasional vomiting, nervousness, prostration, muscle twitchings, loss of strength, and weight loss. Six years later, the man still was weak and thin, and was reported to be mentally incompetent and unstable. However, a report 11 years after solvent exposure indicated that the man was mentally alert and agile but still thin.

Hayhurst [35] also described seven other workers exposed to petroleum naphtha. The workers cleaned metal trays with the solvent in preparation for an enameling process. The work area did not have adequate ventilation. In general, the symptoms included a burning throat, drowsiness, "smarting" eyes, nausea, loss of appetite, headache, and nervousness.

A female worker who washed household appliance parts with naphtha developed dizziness, fainting, anorexia, and nausea after 1 month of solvent exposure [35]. The author reported that "a number of other girls were carried out unconscious from the plant."

Three workers, 27-41 years old, who were employed in a rubber factory and exposed to petroleum benzine for 2-5 years developed signs of solvent intoxication [35], ie, dizziness, headache, numbness of hands and feet, weight loss, anorexia, nausea, anemia, and bleeding from the nose and gums.

In 1938, Schwartz [36] reported the incidence of dermatoses in "basic" industries in the United States. Petroleum naphtha, benzine, and kerosene were reported to have been the cause of 3, 10, and 8 of 3,136 cases of occupational dermatoses. The author stated that exposure to materials of the broad classification of "solvents" caused 11% of the abnormalities that occurred in the United States and that about 1% of the industrial workers were involved.

Effects on Humans

(a) Petroleum Ether

Petroleum ether is primarily composed of pentanes and hexanes [3,4] and several studies have described the toxicity of these alkanes.

In 1953, Kjaer [37] described an incident in which petroleum ether was mistakenly used as an inhalation anesthetic before a craniotomy. A 56-year-old man developed severe clonic convulsions and considerable brain edema during the operation. According to Kjaer, these effects indicated central nervous system (CNS) irritation. The amount of petroleum ether inhaled was undetermined. Six days later, the patient was well enough to

be discharged from the hospital.

In 1970, Spruit et al [38] applied unspecified amounts of petroleum ether to the forearms of volunteers to observe dermal effects. Contact with the skin for 30 minutes caused disruption of the horny layer as indicated by subsequent skin peeling and increased water vapor loss from the injured skin. The average time of exposure before irritation appeared was about 20 minutes.

In 1936, Oettel [39] reported the effect of alkanes (pentane, hexane, heptane, and octane) on the intact skin of five volunteers. Circular glass dishes, 1 cm in diameter, were filled with the solvent and loosely attached to the forearm of each subject for 1 hour. Dermal exposure to these substances produced irritation characterized by erythema, hyperemia, swelling, and pigmentation. When solvent exposure was discontinued, marked increases in erythema and pigmentation accompanied with pain for up to 24 hours and followed by minor increases up to 96 hours were noted. The blistering properties of these solvents were also investigated by attaching dishes containing the alkanes to the thighs of the volunteers for 5 hours. Blisters formed on the alkane exposed areas. In addition, pentane exposure caused a constant burning sensation accompanied by itching. The intensity of these symptoms increased when the subject was exposed to hexane and heptane. No alkanes caused local anesthetic action. As carbon chain length increased, so did the time for pain to abate after the solvent was removed from the skin. Removal of pentane and hexane from the skin reduced pain in 15 and 90 minutes, respectively. After exposure to the alkanes was discontinued, the injured skin recovered with no scarring, and the author [39] concluded that the acute skin irritation was probably caused by

affected nerve endings and by histamine release and that the delayed effects were probably from cell damage and the accumulation of metabolic products.

Several investigators [40-43] have shown that hexane exposure causes polyneuropathy. Yamamura [42], in 1969, reported the effects on sandal makers of exposure to hexane in glue. The concentration of hexane in the air ranged from 500 to 2,500 ppm (1,759 to 8,793 mg/cu m). The initial symptoms included sensory impairment in the distal portion of the extremities in 88% of the subjects; almost 60% had reddish, rough, and cold skin of the distal portion of the arms. Muscle weakness was observed in 14%. Some of the workers with polyneuropathy also experienced loss of appetite, blurred vision, cold sensations of the extremities, general fatigability, headache, and weight loss. Muscle and nerve biopsies were taken from several workers. Light microscopic examination of the muscle tissues showed minimal fatty degeneration of the muscle fibers, diminution of fiber size, and slight proliferation of the sarcolemmal nuclei which indicated neurogenic atrophy and regeneration. Similar examination of the peripheral nerves generally showed demyelination and a milder axonal degeneration.

Inoue et al [44], in 1970, described the results of an analysis of the hexane solvent in the glue used by the sandal makers studied by Yamamura [42]. Gas chromatographic analysis indicated that the solvent contained 2-methylpentane, 3-methylpentane, methylcyclopentane, and n-hexane. The concentrations of the individual constituents were not given. After visiting the worksites of polyneuropathic sandle makers and measuring airborne hexane, the authors [44] concluded that the polyneuropathy was

probably caused by hexane at concentrations below 500 ppm (1,759 mg/cu m).

In 1971, Herskowitz and associates [40] examined three female employees working in a furniture factory who were exposed to n-hexane. These women worked in an enclosed, poorly ventilated room containing an open 189-liter drum of n-hexane solvent. Their job included dipping rags into the open drum and wiping excess glue from finished cabinets. Air samples of hexane were found to average 650 ppm (2,286 mg/cu m) and peaked at 1,300 ppm (4,573 mg/cu m). The subjects first noticed symptoms 2-4 months after beginning work and were admitted to a hospital 6-10 months later, where they complained of one or more of the following symptoms: abdominal cramps, burning sensations, numbness and weakness of the distal extremities, and paresthesia. Physical examination showed bilateral foot-drop gait, bilateral wrist drop, and absence of Achilles tendon reflexes. Biopsies of the sural nerves and the anterior tibial muscles of two of the patients were made. The muscles contained small angulated fibers and other fibers with clear central zones (denervation-type injury). Electron microscopic examination of small bundles of axons from the muscle sections showed that they contained increased numbers of neurofilaments and abnormal membraneous structures with clumping and degeneration of mitochondria, dense bodies, and bulbous formations. Motor-end plates had swollen terminal axoplasmic expansions, increased glycogen granules, dense bodies, large osmophilic membranes, synaptic folds, and vesicles. The sural nerve sections were normal under light microscopy, but electron microscopic examination revealed an occasional injury to myelinated axons. The authors concluded that all three workers showed signs and symptoms of sensorimotor polyneuropathy.

In 1972, Yamada [41] investigated 17 workers reporting symptoms of intoxication from exposure to hexane vapor. Six worked in small polyethylene laminating plants where hexane was vaporized into the workroom air. The airborne hexane concentration ranged from 1,000 to 2,500 ppm (3,417 to 8,793 mg/cu m). Analysis of the hexane solvent showed that it was composed of 16% methyl pentane, 20% methyl cyclopentane, and 64% n-hexane. Eleven of the 17 workers were employed by a pharmaceutical company and used a 95% hexane solution to remove oil from the surface of tablets. The airborne hexane concentration in the center of the workroom was 500 ppm (1,759 mg/cu m), but in the immediate work area the concentration was 1,000 ppm (3,517 mg/cu m). The initial complaints of the workers were reported within 1 month of exposure and included fatigue, followed by, in 1-3 and 6-9 months at the latest, paresthesia in distal parts of the extremities and difficulty in walking. The author reported that the workers displayed signs and symptoms of polyneuropathy, but that the progress of the disease was halted 3 months after the cessation of exposure and gradual recovery took place over 6-30 months.

In 1975, Takeuchi and coworkers [43] reported on four persons exposed to petroleum benzine. These people worked in a brocade sash cleaning shop that had a small, poorly ventilated workroom. The work process involved placement of a brocade sash on a desk and scrubbing with a brush dipped frequently in petroleum benzine. The sash was then hung in the room to dry. The operation was very busy during the winter months and the employees usually washed sashes 12 hours or more a day. Each worker used 9-12 liters of benzine a day. In other seasons, when the plant was not as busy, the employees worked 8-9 hours/day and only 4.5-6 liters/day/worker

were used. The petroleum benzine was reported to contain 13% n-pentane, 12.5% n-hexane, 10% n-heptane, 7.5% n-octane, 3% benzene, 3% toluene, and 57% unspecified components.

A 16-year-old boy who had worked in the plant for 5 months began losing his appetite and weight and suffered from constipation, cold sensations in the lower extremities, and muscle weakness [43]. After 7 months, he had to quit his job because of great difficulties in walking. After leaving, he became worse, developed upper extremity impairment, and could not walk unaided. Two months later, the sensory disturbances of the extremities began to show some improvement, but, since he still suffered from walking difficulties, he entered a hospital. Neurologic examination showed decreased sensation and moderate symmetrical weakness in the hands and feet, and muscle atrophy in the forearms and beneath the midthighs. The tendon reflexes were diminished in all extremities, and the patellar and Achilles tendon reflexes were absent. No Babinski's sign was present. The abdominal skin reflexes were normal. An electromyogram study showed fibrillation voltages in the distal portion of the extremities. The electroencephalogram was normal. Examination of the blood showed no abnormalities. Urinalysis results indicated only increased urobilinogen.

The second investigation involved a 34-year-old man who started working in a brocade sash shop in 1957 [43]. After 7 years, he bought his own shop where he worked 12 hours/day or more. Seven months later, he began losing weight and appetite and suffered from irritability and insomnia. In the autumn of 1965, when business slackened, his health improved, but, during the winter, he developed paresthesia and decreased sensation in the hands and feet. He eventually could not walk or use his

hands. He left work and 5 months later his condition had improved so that he could do manual work, but he still could not walk. Subsequently, it was noted that his condition worsened from winter to spring and improved from summer to autumn. In 1971, neurologic examination showed weakness and atrophy of the small muscles of his hands and feet. Tendon reflexes of the upper extremities and the Achilles tendon reflexes were diminished, but the patellar tendon reflexes were exaggerated. Ankle clonus was found. There was no Babinski's sign. Abdominal skin reflexes were impaired. The cranial nerves and blood showed no abnormalities.

The third instance involved a 17-year-old boy who, after being employed in the brocade sash cleaning workshop for 7 months, began suffering from insomnia, irritability and walking difficulties [43]. He visited a physician who diagnosed his illness as polyneuropathy, but the treatment (unspecified) was not helpful. He became unable to walk and was admitted to a hospital as a suspected case of poliomyelitis. After 3 months, he left the hospital without any improvement in his condition. In the next 13 months, without any treatment, he gradually recovered.

The final investigation involved a 19-year-old woman who worked in the factory for 6 months before she developed irritability, insomnia, and weight loss [43]. Eight months later, she quit her job after walking became difficult. Three months later, her condition improved, and she went to work in another occupation.

Although determination of the air concentrations of petroleum benzine were not made at the time these workers experienced their illness, analysis of the concentrations of petroleum benzine and its major constituents in the workroom air was subsequently made. The resultant values are given in

Table III-2 [43]. The components were analyzed by gas chromatography, but the assumptions made in determining the total petroleum benzine content (last column in table) were not stated. The concentration of petroleum benzine and n-hexane did not exceed 4,400 and 844 mg/cu m, respectively.

TABLE III-2

CONCENTRATION OF VAPOR IN THE BROCADE SASH WORKROOM

Location in Workroom	Solvent Concentration (ppm)				
	n-Pentane	n-Hexane	n-Heptane	n-Octane	Total Petroleum Benzine*
Under worker's nose	210	240	41	15	1,250 (4,400 mg/cu m)
1.5 meters in front of worker	150	150	38	40	895 (2,800 mg/cu m)
2.0 meters to left of worker	90	100	42	33	545 (1,920 mg/cu m)
Near doorway	20	50	26	13	273 (960 mg/cu m)
Under worker's nose with fan operating	50	60	20	20	445 (1,160 mg/cu m)

*Conversions from ppm to mg/cu m are inconsistent and do not reflect a uniform molecular weight assumption. These values reflect the actual data reported by the authors.

Adapted from Takeuchi et al [43]

The authors indicated that, if the concentration of petroleum benzine rose higher than 4,400 mg/cu m, irritation of the mucous membrane would have become unbearable and a narcotic effect would have occurred. The potential effects of dermal exposure, although not measured, could not be disregarded as a potential route of intoxication. The authors felt that these four subjects represented cases of polyneuropathy that were probably caused by n-hexane exposure.

In 1973, Gaultier and associates [45] studied five workers employed in a belt-manufacturing shop and exposed to unknown concentrations of a solvent vapor. The solvent was composed of 80% pentane, 14% heptane and 5% hexane. Three of the workers were examined and reportedly had anorexia, asthenia, paresthesia, fatigue, and bilateral and symmetrical muscle failure. Recuperation was very slow [45]. The authors concluded that alkanes other than hexane may cause polyneuropathy.

For additional information on pentane and hexane toxicity, the reader is referred to the NIOSH document entitled Criteria and Recommendations.... Occupational Exposure to Alkanes.

(b) Rubber Solvent

In 1975, Carpenter et al [9] studied the odor and sensory thresholds of volunteers exposed to rubber solvent vapor. To determine the odor threshold, six volunteers between the ages of 25 and 49 years were exposed for about 10 seconds to a series of concentrations of rubber solvent vapor. The range of the odor threshold was reported to be between 6.4 and 64 mg/cu m (1.6 and 16 ppm) based on a mean molecular weight of 97 calculated from mass spectrometry data and analyzed by gas chromatography as detected 17 and 75% of the time, respectively. The authors suggested that the most

probable odor threshold concentration was about 40 mg/cu m (10 ppm).

Human sensory response in volunteers, 25-60 years old, was determined in daily 15-minute inhalation studies of measured vapor concentrations of rubber solvent ranging from 1,700 to 8,100 mg/cu m (430 to 2,000 ppm) [9]. Eye and throat irritation responses of volunteers exposed to rubber solvent vapor at 1,700 mg/cu m (430 ppm) were all slight and transitory. One out of seven volunteers noted eye irritation, and two out of seven had throat irritation at 3,100 mg/cu m (780 ppm). Eye irritation and headache in two cases each were reported at 6,700 mg/cu m (1,700 ppm) after the discontinuation of exposure. One of six volunteers had the same symptoms at 8,100 mg/cu m (2,000 ppm), and they subsided unaided within 10 minutes after the discontinuation of exposure. The authors concluded that a concentration of 1,700 mg/cu m (430 ppm) could be tolerated without complaint.

(c) Varnish Makers' and Painters' Naphtha

Carpenter et al [17] carried out inhalation studies on volunteers to determine the odor and sensory threshold for VM and P naphtha vapors. The odor threshold was determined in an exposure chamber using six subjects between 25 and 48 years of age. The subjects were exposed to the solvent vapor for 10 seconds at concentrations ranging from 0 to 70 mg/cu m (0 to 15 ppm based on a mean molecular weight of 114 calculated from mass spectrometry data; analyzed by gas chromatography). The odor threshold was estimated to be about 4 mg/cu m (0.86 ppm). The sensory threshold was determined with seven volunteers between 25 and 59 years of age. Exposures were limited to one 15-minute exposure/day at solvent concentrations ranging from 660 to 4,100 mg/cu m (140 to 880 ppm). Olfactory fatigue was

noted at all concentrations. At the highest concentration tested of 4,100 mg/cu m (880 ppm), definite throat and eye irritation was produced.

In 1976, Wilson [46] reported on the effect of petroleum naphtha vapor exposure on humans. A storage tank of petroleum naphtha at a refinery became overheated and the naphtha vaporized and escaped from the tank. What was described as a vapor cloud was reported to have remained close to the ground for a short, unspecified period of time during which individuals were briefly exposed to the vapor. Although the concentration of vapor was not measured, it was sufficiently high enough to stall the engines of two motor vehicles which were driven into the vapor cloud, suggesting to Wilson that a possible oxygen deficiency within the cloud might have occured. The petroleum naphtha had a boiling range of 84-164 C (183-327 F) and was composed of 84% paraffins, 3% olefins, 11% naphthenes, and 2% aromatics, and therefore may be considered similar to both VM and P naphtha and rubber solvent. There was probably little or no benzene in the petroleum naphtha since benzene boils at 80.1 C.

Eighteen of the 19 individuals were examined by Wilson [46] immediately after exposure. They all had labored breathing and two were cyanotic. Several were excited and hyperactive but none were drowsy. There were no signs of burns or irritation of the mucous membranes. The lungs of all the subjects were clear to auscultation. Treatment consisted of oxygen administration, and the labored breathing and cyanosis disappeared. Chest roentgenograms showed no abnormalities. One individual was reported to have premature ventricular contractions. No other individuals had any cardiac arrhythmia. All of the individuals had tremors and complained of mild nausea shortly after cessation of the oxygen

therapy. These symptoms were eliminated by the use of a sedative-antispasmodic drug. All the individuals returned to work 30 minutes after their arrival to the health center except for one older person who had remained in the vapors longer than the others. He was free of symptoms within 30 minutes but was observed a little longer as a safety precaution. Blood counts and urinalyses were made on all of the exposed individuals and the results were all normal. A followup examination after 5 years showed no medical problems that could be attributed to the petroleum naphtha vapor exposure.

(d) Mineral Spirits

In 1958, Kegels [47] reported the effects of white spirits on a 36-year-old man who cleaned floors with copious amounts of the solvent. He had no previous history of serious illness. The man and several women had been exposed to white spirits for at least 4 months. He was constantly surrounded by "clouds" of solvent, but neither airborne measurements of white spirits nor daily exposure times were quantitated. When some women complained of nausea and vomiting, the use of white spirits was stopped. The author indicated that the white spirits boiled between 153 and 185 C and contained 83% paraffins and 17% aromatics.

The man showed no blood abnormalities when medically examined, but 3 months later, he complained of fatigue and pallor [47]. A physician's diagnosis was that he was suffering from overwork. Several months later, the patient still had abnormal symptoms. A second physician performed a blood analysis and sternal puncture and indicated that the subject had either aplastic anemia or aleukemic leukemia. Subsequently, he was

diagnosed as having aplastic anemia with thrombocytopenia and leukopenia (80% lymphocytes and 20% neutrophils).

Treatment consisted of three blood transfusions, but his condition did not improve and he was admitted to a hospital [47]. Signs of purpura on the skin and mucous membranes now appeared. The initial blood analysis showed decreased erythrocytes (2,480,000/cu mm), leukocytes (2,300/cu mm), platelets (34,000/cu mm), and hemoglobin (45%). After several blood transfusions and iron and liver extract injections, the employee's condition improved and he returned to work. However, shortly thereafter, he developed articular rheumatism which was treated with cortisone. He was treated continuously for aplastic anemia and rheumatism by blood transfusions and iron, liver extract, and adrenocorticotropic hormone injections.

About 2 years later, after several intermittent periods of infection, the patient again felt fatigued and weak [47]. Hematologic examination showed severe decreases in erythrocytes (1,710,000/cu mm) and leukocytes (2,800/cu mm). A sternal puncture biopsy examination showed marked hypocellularity. Urobilinogen was present in the urine, indicating signs of liver dysfunction probably caused by hemosiderosis. The subject died a few months later from septicemia. Kegels indicated that this subject probably had a sensitivity to white spirits, since other workers exposed to white spirits did not develop aplastic anemia. The possible role of benzene in the etiology of the disease should be considered, even though the boiling range of white spirits should preclude any benzene being present, since trace amounts of benzene could have been present in the solvent as contaminants.

In 1975, Astrand and associates [48] examined the effects of white spirits on human alveolar air and blood solvent concentrations during rest and exercise. The white spirits used in the study consisted of 83% aliphatic and 17% aromatic components.

Fifteen men, 20-34 years of age, were used in the study [48]. In initial trials, subjects were exposed to 2,500 or 5,000 mg/cu m of white spirits. The concentrations of mineral spirits were determined by gas chromatography. The duration of exposure was not reported. Nausea and vertigo were apparent at both concentrations.

The authors [48] decided that subsequent experiments should be conducted with white spirits at concentrations that ranged from 1,000 to 2,500 mg/cu m to reduce the discomfort of the men and to accurately analyze the solvent content in alveolar air and blood. Five subjects each inhaled both 1,250 and 2,500 mg/cu m of white spirits for 30 minutes at rest and then during exercise at an intensity of 50 watts. Four subjects were exposed at 1,250 mg/cu m for 30 minutes during rest and in three 20-minute exercise periods at intensities of 50, 100, and 150 watts which are equivalent to the amount of energy used in light industrial work, manual labor, and heavy manual work, respectively [49]. Two subjects were first exposed for 30 minutes to 2,500 mg/cu m of white spirits in atmospheric air (20.90% oxygen, 0.04% carbon dioxide, and 79% nitrogen) and then to the solvent in a mixture of 21% oxygen, 4% carbon dioxide, and 75% nitrogen during a 30-minute rest period and a 30-minute exercise period (intensity of 50 watts). Two subjects were exposed to white spirits at 1,250 mg/cu m in the air for 30 minutes during rest followed by three 30-minute exposures during exercise at an intensity of 100 watts. The two remaining subjects

were each exposed at rest to 1,000, 2,500, 1,500, and 2,000 mg/cu m for one 30-minute period. The white spirits concentration or work rate changes were made after each 30-minute period without interrupting exposure. Alveolar air samples were collected during exposure, and arterial and venous blood samples were taken from preplaced catheters in the brachial artery and medial cubital vein, respectively. Heart rate and blood lactic acid content were determined in some subjects at the end of each exposure period. Cardiac output, oxygen uptake, and volume of expiratory and alveolar air were determined in all subjects after 20 minutes of each exposure period.

During exercise, three subjects had occasional premature atrial beats as shown by electrocardiograms; however, they were of the same type as those observed during rest [48]. One man developed premature atrial beats exclusively in conjunction with solvent exposure (concentration not reported). Another displayed gradual flattening, and, ultimately, inversion of the T wave during exposure to white spirits. This subject had no symptoms, and the electrocardiogram became normal a few days after solvent exposure (concentration not reported). No differences were noted in heart rate, alveolar ventilation, or oxygen uptake either at rest or during exercise at an intensity of 50 watts during exposure at 1,250 and 2,500 mg/cu m of white spirits. Cardiac output was normal at rest and increased in an normal manner as work increased during exposure at 1,250 and 2,500 mg/cu m of white spirits. Blood lactate content was unaffected by white spirits exposure.

The authors [48] found that the concentrations of aliphatic and aromatic white spirits components in the air and blood differed

considerably. After a 30-minute exposure at rest to white spirits at 1,250 mg/cu m (1,038 mg/cu m of the aliphatic component), the concentration of the aliphatic component in the alveolar air was 255 mg/cu m (25% of the concentration in the inhaled air). The corresponding arterial and venous blood concentrations were 1.7 and 1.3 mg/kg, respectively. During the 50-watt exercise, the alveolar aliphatic component concentration increased to about 515 mg/cu m or about 50% of the concentration in the inhaled air. The arterial and venous blood concentrations were 3.5 and 2.4 mg/kg, respectively. During exposure at rest to about 210 mg/cu m of the aromatic components of white spirits (at a white spirits concentration of 1,250 mg/cu m), the aromatic concentration in the alveolar air after 30 minutes was about 30 mg/cu m, about 15% of the concentration in the inhaled air. The corresponding arterial and venous blood concentrations were both 0.2 mg/kg. During exercise at 50 watts, the alveolar concentration of the aromatic components increased to about 20% of the concentration in the inhaled air. The aromatic component concentrations in the arterial and venous blood were 0.9 and 0.6 mg/kg, respectively.

Exposure to white spirits at a concentration of 2,500 mg/cu m (2,075 and 425 mg/cu m of the aliphatic and aromatic components, respectively) at rest produced alveolar concentrations of the aliphatic and aromatic components of 563 and 56.4 mg/cu m, respectively [48]. The arterial and venous aliphatic component concentrations were 3.4 and 2.2 mg/kg, respectively, while the arterial and venous aromatic components concentrations were 0.6 and 0.4 mg/kg. Alveolar air and arterial blood concentrations of the aliphatic components after white spirits exposure at 2,500 mg/cu m during exercise were approximately double those at the

resting level. The aromatic components in the alveolar air during exercise, however, were only 50% of those at the resting level. The increases in the aromatic components of the arterial and venous blood during exercise were similar to those seen for the aliphatic components.

When exercise intensity was increased successively to 150 watts during exposure to white spirits at a concentration of 1,250 mg/cu m, the alveolar aliphatic component concentration rose in steps from 256 to 622 mg/cu m, while the aromatic components rose from 28 to 59 mg/cu m [48]. In general, the alveolar concentrations of the aliphatic and aromatic components of white spirits in these studies leveled off after 10 minutes exposure and remained relatively unchanged during the rest of the exposure period. In contrast, the arterial and venous blood concentrations rose continuously throughout each exposure. The blood concentrations did show a plateau only after exposure at 1,250 mg/cu m of white spirits for 90 minutes.

In these studies, the authors [48] found a linear relationship between the arterial and alveolar concentrations of the aliphatic and aromatic components; the venous concentrations paralleled arterial concentrations. The total uptake of the aliphatic and aromatic components by the subjects was determined at rest during four consecutive 30-minute exposure periods. The uptake values were 59, 53, 47, and 46% of the total amount of the aliphatic components and 70, 64, 59, and 58% of the total amount of the aromatic components. During 50-watt exercise, the uptake was about 39% for the aliphatic components and 69% for the aromatic components. Thus, the proportion of aliphatic to aromatic components taken up decreased during exercise. However, the total uptake, measured in milligrams/period

of exposure, was slightly greater during exercise than at rest for both the aliphatic and aromatic components.

Astrand et al [48] concluded that measuring the solvent content of the inhaled or alveolar air was less reliable than measuring the blood concentration of aliphatic and aromatic components when assessing uptake, since the aliphatic components reacted as if they were not very soluble in blood while the aromatic components were relatively soluble. The authors noted that more solvent reached the blood during exercise than during rest. Thus, as would be expected, the degree of physical activity associated with a worker's job may influence solvent vapor toxicity.

In 1975, Gamberale and coworkers [50] studied the effects of exposure to white spirits (mineral spirits) on humans. Performance tests were conducted in perceptual speed, reaction time, short-term memory, numerical ability, and manual dexterity. Two sets of experiments were performed. In the first experimental series, 14 men, 18-34 years of age, were separated into 2 equal groups. One group was first studied under experimental conditions with exposure to white spirits and then, 7 days later, with exposure to air. The subjects in the second group were studied in a similar manner but in the reverse order. Under the experimental conditions, the first group was exposed to white spirits at 625, 1,250, 1,875, and 2,500 mg/cu m for four consecutive 30-minute periods. The concentration was increased after each 30-minute period without interrupting exposure. Gas chromatography was used to determine the white spirits concentration. The white spirits were supplied through a low air resistance breathing valve and mouthpiece. The presence or absence of white spirits was disguised by the introduction of menthol crystals into

the mouthpiece, since previous studies indicated that the subjects might taste and smell the solvent [48] which might, therefore, influence the experimental results. The five performance tests were always carried out in the same sequence during the final 20 minutes of each exposure period. Alveolar air samples were taken every 5 minutes and heart rate was monitored. At the termination of the experiment, the subjects were asked several questions to ascertain their perception of the experimental conditions.

From the answers to these questions, the authors [50] concluded that exposure to white spirits probably did not affect the subjective reactions in the psychologic experimental series. No difference in the heart rate of the subjects was noted between treatment and control situations. There was no impairment of the five performance tests as a result of solvent exposure. The resulting air concentrations of aliphatic components of the white spirits were about 175, 300, 450, and 600 mg/cu m at the 625, 1,250, 1,975, and 2,500 mg/cu m exposures, respectively; aromatic component concentrations at these exposures were about 25, 40, 50, and 75 mg/cu m. The solvent vapor concentrations were determined by gas chromatography.

In the second experiment [50], eight of the subjects who participated in the first experiment were exposed to 4,000 mg/cu m of white spirits for 50 minutes. During the final 20 minutes of exposure, the same performance tests used in the first experiment were performed. The subjects were also studied under control conditions without exposure to white spirits, as in the previous experiment. Half of the subjects were studied during control conditions 2 days before and the other half 2 days after the experimental trial. White spirits had no effect on perceptual speed, numerical ability,

and manual dexterity [50]. There was, however, a definite prolongation of reaction time and a possible impairment of short-term memory as a result of exposure at 4,000 mg/cu m. The alveolar concentrations of the aliphatic and aromatic components of the white spirits were about 850 and 100 mg/cu m, respectively.

(e) Stoddard Solvent

In 1940, Braunstein [51] reported that a 26-year-old man who worked in a drycleaning factory and had his forearms and hands wetted with or immersed in Stoddard solvent during most of the workday developed follicular dermatitis of the exposed skin after 2 weeks of employment. In the following 1 or 2 weeks, he felt nauseated after inhaling the fumes in the workroom. He continued to work in the factory for about 8 weeks longer before seeking medical aid after yellowing of the skin and four or five vomiting episodes had occurred. He was admitted to a hospital about 3 months after his first exposure to solvent.

The patient felt weak and had lost 6 pounds during the previous 2 months; however, he regained this loss by the time of discharge from the hospital 1 month later [51]. Abnormalities shown by physical examination were jaundiced skin and eyes and a moderately enlarged liver. Temperature, pulse, and respiration values were normal. A roentgenogram of the abdomen was normal. He had an increased serum icteric index, decreased glucose tolerance, and increased erythrocyte resistance to hemolysis. The urine had traces of albumin, sugar, and urobilin; the feces contained bile. The blood urea nitrogen (BUN) content was increased; total erythrocyte count and hemoglobin value were decreased; total leukocyte count was normal; and some abnormal-sized erythrocytes were noted. A skin sensitization test

with Stoddard solvent was "highly" positive. The diagnosis was obstructive jaundice originating in the liver parenchyma and subacute yellow atrophy of the liver. In the next 3 weeks, the values for bile retention gradually returned toward normal and the dermatitis disappeared. One year later, the blood icteric index was again elevated, which, in the opinion of the author, meant that the man had latent jaundice and possibly permanent liver damage.

The clinical histories of four people reported to have aplastic anemia as a result of exposure to Stoddard or Stoddard-like commercial solvents were discussed by Scott et al [52] in 1959. Three of the subjects died. In the first fatality, a housewife used a Stoddard-type solvent as well as carbon tetrachloride for spot-cleaning household rugs two or three times a month for 2 years before excessive uterine bleeding and purpura appeared. No history of exposures other than to the two mentioned solvents could be obtained. A bone marrow smear was classified as hypocellular, ie, there were 4% normoblasts, 26.5% lymphocytes, 4% plasma cells, no megakaryocytes, and a myeloid/erythroid ratio of 5:1. A sternal bone marrow biopsy showed moderate hypoplasia, since there was a slight decrease in the overall number of cells and an increased number of lymphoid elements. At autopsy, focal hyperplasia was found.

The second fatal case was a high school student who had cleaned his hands in Stoddard solvent, four or five times/week, during a 6-month course in automotive mechanics [52]. He had been taking tripelennamine hydrochloride and diphenhydramine hydrochloride, both reported by the authors to be potential myelodepressants, for several years for his seasonal allergy. Two months after the automotive mechanics course ended,

the student became bruised easily and had symptoms of anemia. The patient's bone marrow aspirate smear was hypocellular: 34.0% normoblasts, 34.5% lymphocytes, 0.3% plasma cells, decreased megakaryocytes, and a myeloid/erythroid ratio of 1:1. A sternal bone marrow biopsy showed marked hypoplasia since there was severe hypocellularity with a predominance of lymphoid elements. The autopsy report indicated moderate hypoplasia with all normal elements present.

The third fatal case was a man who periodically over 2 years used Stoddard solvent to remove paint from his hands [52]. The patient denied using other potentially toxic agents. An episode of purpura, pallor, and fatigue occurred 1 year before his illness was first recognized, and it apparently subsided spontaneously. There was no clear chronologic relationship between the intermittent symptoms and the periods of exposures to the solvent. The bone marrow aspirate smear was classified as slightly hypocellular: 14.5% normoblasts, 35.7% lymphocytes, 1.0% plasma cells, decreased megakaryocytes, and a myeloid/erythroid ratio of 3.2:1. Autopsy findings showed marked hypoplasia of the bone marrow with alternating areas of aplasia and hypercellularity resulting from an increase in lymphoreticular elements.

The fourth patient was a housewife who had used a Stoddard-type solvent as a drycleaning agent for 20 years [52]. Once every year, she immersed the family clothing in a large open tub containing the solvent, usually working indoors. Nothing else in the woman's medical history indicated other types of exposure that could have resulted in her illness. The patient's bone marrow smear was classified as normal in cell number: 63.9% normoblasts, 13% lymphocytes, 2.3% plasma cells, decreased

megakaryocytes, and a myeloid/erythroid ratio of 0.3:1. The sternal bone marrow biopsy showed normal bone development with an increase in the lymphoid elements. After splenectomy, which was also performed on the first and third patients, this patient's condition improved and she was listed as surviving.

The authors [52] concluded that these four cases implicated Stoddard-type solvents as possible myelotoxic agents capable of producing aplastic anemia. However, they gave no information on the composition of the solvent and were thus not in a position to rule out a possible role of myelotoxic compounds such as benzene.

In 1970, Prager and Peters [53] described a 41-year-old man who had been frequently exposed to "Solvasol #5," a Stoddard-type solvent, for 16 years in the course of his employment as a heavy-equipment mechanic. The patient had been well until 3 months before his admittance to the hospital, during which period he felt progressively more tired and lightheaded and bruised easily. Physical examination showed diffuse petechiae and some ecchymotic areas of the skin. No enlargement of the liver or spleen was found by palpation. Blood tests showed an initital hemoglobin level of 7.9 g%, a hematocrit reading of 22%, and a leukocyte count of 2,000 cells/cu mm with 18% segmented cells, 77% mature lymphocytes, 3% atypical lymphocytes, and 2% monocytes. The platelet count was 9,000 cells/cu mm. A sample of sternal bone marrow showed no marrow particles. Bone marrow taken from the ilium showed a marked decrease in the number of cells and in all cellular elements. The results from the following laboratory tests were either negative or normal: buffy coat smear, leukocyte alkaline phosphatase, haptoglobin, fluorescent antinuclear antibodies, and thrombin. The patient

was diagnosed as having aplastic anemia. He died 11 months later. Post-mortem examination showed a diffuse intracerebral hemorrhage of the right occipital lobe. The bone marrow smear showed a marked decrease from normal in the number of cells and in all cellular elements. The authors suggested that Stoddard solvents, although presumably free of benzene because of the solvent's boiling range, might contain a myelotoxic agent which remains to be identified.

Grant [54], in 1974, reported that Stoddard solvent was essentially innocuous to the human cornea. No details were given.

However, in 1943, Nelson et al [55] had described the subjective sensory responses (eye, nose, and throat irritation) of 10 men and women to Stoddard solvent at a given concentration for 3-5 minutes. The authors had observed that solvent concentrations greater than 400 ppm were irritating to the eyes, nose, and throat of most subjects. The concentration that volunteers thought would be satisfactory (presumably in terms of comfort) for an 8-hour exposure was less than 400 ppm. No analytical method or assumption on molecular weight was reported; however, if the average molecular weight were 140, the equivalent concentration would be 2,290 mg/cu m.

In 1975, Carpenter and associates [21] used six volunteers, ages 25 to 48, to determine the odor threshold for Stoddard solvent. The volunteers were exposed to Stoddard solvent at graded concentrations ranging from 0 to 50 mg/cu m (0 to 9 ppm) based on a mean molecular weight of 144; this weight was calculated from mass spectrometry data and analyzed by gas chromatography for 10 seconds. The odor threshold was between 0.5 mg/cu m (0.09 ppm) and 5 mg/cu m (0.9 ppm). The sensory threshold to

vapors of Stoddard solvent was determined for six volunteers, ages 25-59. The volunteers were subjected to the solvent at concentrations of 140, 850, and 2,700 mg/cu m (24, 150, and 470 ppm) for a 15-minute exposure. No eye irritation was noted at 140 mg/cu m, but slight and transitory eye irritation occurred in one of six volunteers at 850 mg/cu m (150 ppm). At 2,700 mg/cu m (470 ppm), all six experienced eye irritation, three with tearing. Slight dizziness also was reported by two subjects at the 2,700 mg/cu m concentration (470 ppm). Olfactory fatigue occurred at all concentrations tested. Volunteers who experienced olfactory fatigue recovered full acuity within 10 minutes after they were removed from exposure.

In 1975, Carpenter et al [56] examined the odor and sensory thresholds to 140 flash aliphatic solvent, a type of Stoddard solvent, in humans. To determine the odor threshold, a group of six volunteers, 22-49 years old, inhaled the solvent at a series of vapor concentrations for about 10 seconds each in the following sequence: 4, 0.4, 0, 40, 4, 0, 40 and 0.4 mg/cu m. Sixty percent of the volunteers perceived the 4 mg/cu m concentration (0.6 ppm), but none could detect the 0.4 mg/cu m level (0.06 ppm based on a mean molecular weight of 154, calculated from mass spectrometry data and analyzed by gas chromatography).

The sensory threshold was determined in six subjects, 22-61 years old. They inhaled the 140 flash aliphatic solvent at concentrations of 110 mg/cu m (17 ppm) and 310 mg/cu m (49 ppm) for 15-minute periods. The solvent was inhaled at each concentration once daily for 2 days. Slight dryness of the eyes was reported by one of the subjects during the inhalation of 110 and 310 mg/liter (17 and 49 ppm, respectively) of the

solvent. This response did not persist after exposure ended. No other volunteers reported discomfort at either solvent concentration. Olfactory fatigue occurred within the first 6 minutes of inhalation of the solvent at either concentration. The volunteers stated that exposures at concentrations of 110 or 310 mg/cu m would be acceptable for an 8-hour workday.

(f) Kerosene

In 1939, Cavanagh and Wilner [57] described a case of aplastic anemia in a 59-year-old woman who, for several months before the onset of her illness, rubbed household kerosene on her legs every night as a remedy for "stiff joints." Her initial complaints were shortness of breath, weakness, easy fatigability, and several unaccountable nosebleeds. She also discovered black and blue marks scattered over her body. These symptoms gradually progressed until she required bedrest. Physical examination revealed that the patient was obese and had a waxy pallor. Her blood pressure was 120/80, pulse rate was 80 beats/minute, and respiration rate was 20 breaths/minute. There were no heart or lung abnormalities. The liver was palpable.

The patient was hospitalized for 4 months before succumbing to a gas gangrene infection [57]. During this period, frequent nosebleeds occurred and there were marked weakness and mental depression. The erythrocyte count ranged from 950,000 to 3,400,000; abnormal erythrocytes were observed several times. Hemoglobin content varied from 14 to 64%, the leukocyte count diminished progressively, reaching 900 with decreased neutrophils predominating, and the platelet count never exceeded 10,000. At autopsy, the sternal bone marrow showed a marked aplastic state that involved

primarily granulocytes and platelets. The authors suggested that the aplastic anemia seen in the patient may have been the result of the aromatic hydrocarbon content of the kerosene, but they gave no supporting detail.

In 1955, Johnson [58] related the case of a 58-year-old man exposed to a degreasing solvent containing kerosene. This man, who was hospitalized in April 1955 and expired in June 1955, was employed from 1928 to 1930 in a factory plating lead batteries. When "lead poisoning showed up in the blood," he was transferred from that job. From 1952 to 1955, he worked in a machine shop where his job involved delivering airplane parts, and he also spent 3 or 4 days every week degreasing airplane parts. Usually, he immersed his hands in a solvent composed of 29 parts kerosene and 1 part paraffin jelly, cosmoline, the latter being incorporated for the purpose of reducing skin irritation. In February 1955, the man began having fever, chills, coughing, and pleuritic chest pain and was hospitalized. Severe anemia was diagnosed. The patient was treated with 10 blood transfusions, penicillin, and tetracycline. He returned to work in spite of continued chest pain and intermittent fever and felt progressively weaker and fatigued. In April 1955, he was rehospitalized with persistent blood-stained sputum and fever and was transferred to another hospital where he died in June. The patient's illness was diagnosed as typical hypoplastic anemia with pancytopenia and hypoplastic marrow with no evidence of leukemia. Johnson considered it probable that this patient had a particular sensitivity to the solvent. Further, she suggested that benzene or other aromatic compounds were components of kerosene and might have been responsible for the blood effects, but she did

not have quantitive data on the benzene content.

Hiebel et al [59], in 1963, found three incidents of bone marrow suppression associated with dermal and oral exposure to kerosene. The first incident involved a 52-year-old woman who, for 34 years, had applied kerosene poultices to a painful lumbar area about two or three times a year. The poultices were prepared by soaking cotton balls with kerosene, applying them to the back with adhesive tape and leaving them in contact with the skin for 1-3 days until blistering occurred. The patient had on two occasions mixed kerosene with sugar, ignited the mixture, and, after the flame had extinguished itself, ingested the charred sugar. On physical examination, the patient was noted to be obese and to have hypertension. Hematologic examination showed an erythrocyte count of 1.99 million cells/cu mm, a leukocyte count of 5,850 cells/cu mm (42% neutrophils, 4% immature neutrophils, 4% eosinophils, 36% lymphocytes, 13% monocytes, and 1% basophils), and a normal platelet count. A sternal bone marrow smear was slightly hypocellular. Erythropoiesis was greatly depressed and both eosinophils and lymphocytes were increased. Study of the bone marrow suggested a lymphoma. The diagnosis was aplastic anemia from long-term exposure to kerosene.

The second incident involved a 71-year-old male who had generalized aches and pains in most of his joints for the preceding 3 years and had treated these with a kerosene massage two or three times a week [59]. The patient had a hemoglobin level of 11.2 g/100 ml, an erythrocyte count of 3.84 million cells/cu mm, a leukocyte count of 1,750 cells/cu mm (24% neutrophils, 5% immature neutrophils, 11% lymphocytes, and 10% monocytes), and a platelet count of 366,000 cells/cu mm. Bone marrow specimens were

hypocellular. The authors suggested that the decrease in neutrophils resulted from kerosene-induced bone marrow suppression.

The third incident involved a 52-year-old woman who took a teaspoon of kerosene and sugar to treat her colds [59]. She averaged three colds a year, and she had used this cold remedy for approximately 45 years. In addition, for about 40 years, she had used a dust cloth saturated with kerosene to clean her furniture. The patient's blood pressure was 180/100 mmHg. Analysis of the blood showed a hemoglobin level of 14.1 g/100 ml and a leukocyte count of 2,500 cells/cu mm (36% neutrophils, 49% lymphocytes, 13% monocytes, and 2% eosinophils). The bone marrow was hypocellular with normoblastic erythropoiesis, "toxic" granulopoiesis, and increased eosinophils. The diagnoses were leukopenia secondary to kerosene exposure, essential hypertension, and arteriosclerotic heart disease. The possibility of exposure to aromatic hydrocarbons as components of the kerosene was not commented upon by the author.

In 1947, Klauder and Brill [60] described the effects of kerosene on human skin. Kerosene of a paraffinic nature (composition not given) was applied in a patch test to an unspecified site on 20 white and 14 black subjects. In performing the patch test, six drops of kerosene were applied to a piece of gauze (1-inch square) and then placed on the skin. The gauze was covered with wax paper and kept in contact with the skin for 24 hours. The skin was then graded from 0 to 4+ (1+, mild erythema; 2+, well-defined erythema; 3+, erythema with edema, and with or without a few blisters; and 4+, erythema, edema, and many blisters, or serous exudation.)

All of the white subjects reacted to the paraffinic type kerosene: 4 had reactions of 2+ or less, 10 had 3+ reactions, and 6 had 4+ reactions

[59]. Of the 14 black subjects tested, six did not react, seven had reactions of 2+ or less, and one had a 4+ reaction. Patch tests were also performed with a naphthenic-type kerosene (composition was not specified) on white subjects. All reacted positively, and seven had 4+ reactions.

The authors [60] concluded that the skin of black subjects was more resistant to kerosene-induced irritation than the skin of white subjects and that naphthenic kerosene was a greater irritant than paraffinic kerosene. They found that, of the substances tested, solvents boiling below 232 C (450 F) were primary irritants and indicated that the correlation of boiling range with irritant action applied to the paraffin type of petroleum products and not to the naphthenic type or highly aromatic products, whether derived from petroleum or other sources.

In 1973, Tagami and Ogino [61] reported four cases of dermatitis caused by kerosene. The first case involved an 8-year-old boy who had handled kerosene the previous night. On physical examination, a strong smell of kerosene was noted. There was a well-defined reddened area on the arm topped with a large, sterile, 2 cm, soft, pus-containing blister and scattered smaller blisters. The second case was a 2-year-old boy who complained of soreness in the genital region about 10 hours after playing with a kerosene can. Physical examination was made the following day and showed diffuse well-defined redness and swelling in the genitocrural region. There were two denuded areas with tiny, soft elevations of the skin containing pus. The third case concerned a 2-year-old girl who had played with a kerosene pump. She complained of burning on the right arm the following day. Physical examination showed diffuse redness near the elbow with a scattering of small pus-containing blisters and a large area

of denudation. A definite odor of kerosene was perceived on the skin. In the fourth case, a 15-year-old boy noted a burning eruption on his neck with a well-defined reddened area with small pus-containing blisters, a day after he handled kerosene. The neck portion of his sweater smelled of kerosene. Oral and dermal corticosteroids brought about improvement of the skin irritation.

To experimentally reproduce the four previously described clinical cases, Tagami and Ogino [61] performed several studies on the effects of dermal kerosene administration. The forearm of one volunteer was exposed in a patch test to kerosene. One hour after kerosene application, a burning sensation developed and was followed at 2 hours by slight redness. By 7 hours, the skin was very tender and red, extending beyond the patch test site. A large firm blister with several small blisters was observed at 12 hours, but there was no longer any burning sensation. After 24 hours, the large blister became soft and filled with pus. The blister broke easily leaving a raw surface. The authors concluded that the experimental lesion corresponded with those seen in clinical cases of kerosene dermatitis.

Tagami and Ogino [61] also used patch tests to study the effects on skin of different concentrations of kerosene. Refined kerosene was used as the test material and diluted to 40, 55, 70 and 85% concentrations in mineral oil. The subjects were 22 white and 12 black adult male volunteers. About 0.1 ml of the material was placed on a 1.5-sq cm cloth and then sealed to the midback skin under impermeable plastic tape. After 24 hours, the patches were removed and the skin was graded on a scale of 0-5 for irritation.

All volunteers showed skin irritation to the 85% kerosene solution [61]. The 70 and 55% kerosene solutions caused skin irritation in 85 and 24% of the volunteers, respectively. No skin irritation was reported at the 40% kerosene concentration. The authors noted that 85% kerosene was more toxic to the skin of whites than to the skin of blacks, 2.95 versus 2.50. Microscopic examination of skin biopsy samples were made 7 and 24 hours after kerosene application. At 7 hours, there were intercellular and intracellular edema, pyknosis, and eosinophilic cytoplasm of the upper epidermal cells. Dense perivascular lymphocytic infiltration was observed in the upper dermis. After 24 hours, the epidermis showed prominent spongiosis, exocytosis, and blister formation. The blisters were intraepidermal, often subcorneal. The intravesicular cells were composed of lymphocytes with some eosinophils and neutrophils.

Tagami and Ogino [61] also investigated the effect of age and the influence of skin region on kerosene-induced skin irritation. To assess the effect of age on kerosene-induced skin irritation, young male whites, 21-31 years old (average 26.4), and 10 older male whites, 58-82 years old (average 68.3), were patch-tested with 85% kerosene on the midback. No significant differences in skin irritation were noted between the age groups. To assess the influence of skin region on kerosene-induced skin irritation, patches of 85% kerosene were applied for 24 hours on the midback, abdomen, forearm, forehead, and lower leg of nine male blacks. The results indicated that the forehead was the least susceptible region. The authors suggested that the decreased sensitivity of the forehead to kerosene was caused by the extensive blood supply of this region which rapidly removed kerosene from the skin before extensive damage could occur.

To test this possibility, four subjects were given patch-tests with 85% kerosene on a site previously injected intradermally with 0.1% naphazoline hydrochloride, a vasoconstrictor, at a dose of 0.1 ml in normal saline [61]. Seventy-five percent of the volunteers showed more pronounced skin irritation on the naphazoline-treated area. Thus, the extent of skin irritation was related to blood flow through the exposed area.

Using 17 subjects previously exposed topically on the midback to an 85% kerosene-15% mineral oil mixture, Tagami and Ogino [61] studied the permeability of the stratum corneum to a solution of 1.5% 3,3,4,5-tetrachlorosalicylanilide (TCSA) in ethylene glycol monomethyl ether. No correlation was found between skin irritation and the penetration time of TCSA, and the authors concluded that irritability was related to the inherent reactivity of the skin.

In 1973, Lupulescu et al [62] described the effects on the ultrastructure of the skin of six men from dermal applications of kerosene. Four small glass tubes, each containing about 1 ml of kerosene, were taped in a vertical position on the forearms. The kerosene was left in contact with the skin for 30 or 90 minutes. Skin sections, 4 mm in diameter, were removed from two of the sites on each man's arm immediately after exposure; similar sections were removed 72 hours later. Control specimens were taken from each subject before exposure. The test sites were not cleaned either before or after the procedure. The samples were fixed and examined with an electron microscope at magnifications of 5,600-18,000 X.

Specific changes were observed in the skin ultrastructure after the 90-minute skin exposure to kerosene [61]. The number of skin horny layers was reduced and the keratin pattern was disorganized in the samples taken

immediately after exposure. Large lacunar formations which contained fibrils in their lumina were present. The plasma membranes appeared thick and some horny cells were disrupted and disintegrated. Some keratinocytes were severely damaged, cell membranes were thick and disrupted, and tonofilaments were clumped. Advanced cell damage was seen in the stratum spinosum. Several spinous cells were undergoing destruction, and most of the cytoplasm appeared homogenous and structureless. The nuclei were reduced in size and indented with peripheral chromatin. A fine granular material had largely replaced the cytoplasm. The nucleus was elongated and poor in chromatin and contained a granular-globular structure. In the 72-hour samples, Langerhans cells retained their ultrastructural pattern. No mitotic figures were observed. Skin specimens examined 72 hours after the 90-minute exposure were similar to those of the controls. The skin that was exposed to kerosene for only 30 minutes showed appreciably fewer changes than the skin exposed for 90 minutes. Few cells underwent destruction or vacuolation. The intracellular spaces were enlarged and the desmosomes were disrupted. The changes seen in the stratum corneum were similar to those seen after the 90-minute kerosene exposure, but were less pronounced.

The authors [62] concluded that exposure of the skin to liquid kerosene caused large lacunae in the horny spinous cells and marked nuclear changes after the 90-minute exposure. Both the stratum corneum and stratum spinosum were affected by kerosene. While intercellular edema and disruption of the tonofilaments occurred in many types of epidermal damage, Lupulescu and associates considered the observed changes in the keratin pattern to be specific effects of liquid kerosene exposure.

In another 1973 report, Lupulescu et al [63] described the penetration and transport of kerosene. Human skin (healthy and psoriatic) was exposed to tritiated kerosene for 90 minutes. Electron microscopic autoradiography findings showed that most of the kerosene was present over the horny layers, in the intracellular spaces of the stratum spinosum, and between desmosomes. Kerosene was also found surrounding the nuclear chromatin of spinous cells. In the authors' opinion, the presence of labeled kerosene in the nucleus suggested that the solvent may have interfered with mitosis. Forty-eight hours after exposure to kerosene, only small traces of the solvent were found and these were located near the collagen fibers in the upper corneum. The only major difference between healthy and psoriatic skin was that, in the latter, more kerosene was seen between collagen fibers. From this observation, Lupulescu and coworkers suggested that a more rapid penetration of the solvent had occurred through psoriatic skin.

In 1975, Lupulescu and Birmingham [64] used electron autoradiographic techniques to study the effects of kerosene on DNA, collagen, and protein synthesis in humans. The effects of kerosene, which was administered dermally at a dose of 1 ml on the forearm, were measured in terms of DNA incorporation of tritiated methylthymidine, collagen incorporation of tritiated proline, or protein incorporation of tritiated leucine during the respective syntheses of these cellular components. Quantitative analysis after the concomitant administration of tritiated leucine intradermally at a dose of 20 microcuries, after 90 minutes of exposure, showed a marked decrease in silver grains in the photographic plate as compared with controls or untreated areas, indicating a decrease in protein synthesis in

the exposed areas. Intradermally injected tritiated methylthymidine at a dose of 20 microcuries or tritiated proline at a dose of 20 microcuries was used to examine the effects on DNA and on collagen synthesis, respectively. Analysis of electron microscopic autoradiograms after 90 minutes of exposure showed that kerosene had no effect on either DNA or collagen synthesis. Thus, the authors concluded that the dermal cellular damage resulting from kerosene exposure was probably caused by inhibition of protein synthesis.

In 1952, Downing [65] reported a clinical case in which an epidermoid carcinoma developed on the dorsum of the left hand of a 63-year-old man, who had been employed as a grease-pit worker at a service station for 20 years. (The article stated 20 years in the case report and 30 years in one of the figures.) His job entailed cleaning trucks with gasoline and performing general maintenance work with kerosene and various other unspecified solvents. Prior to May 1947, a large lump developed on the back of the worker's left hand. The lump was surgically removed and microscopic analysis of the excised tissue showed that the lump was a epidermoid carcinoma. Since the initial surgery, the man had returned to work and had persistent dermatitis on both hands; keratoses and benign epitheliomas, as well as small recurring epidermoid carcinomas, had developed. In addition, the man received x-ray therapy on his left hand. While not stated in the article, it is believed that the x-ray therapy was initiated when the smaller lesions occurred.

The data presented in this case report [65] are insufficient to implicate kerosene as the agent that caused the epidermoid carcinoma, as gasoline and many other undefined solvents were used by the worker. In

addition, there was no medical or occupational history prior to the man's employment at the service station.

Grant [54], in 1974, has commented that kerosene and deodorized kerosene were essentially innocuous to the human cornea. No details were given.

In 1964, Davies [66] cited an incident of a man becoming intoxicated from inhaling jet fuel vapor. The jet fuel was type JP-4 and was described as being more like the composition of kerosene than that of gasoline. No other composition data were given. The 32-year-old male pilot was in flight for 7 minutes when he began to feel groggy and weak. He immediately started breathing 100% oxygen and subsequently the oxygen was filtered through water and under pressure, but there was only a slight alleviation of the symptoms. The pilot also noted that the engine was making an unusually loud noise and he decreased power. A distinct but unidentifiable odor was perceived by the pilot. Being unable to alleviate his symptoms, the pilot landed the plane and was taken to an infirmary.

Physical examination showed a well-developed, well-nourished male who was dressed in clothing that smelled of fuel [66]. He appeared moderately intoxicated and was excessively jovial. There was a slight stagger in his gait, and he complained of a mild headache. No other abnormalities were noted. Neurologic examination showed the following positive findings: slight staggering on walking; slight but definite slurring of speech; a loss of position sense in which the patient failed to maintain equilibrium when standing with feet together and eyes closed; and possible decreased sensation to painful stimuli. The only laboratory study performed was for carboxyhemoglobin which was normal. After examination, the pilot was given

rest. After 26 hours, he reported that he still did not feel normal. One week after the incident, there were no adverse effects of intoxication, and he returned to work. He stated that hypoxia had not caused the condition. The airplane and breathing equipment were examined to determine if a leak caused the intoxication. The breathing mask was found to be in good condition, but the aircraft engine had developed a fuel leak. Fuel fumes were not noticed in the cockpit but, had the access doors of the plane been closed and had the engine heat vaporized the fuel, fumes would have entered the cockpit in high concentrations through the compressor system. The author suggested that, based on the assumption that JP-4 fuel is similar in CNS toxicity to gasoline, the concentration of fuel in the cockpit must have been 3,000-7,000 ppm to intoxicate the pilot within 7 minutes.

In 1976, Carpenter and colleagues [67] described the odor and sensory irritation thresholds of humans exposed to airborne concentrations of deodorized kerosene. The odor threshold was based on the responses of six volunteers ranging in age from 23 to 49 years to a series of airborne concentrations given for approximately 10 seconds each/day for 2 days. The odor threshold for this solvent was found to lie in the range from 0.2 to 2 mg/cu m (0.03 to 0.3 ppm) based on a mean molucular weight of 171 calculated from mass spectrometry data and analyzed by gas chromatography. The authors stated that the odor threshold was probably 0.6 mg/cu m (0.09 ppm).

To determine the sensory threshold, six volunteers, ranging from 20 to 63 years in age, inhaled a vapor concentration of 140 mg/cu m (20 ppm) for 15 minutes [67]. The authors stated that 140 mg/cu m (20 ppm), as measured by gas chromatography, probably represented the maximum airborne

concentration at which this deodorized kerosene vapor is representative of its liquid phase. This exposure concentration was easily tolerated by the volunteers, with none reporting any discomfort or irritation. Two did, however, report a slight decrease in olfactory acuity but not complete olfactory fatigue. The volunteers judged that 140 mg/cu m (20 ppm) of deodorized kerosene, based on a 15-minute exposure, would be acceptable for an 8-hour workday.

There are numerous cases of kerosene poisoning by aspiration or ingestion of the liquid [59,68-70]. In 1934, Nunn and Martin [68] reported 65 cases of kerosene poisoning in children with an overall mortality of 9.2%. In the fatal incidents, the patients lived 2-18 hours after ingestion and aspiration of the kerosene. These subjects were cyanotic and had moist rales in both lungs and rapid, shallow respirations. In the nonfatal episodes, 32% showed evidence of pneumonitis. Body temperature and pulse rates ranged from 97 to 106 F and 110 to 150 beats/minute, respectively. Respiration rates were very rapid, ranging from 50 to 80 breaths/minute in those patients who developed pneumonitis. Erythrocyte and hemoglobin counts were within normal limits, but leukocyte counts varied from normal to 21,000 cells/cu mm. Occasionally, urinalysis showed the presence of albumin.

In 1956, McNally [69] reviewed the major findings on 204 children admitted from 1946 to 1954 to an Alabama hospital after ingesting kerosene. All of the patients showed upper respiratory tract infections and rales and rhonchi were heard in 10% of the subjects. Thirty percent of the patients were diagnosed as having pneumonia. The roentgenologic reports of the chest varied from patchy infiltration to diffuse interstitial pneumonia.

Forty percent of the patients were lethargic, 8% were semicomatose, and none had convulsions. Urinalysis findings showed the presence of albumin in 30% of the incidents, ranging from a trace to 3+. Leukocyte counts varied from 4,500-31,900 cells/cu mm and the lymphocytes varied from 10-79%. The hemoglobin content ranged from 7 to 11.5 g/100 ml.

Truffa and Montalenti [70], in 1969, described an incident of acute lung disease and jaundice from accidental ingestion of kerosene. A man had ingested and possibly aspirated an unknown quantity of kerosene while he attempted to syphon this substance. There were no immediate disturbances, but, a few hours later, he developed a headache and an intense difficulty in breathing followed subsequently by vomiting, epigastric pain, and malaise. On physical examination, the following abnormalities were found: moderate blueness of the lips, evidence of right lung congestion, small inhalation rales and harsh breathing, intensified abdominal pain upon pressure, moderate fever (38.3 C), and marked jaundice. A chest roentgenogram showed the presence of zonal parenchymal thickening. There was an elevation of the serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase. The patient fully recovered several weeks after the kerosene ingestion.

Epidemiologic Studies

Epidemiologic studies indicated that refined petroleum solvents can cause dermal, eye, nose, and throat irritation. Menstrual disturbances and leukemia may develop as a result of exposure to solvents containing benzene. Polyneuropathy was reported to develop in workers exposed to jet fuel that was composed of raw gasoline and kerosene. Thus, neurologic

dysfunction may result from exposure to solvents.

In 1944, Hamilton-Paterson and Browning [71] investigated the toxic effects on women exposed to industrial rubber solutions. The investigation was conducted in two parts. In the first, sample groups from 13 factories (a total of 200 women were studied) were clinically examined and had blood counts made. These blood counts were compared with the counts of 200 control women. In the second part of the study, all the women working in one factory were similarly compared with a group of women in the same factory who had never been in contact with rubber solutions. The effects of rest were also examined in this group of women. The rubber solution used in these factories contained varying amounts of benzine and aromatic hydrocarbons (5-20%). Although adequate ventilation was provided, it was not possible for the workers to avoid inhaling the fumes. Approximately 41% of the workers complained of symptoms probably related to their occupations. The major symptoms were: exhaustion, headache, dizziness, nausea, vomiting, and difficulty in breathing. The pertinent blood finding was a decreased leukocyte count which resulted primarily from a decrease in neutrophils. There was no significant variation from controls in the erythrocyte count, and it was not possible to evaluate the results of hemoglobin measurements because they varied unreasonably, having been done at different laboratories. After the workers had been free from exposure to the rubber solution for 3 months, their blood findings returned to control levels. The authors [71] suggested that the decreased leukocyte count resulted from benzene exposure, but neither the benzene content of the solution nor of the air was determined. Excessive uterine bleeding was observed in 7 of 45 women, 40-50 years old, and 4 of 131 women between 19

and 39 years old complained of increased frequency of menstrual periods. The authors felt that these menstrual disturbances may have been the result of benzene poisoning, but they also indicated that the uterine bleeding may have been a menopausal symptom or a response to uterine disease, and that the increase in menstrual frequency may have been associated with the change from domestic to factory work. No gynecologic examinations were performed on the women, and no definite conclusions were made concerning the etiology of the menstrual disturbances.

In 1962, Kaplan and Zeligman [72] found that the use of kerosene or mineral spirits mostly for cleaning caused dermatitis in 10 of 98 railroad maintenance workers. The extent or duration of vapor exposure or liquid contact was not reported.

In 1973, Ramos and Shama [73] reported that exposure to petroleum distillate (naphtha) caused dry throats, burning or tearing of eyes, mild headaches, dizziness, respiratory irritation, and, in some cases, dermatitis in workers of an electric company. They determined that the TWA exposures to the distillate vapors ranged from about 25 to 274 mg/cu m based on charcoal sampling and gas-chromatographic analysis. There was no apparent relationship between solvent concentration and symptom development. The dermatitis was believed to be caused by direct contact with the petroleum distillate, and it ranged from mild redness to fissuring and blister formation.

Markel and Shmunes [74], in 1974, described the evaluation of Stoddard solvent hazard at a greeting-card company. Twelve workers were exposed to a concentration of Stoddard solvent of 99-1,906 mg/cu m (average, 438 mg/cu m) in their working environment. Gas chromatographic

techniques were used to determine the solvent vapor concentration. The author concluded on the basis of pulmonary function tests (forced expiration volume, and forced vital capacity) and a serologic antigen test that, under the conditions found at the time of the survey, Stoddard solvent did not constitute a hazard to the health of the workers.

In 1974, Larsen and Shmunes [75] reported that Stoddard solvent used to clean polishing machines were probably the cause of dermatitis in several industrial workers. The workers also complained of headaches and eye and nose irritation. Although the detectable concentrations of Stoddard solvent were less than 20 ppm (115 mg/cu m), the authors felt that higher concentrations could have occurred immediately after the polishing machines were cleaned with Stoddard solvent, which could have caused the headache and eye and throat irritation. The analytical method and assumption used in converting the data to ppm were not stated in the paper.

McMichael and associates [76], in 1975, presented an epidemiologic study involving rubber workers that indicated an association between leukemia and jobs entailing exposure to solvents. The authors did not specify which types of solvents were used by the workers, although they mentioned that benzene was once the solvent of choice. After noting that leukemias in general demonstrated a threefold excess in mortality in the 40-64 age range, and with further subclassification of the International Classification of Diseases categories to identify specific leukemias, a sevenfold excess of deaths from lymphatic leukemia in the 40-64 age range was observed. Six of eight deaths were from chronic lymphatic leukemia. Myeloid leukemia was the next highest category in this age range, showing a twofold excess. The question of whether the observed mortality excesses

were associated with specific job categories within the rubber industry was then investigated. Nineteen of 70 occupational titles were associated with solvent exposure and were grouped as heavy, medium, and light solvent exposure. A discriminant function analysis based on time spent in various work groups and independent of the previously observed mortality excess revealed a statistically significant positive association between solvent exposure and lymphatic leukemia. The average solvent exposure time was approximately 11 years. The leukemia seen in these affected workers was lymphatic in character. In benzene poisoning, the leukemia tends to be either the hemocytoblastic (or stem cell) or the myeloblastic type. Thus, benzene may not have been the agent causing the leukemia in the present study. The authors suggested that an unidentified substance presently being used may have been the carcinogen, since four cases of leukemia developed in workers employed in recent decades.

In 1976, Knave and coworkers [77] reported the effects of long-term exposure to jet fuels in aircraft factory workers. The jet fuels were types MC 75 and MC 77 and had raw gasoline and kerosene as their principal components. The workers were exposed to the fuel during the production, installation, and testing of fuel systems for planes. The airborne concentrations of fuel were not routinely determined, but the authors indicated that, on one occasion, the airborne levels were measured in three workrooms. The concentrations were between 500 and 3,000 ppm (3,476 and 20,859 mg/cu m assuming a molecular weight of 170).

From employer's records and interviews with workers, 29 employees considerably exposed to fuel vapors from 1955 on were selected for the study [77]. The exposed workers were divided into two groups, depending on

the degree of exposure. The 13 workers belonging to group A were either continuously exposed for several hours daily to "high" concentrations of jet fuel or were exposed for no less than 20 minutes to "high" concentrations at least every 2nd or 3rd week. The 16 members of group B were exposed intermittently but exposure was less frequent than that found in group A. All 29 workers were exposed for at least 29 years. They were given a neurologic examination and were questioned about the occurrence of "restless legs," muscle cramps, pain in the extremities, distal paresthesia, numbness, and paresis.

All workers in group A stated that they repeatedly experienced one or more of the following symptoms when exposed to the fuel vapors: dizziness, headache, nausea, palpitations and pressure on the chest, a slight cough, and pain upon inhalation [77]. Seven of 16 workers in group B experienced similar acute symptoms. The authors reported that 92 and 56% of the workers in groups A and B had one or more of these symptoms and that the symptoms were chronic, neurasthenic, and psychasthenic. In groups A and B, 85 and 38%, respectively, of the workers had symptoms, and 77 and 44% had signs of polyneuropathy. Fuel vapor exposure did not affect the vibration sensation threshold and nerve conduction velocity, although conduction velocities tended to decrease.

The authors [77] concluded that many of the workers studied had definite signs and symptoms of neurasthenia, psychasthenia, and polyneuropathy. This study did not establish a definite relationship between exposure to pure kerosene and polyneuropathy since n-hexane, an agent known to cause polyneuropathy [78], may have been a part of the fuel mixture.

The authors [77] pointed out that obvious eye irritation was not present in exposed workers; they suggested that kerosene was not an eye irritant, in contrast to gasoline, apparently interpreting that most of the exposures were from kerosene. Since the exposures stemmed from installation and testing of fuel systems rather than from spills, the less volatile kerosene might have been volatilized to a greater extent than gasoline, if temperatures, air movements, and proportions of components of the fuels were appropirate.

Animal Toxicity

(a) Petroleum Ether

There are several animal toxicity studies on individual alkanes and alkane mixtures that demonstrate that one or more of these materials can cause peripheral nerve disorders, CNS depression, and skin and respiratory irritation, and they are reviewed in detail in the NIOSH criteria document on alkanes [78]. To evaluate the toxicity of petroleum ether, its two major components, pentanes and hexane, will be briefly discussed.

Miyagaki [79], in 1967, reported the neurotoxic effects of n-hexane exposure on 8-week old male mice. The mice were separated into 6 groups of 10 each and exposed to either 0, 100, 250, 500, 1,000, or 2,000 ppm (0, 352, 879, 1,759, 3,517, or 7,035 mg/cu m) of n-hexane for 24 hours/day, 6 days/week, for 1 year. Tests designed to evaluate neurotoxicity were made on the distal portion of the lower extremities and they included electromyography, strength duration curves, electrical reaction time, and determination of the flexor-extensor chronaxy ratio. Evaluations of the effect of n-hexane on gait, posture, and muscular atrophy were also made.

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Microscopic examinations of the distal lower extremity muscles of some of the animals were performed.

Mice exposed to 3,517 mg/cu m of n-hexane or greater showed abnormal electromyography, strength-duration curves indicative of denervation, prolongation of the electrical reaction time, depression of the flexor-extensor chronaxy reaction time, abnormal gait posture, decreased muscle mass, and degeneration of muscle fiber cells [79]. Mice exposed at 879 or 1,759 mg/cu m of n-hexane developed only abnormal electromyography patterns and altered strength-duration curves indicative of incomplete denervation. No neurotoxicity was observed in mice exposed at n-hexane concentrations of 100 ppm. The author concluded that peripheral nerve disorders were caused by a 1-year exposure to n-hexane at concentrations of 879 mg/cu m or greater.

Truhaut and associates [80], in 1973, exposed rats to airborne hexane at a concentration of 2,000 ppm (7,035 mg/cu m), 5 hours/day, 5 days/week, for 1-6 months. Technical grade hexane was used for the investigation. Analysis of the hexane gave the following results based on total volume: 0.3% n-pentane, 25.1% 2-methylpentane plus cyclopentane, 18.4% 3-methylpentane, 48.8% n-hexane, 8% methylcyclopentane, 1.2% methylhexane, and 1.2% benzene. The sciatic and saphenous nerves were removed from anesthetized rats at the end of the 5- to 6-month exposure period, mounted in a nerve chamber, and stimulated by square pulses of various voltages. The studies showed a decrease in the conduction rate of the nerves, an increase in the refractory periods, and a decrease in the excitability of the nerves. Microscopic examination of the nerves following 5-6 months of exposure to hexane showed retraction of the myelin sheaths and, in some

cases, a rupture of the Schwann cell membranes. The authors noted that impurities, such as 3-methylpentane, the cycloalkanes, and benzene in the technical grade hexane used for the studies, might have been responsible for some of the results observed.

In 1974, Swann et al [81] discussed the inhalation effects of various hydrocarbons, including n-pentane and n-hexane, on animal toxicity. Groups of four mice, weighing about 25 g each, were exposed to n-pentane and n-hexane at concentrations of 1,000, 2,000, 4,000, 8,000, 16,000, 32,000, 64,000, or 128,000 ppm (3,517, 7,035, 14,070, 28,139, 56,278, 112,556, 225,112, or 450,225 mg/cu m). Exposures were for 5-minute periods. The exposures were made in a chamber which allowed only the heads of the mice to be exposed to the solvent vapor while the rest of their bodies were enclosed in plethysmographs. Respiration patterns were recorded during the exposure period. Exposure to pentane up to 56,278 mg/cu m produced no anesthesia. Anesthesia was noted during the recovery period after exposures at 112,556 and 225,112 mg/cu m. At 450,225 mg/cu m, deep anesthesia was produced during the exposure period. Respiratory arrest occurred in one mouse about 4.8 minutes after exposure to pentane at 450,225 mg/cu m began. Respiratory irritation was noted at 225,112 and 450,225 mg/cu m. Concentrations of n-hexane up to 56,278 mg/cu m failed to produce anesthesia. At 112,556 mg/cu m of n-hexane, deep anesthesia was produced. At 225,112 mg/cu m, all mice experienced respiratory arrest, the first after 2.5 minutes and the last after 4.5 minutes of exposure.

(b) Rubber Solvent

In 1975, Carpenter and associates [9] examined, in a series of experiments, the toxic effects of rubber solvent vapor inhalation on male

rats, cats, and mice, and female dogs. Groups of 15 rats (100-200 g) were exposed to rubber solvent vapor at concentrations of 11,000, 21,000, 39,000, or 96,000 mg/cu m (about 2,800, 5,300, 9,800, or 24,200 ppm) based on a mean molecular weight of 97 calculated by mass spectrometry data and analyzed by gas chromatography for a single 4-hour period to determine an LC50 or to detect possible cellular damage. After the 4-hour exposure period, 5 rats were immediately killed and their organs examined microscopically, while the remaining 10 animals were observed for an additional 14 days.

Impairment of motor coordination and eye irritation were observed at vapor concentrations of 21,000 and 39,000 mg/cu m, respectively [9]. Convulsions followed by death were observed in all animals exposed to rubber solvent vapor at 96,000 mg/cu m. There were no toxic effects noted at the 11,000 mg/cu m concentration. Microscopic findings of liver sections were hyperplasia of Kupffer cells and increased hepatic mitotic figures which occurred at only the 96,000 mg/cu m concentration. No other microscopic changes were reported. The 4-hour LC50 was estimated to be 61,000 mg/cu m (15,000 ppm).

Female beagles were exposed to rubber solvent vapors, one each, at concentrations of either 5,900, 13,000, or 25,000 mg/cu m (1,500, 3,300, or 6,300 ppm) for a single 4-hour period to determine the earliest persistent signs of toxicity and to ascertain an appropriate level to be used in a subacute study [9]. Loss of coordination was observed at concentrations of 13,000 mg/cu m or greater, and eye irritation was noted at 25,000 mg/cu m. The eye irritation was more severe in the beagle exposed at 25,000 mg/cu m than the eye irritation seen in rats exposed at a similar concentration.

No observable effects occurred at 5,900 mg/cu m.

The acute CNS effects of a 4-hour exposure to rubber solvent vapor at a concentration of 49,000 mg/cu m (12,000 ppm) were examined in four male cats [9]. A time-related depression followed a sequential pattern that included ataxia, loss of proprioception, salivation, relaxation of the nictitating membrane, unconsciousness, tremors, and convulsions. One animal died 3 days after exposure to the solvent vapor. No other deaths or gross or microscopic tissue damage were reported to have occurred from this exposure.

Fifteen male rats (100-200 g) were used to determine the LT50 (time required to cause the death of 50% of the animals) of saturated rubber solvent vapor at a concentration of 180,000 mg/cu m (45,000 ppm) [9]. The animals were exposed to the solvent for 2, 4, or 8 minutes. The LT50 was calculated to be 4.3 minutes. Microscopic examination of the lungs of the animals exposed for 8 minutes showed areas of hemorrhage and perivascular edema.

Male rats (about 6 weeks old) and male beagles (under 2 years old) were divided into four groups of 25 and 4 each, respectively, and placed in inhalation chambers containing rubber solvent vapors at a concentration of 0, 1,900, 3,700, or 7,900 mg/cu m (0, 480, 930, or 2,000 ppm) based on a mean molecular weight of 97 calculated from mass spectrometry data [9]. The animals were exposed for 6 hours/day, 5 days/week. Three rats from each exposure concentration were killed for microscopic examination after 15 and 40 exposure days. All but 10 of the remaining rats (used for another experiment) and all of the beagles were killed after 62 and 63 days of vapor exposure, respectively. There were no animal deaths attributed to

rubber solvent vapor. Body weight gain was no different than that of the controls. No significant changes in blood urea nitrogen, serum glutamic-oxaloacetic transaminase, and serum glutamic-pyruvic transaminase tests and erythrocyte, and total and differential leukocyte counts resulted from solvent vapor inhalation at any exposure duration or concentration in the rats or dogs. Serum alkaline phosphatase was significantly higher after 62 days in all rats exposed to the rubber solvent vapor, but the authors concluded that this finding was an artifact which resulted from very low control alkaline phosphatase values. Microscopic examination of the various organ sections showed no tissue damage that could be attributed to the solvent vapors. Urinalysis showed an increase in specific gravity in the dogs exposed to rubber solvent vapors at 7,900 mg/cu m (2,000 ppm) for 63 days. The significance of this finding was unknown.

At the termination of the 62-day solvent inhalation period, 10 rats from each exposure concentration were exposed to rubber solvent vapor at 80,000 mg/cu m (20,000 ppm) for 5 hours to determine the animals' resistance to the toxic effects of the vapor [9]. No difference in mortality and in the median time of death were noted.

The authors [9] concluded that, since exposure of rats and dogs to 1,900 mg/cu m did not produce significant signs of toxicity and acute exposure of humans to 1,700 mg/cu m produced only slight eye and throat irritation, a hygienic standard for rubber solvent should be set at 1,700 mg/cu m (430 ppm).

(c) Varnish Makers' and Painters' Naphtha

In 1975, Carpenter et al [17] reported the effects of exposure to the vapors of varnish makers' and painters' (VM and P) naphtha in rats, dogs,

and cats. In a single exposure inhalation study, male rats were exposed to VM and P naphtha vapors at concentrations of 4,400, 9,800. or 26,000 mg/cu m (940, 2,100, or 5,600 ppm) based on a mean molecular weight of 114 calculated from mass spectrometry data and analyzed by gas chromatography for 4 hours. Rats at the higher concentration showed responses that were consistently dose related, which included eye irritation and CNS depression characterized by poor coordination and convulsions preceding death. Rats at the 26,000 mg/cu m concentration that died during or shortly after exposure had congested lungs and livers. Bile duct proliferation was noted in three of six livers examined microscopically, and sinusoids of the spleen contained increased numbers of leukocytes in three rats. Examined rats at the 9,800 and 4,400 mg/cu m VM and P naphtha concentrations had no appreciable abnormalities. Animals inhaling VM and P naphtha at 4,400 mg/cu m were reported not to have signs of intoxication during and after exposure and to have gained weight normally during the subsequent 14-day observation period. The authors estimated a single exposure 4-hour inhalation LC50 to be about 16,000 mg/cu m (34,000 ppm) for rats exposed to VM and P naphtha vapor.

Two dogs (one male, one female) were exposed to VM and P naphtha at a nominal concentration of 16,000 mg/cu m for 2 hours [17]. Eye irritation occurred in 30 minutes, tremors and mild ataxia in 1 hour, and dilation of the pupils in 1.5 hours. The male dog was prostrate in 1.5 hours. Apparent recovery occurred within 2 hours after cessation of the exposure. A third dog (male), exposed to VM and P naphtha vapor at 8,000 mg/cu m (1,700 ppm) for 4 hours, appeared normal during the exposure and thereafter.

Four male cats inhaling VM and P naphtha at 19,000 mg/cu m (4,100 ppm) for 4 hours exhibited progressive symptoms usually indicative of CNS depressive effects: salivation, dilation of the pupils, body tremors, prolapse of the nictitating membrane, poor coordination, vomiting, convulsions, and prostration [17]. All animals survived the exposure period, but one became moribund on the 5th day and was killed. Autopsy findings showed suppurative pneumonia.

To evaluate the effects of brief exposures to high concentrations, Carpenter et al exposed male rats to saturated VM and P naphtha vapor at 71,000 mg/cu m (15,000 ppm) [17]. The rats were exposed to the solvent vapor for 57, 30, 15, or 7.5 minutes and had mortality ratios of 5/5, 1/5, 0/5, and 0/5, respectively. The LT50 was estimated to be 37 minutes. Loss of coordination and convulsions were observed in rats which inhaled the vapor for 15 minutes or longer, but no signs of distress were observed during or after 7.5 minutes of exposure.

There was no increase in erythrocyte osmotic fragility in four rats that inhaled 22,000 mg/cu m (4,700 ppm) of VM and P naphtha for 35 minutes [17]. The mean initial hemolysis was in 0.46% and the final in 0.29% saline solution compared to mean control values of 0.50 and 0.31%.

In short-term inhalation experiments, Carpenter and associates [17] subjected 25 male rats and 4 male dogs to repeated daily inhalations of VM and P naphtha for 6 hours/day, 5 days/week, for 65 days. Naphtha at 0, 1,300, 2,800, or 5,800 mg/cu m (0, 280, 600, or 1,200 ppm) was inhaled by randomly assigned groups of animals. No outward signs of distress were observed in either species during the 65-day study. After 40 days, the rats at the 5,800 mg/cu m concentration had a significantly higher

percentage of neutrophils (24%), but a 9% lower lymphocyte count than controls. The total leukocyte count was not affected. These effects were not seen when the rats were killed after 65 days of exposure and therefore were not considered to be related to treatment. After 65 days of exposure, the rats had a significant (9%) lowering in erythrocyte count as compared to controls. There were no statistically significant differences between treated and control groups of rats in weight or in most measured blood chemistry values. Statistically significant differences were noted in the dogs exposed for 60 days to varnish makers' and painters' naphtha, viz: an increase in serum alkaline phosphatase activity (80%) and in reticulocyte count (47%) at the 5,800 mg/cu m concentration, a decrease in the serum glutamic-oxaloacetic transaminase activity (26%) at the 5,800 mg/cu m concentration, an increase in the liver weight to body weight ratio (21%) and a decrease in the reticulocyte count (25%) at the 2,800 mg/cu m concentration, and an increase in the reticulocyte count (4%) at the 1,300 mg/cu m concentration. The authors indicated that, because the values were in the normal ranges of their experimental animals and there were no specific anatomical lesions, the changes might be experimental artifacts rather than deleterious effects. There were no solvent-related microscopic changes seen in either the rats or dogs. Nephrosis was prevalent in the rats and may have masked solvent-related renal damage.

In an additional experiment, Carpenter et al [17] subjected rats surviving the 65-day exposure to VM and P naphtha to a "challenge" concentration of 27,000 mg/cu m for 4 hours (1.7 times the approximate 4-hour LC50 of 16,000 mg/cu m). The surviving rats from the two higher concentrations were found to be more resistant to the increased

concentration than air controls and naive controls (animals never used in the experiment). Animals dying during or shortly after exposure showed marked congested or hemorrhagic lungs, whereas survivors after 24 hours showed no remaining irritation.

The authors [17] concluded that, since exposure of rats and dogs at 2,800 mg/cu m did not produce treatment-related signs of toxicity, and acute exposure of humans at 4,100 mg/cu m, but not at 660 mg/cu m, produced eye, nose, and throat irritation, a hygienic standard for VM and P naphtha should be set at 2,000 mg/cu m (430 ppm).

(d) Mineral Spirits

In 1966, Rector and coworkers [82] reported the effects of a paint thinner on five species of animals exposed continuously (23.5 hours/day, 7 days/week) for 60-90 days or intermittently for 8 hours/day, 5 days/week, for a total of 30 exposures. The mineral spirits used in this study were obtained from a Navy supply depot under the listing of "Paint Thinner, Mineral Spirits Grade I." This type of mineral spirits had a boiling point range of 140-190 C, a mean molecular weight of 144-169, and a specific gravity of 0.786-0.787. The compound was analyzed as a complex mixture of 80-86% saturated hydrocarbons, 1% olefins, and 13-19% aromatics.

Air concentrations of mineral spirits for this study [82] were calculated from nominal input since no satisfactory analytical procedure was available at the time the experiments were begun. Later in the study, the airborne concentration of mineral spirits was monitored and found to be 95% of the calculated nominal input with an average deviation of 4.8%. The concentration of airborne mineral spirits remained relatively constant in monitored experiments.

In continuous 90-day exposure experiments, rats, guinea pigs, rabbits of both sexes, and male dogs and monkeys were exposed to mineral spirits with concentrations ranging from 114 to 1,271 mg/cu m except for approximately 30 minutes/day, which were required for feeding and servicing of cages and chambers [82]. Exposure of the dogs, monkeys, and rabbits to the mineral spirits at any of these concentrations failed to produce death. An occasional death was noted in the rats exposed to the mineral spirits but the number of deaths (3/106) was similar to that of the controls (6/224). In contrast, guinea pigs were very susceptible to the mineral spirits with deaths occurring in all groups exposed at a concentration of 363 mg/cu m or more. The rate of body weight gain was generally similar in test animals and in controls, except in guinea pigs and monkeys. The decline in body weight became apparent in guinea pigs at 619 mg/cu m and in monkeys at 555 mg/cu m, in continuous exposure experiments. Continuous exposure of the guinea pigs and monkeys to mineral spirits at a concentration of 1,271 mg/cu m for 90 days resulted in body weight losses of 4 and 9%, respectively.

In dogs exposed to mineral spirits at 238 and 619 mg/cu m, a marked alteration between the preexposure and postexposure leukocyte counts was found [82]. The differential leukocyte counts and hematocrit and hemoglobin values were within normal limits. No consistent pattern of dose-response blood relationships was found except for a minor, but consistent, increase in the postexposure leukocyte counts in both rabbits and guinea pigs. This change was seen in both exposed animals and chamber controls. Hematologic data from the animals exposed at 1,271 mg/cu m were not reported.

Gross examinations of all animals were conducted at the end of each study [82]. While no remarkable changes were noted, irritation and congestion of the lungs were commonly found in all species. The severity of the irritation and the number of animals involved appeared to be dose-related. The livers of several guinea pigs appeared "discolored and wrinkled." No gross abnormalities were seen in the spleen, kidneys, or heart of any other species that could be attributed to solvent exposure.

Microscopic examination of the heart, lungs, liver, spleen, and kidneys was carried out on all surviving dogs, rabbits, and monkeys, and on 50% of the surviving guinea pigs and rats [82]. In general, congested lungs were found only in animals exposed to mineral spirits at a concentration of 1,271 mg/cu m. At this level, the lung tissue of all species showed evidence of bronchitis and mixed inflammatory cell infiltration. While occasional signs of lung irritation were seen at lower concentrations, the number of animals involved was such that the lung irritation could not be definitely related to the exposure. Microscopic examination of the heart, spleen, and kidney sections showed no findings that could be related to the exposure, but examinations of the liver yielded a mixed pattern. Focal necrosis, sometimes associated with worms, was seen in the livers of rats, rabbits, dogs, and monkeys. Mild-to-moderate vacuolar changes in the plate cells were noted in some guinea pigs and monkeys exposed at 363 mg/cu m and higher. This finding, however, was variable, and the incidence of liver damage did not correlate well with the exposure concentration. The vacuolar changes seen in the livers of guinea pigs were distributed in the peripheral area of lobules, although central and diffuse changes were also commonly seen. While no peripheral vacuolar

changes in the hepatic plate cells were seen in the control guinea pigs, some patchy vacuolar changes were observed. The authors concluded that only the hepatic changes noted in the animals exposed at 513 and 1,271 mg/cu m of mineral spirits were likely to have been caused by solvent exposure.

To find the explanation for the high mortality seen in guinea pigs exposed to mineral spirits at concentrations of 550 mg/cu m, Rector et al [82] investigated the serum alkaline phosphatase activity, serum isocitric dehydrogenase activity, liver lactate production, and serum or plasma urea levels in 10 treated and 10 control guinea pigs. However, the results of this experiment did not explain the high mortality in the guinea pigs.

The authors [82] also conducted three intermittent exposure studies in which the same five species, viz, rats, guinea pigs, rabbits, dogs, and monkeys, were exposed 8 hours/day, 5 days/week, for 30-60 exposures to mineral spirits at concentrations of 593, 596, or 1,353 mg/cu m. In the first study, animals exposed at 1,353 mg/cu m for 6 weeks showed no toxic signs. Body weight gains and blood values were similar in both exposed and control animals. No consistent microscopic changes were found except for possible lung irritation in guinea pigs. Seven of eight guinea pigs exposed at 1,353 mg/cu m showed some lung congestion and emphysema, which were not seen in the controls, and one of seven showed vacuolar changes in hepatic plate cells. In the second study, animals exposed at 596 mg/cu m for 6 weeks showed no signs of toxicity, and body weights and the hematocrit, hemoglobin, and total leukocyte count were all within normal limits. One-half of the rats and guinea pigs were killed and their tissues were examined microscopically. No noteworthy changes were found. After a

2-week nonexposure interval, the remaining half of the rats and guinea pigs were reexposed for a second series of 30 exposures at 593 mg/cu m. No noticeable signs of toxicity occurred during this second reexposure period, and the hematocrit, hemoglobin content, and total leukocyte count were within normal limits. Following a 17-day observation period, the animals were killed for necropsy. Microscopic findings indicated greater focal lymphocytic involvement in the lungs of several exposed guinea pigs than in the controls. No noteworthy microscopic changes were reported in any other tested species. There were no deaths in the animals exposed at 593 mg/cu m of mineral spirits.

Of the five species examined in this study, the guinea pigs were found to be particularly susceptible to mineral spirits [82]. As the air concentration of mineral spirits increased above 363 mg/cu m, guinea pigs began to die. No deaths occurred in guinea pigs during continuous exposures at 114 and 238 mg/cu m; no adverse changes were noted at these levels in any other species exposed. From these short- and long-term inhalation studies, the authors recommended that a guideline for a 90-day exposure period in submarines to mineral spirits containing 15-20% aromatic hydrocarbons be set at 40 mg/cu m.

In 1974, Gillespie et al [83] reported the effects of various paint components, including mineral spirits, on inflammatory response and tissue resistance to infection. Albino rabbits (2-3 kg) were used to assess the inflammatory response to the various paint components. A subcutaneous injection of mineral spirits at a dose of 0.1 ml was made into a shaved portion of the rabbit's back, and 4 days later the diameter of the indurated margins of the skin was measured. The indurated margin was about

2.4 cm in diameter and was greater than the indurated margins caused by most of the other paint components. The assessment of the resistance of tissue to infection was accomplished by subcutaneous injection of 0.1 ml of bacterial inoculum (10,000 or 100,000 Staphylococcus aureus) and a mineral solvents sample (injected at an unknown volume) and by measuring the inflammatory responses in terms of amount of induration and pus formation 4 days later. Mineral spirits caused increased induration, inflammation, and tissue necrosis but did not impair the ability of the wound to resist infection. Similar results were seen with other paint solvents and pigments.

(e) Stoddard Solvent

In 1974, Grant [54] reported that Stoddard solvent was essentially innocuous to the rabbit cornea. No details were given.

In 1975, Carpenter et al [21] reported the effects on rats of the inhalation of Stoddard solvent at 2,400, 4,600, or 8,200 mg/cu m (420, 800, or 1,400 ppm), based on a mean molecular weight of 144 calculated from mass spectrometry data and analyzed by gas chromatography, for a single 8-hour period. Groups of 15 rats were used at each exposure level. Exposure to 8,200 mg/cu m of Stoddard solvent resulted in the death of one of the rats at the termination of the inhalation period. Eye irritation, slight loss of coordination, and a bloody exudate around the nostrils were noted. A concentration of 4,600 mg/cu m produced similar signs but no loss of coordination. Inhalation of Stoddard solvent at 2,400 mg/cu m for 8 hours failed to cause any visible response during or after exposure; body weight gains were normal during the subsequent 14 days.

When a female beagle was exposed to vapors of Stoddard solvent at a nominal concentration of 4,000 mg/cu m for 8 hours, it developed no signs of toxicity during or after the exposure [21]. Another female beagle inhaling Stoddard solvent at 8,000 mg/cu m (nominal concentration) for 8 hours developed eye irritation after 1 hour, increased salivation at 3 hours, tremors at 4 hours, and clonic spasms after 5 hours but survived the exposure.

Four male cats were exposed to vapors of Stoddard solvent at a nominal concentration of 10,000 mg/cu m until they died within 2.5-7.5 hours after the exposure began [21]. They had signs of CNS disorders which followed a time-related pattern. There was first a slowing of pupillary reaction to light, then tremors, clonic convulsions, and finally death.

In a short-term inhalation experiment, Carpenter et al [21] subjected groups of 25 male rats and 4 male dogs to repeated daily inhalations of Stoddard solvent for 6 hours/day, 5 days/week, for 13 weeks. The measured concentrations of solvent used in this study were 0, 480, 1,100, or 1,900 mg/cu m (0, 84, 190, or 330 ppm). Three rats from each exposure concentration were killed for tissue microscopic examination (adrenals, brain, pituitary, trachea, thyroid, parathyroid, lungs, heart, liver, kidneys, spleen, duodenum, pancreas, ileum, jejunum, colon, skeletal muscle, sciatic nerve, and bone marrow sections) after 14 and 37 exposure days and four from each exposure concentration at 65 exposure days. Ten rats from each level were used for a challenge exposure to determine whether the 65-day survivors were more or less sensitive to Stoddard solvent as a result of repeated vapor inhalation. All dogs and surviving rats were killed after 66 days and tissues were taken for microscopic

examination. Those tissues that were examined in the rats were also examined for the dog, as well as the tracheal bifurcation, pharnyx, tonsil, nasal mucosa, and stomach. Blood analysis (hematocrit, total erythrocyte count, reticulocyte, total and differential leukocyte counts, serum alkaline phosphatase, serum glumatic-pyruvic transaminase, serum glutamic-oxalacetic transaminase and blood urea nitrogen) was performed on rats killed after 3, 8, or 13 weeks and on dogs killed after 13 weeks.

The hematologic findings on rats killed after 40 days of solvent exposure showed a 10, 14, and 11% lower erythrocyte count and a 4, 6, and 6% lower hematocrit at the 1,900, 1,100, and 480 mg/cu m concentrations as compared to controls, respectively [21]. Hemoglobin values were not statistically different at the 1,900 mg/cu m (330 ppm) concentration but were 7 and 9% lower than control values at the 1,100 and 480 mg/cu m concentrations, respectively. The authors did not consider these differences to be important since they were not dose related; the values were all within the range of normal values, and similar results were not seen at the termination of the experiment. Blood urea nitrogen was 31% higher in the rats exposed at 1,900 mg/cu m for 13 weeks. No other alterations in blood chemistry were noted.

Marked tubular regeneration in the kidneys and dilation of the loops of Henle which contained homogeneous eosinophilic and amorphous debris were evident in the rats exposed to vapors of Stoddard solvent at 1,900 mg/cu m (330 ppm) for either 8 or 13 weeks [21]. What was described by the authors as marked tubular regenerative changes of the kidneys may in fact indicate kidney damage. Dilation of the loop of Henle was also noted in three of nine rats exposed to 1,100 mg/cu m (190 ppm) for 13 weeks. In addition,

two out of nine rats exposed to 1,100 mg/cu m for 13 weeks showed evidence of marked tubular regeneration. The authors reported that the number of animals that showed dilation of the loops of Henle at the 1,100 mg/cu m concentration were not significantly different from control values. No microscopic abnormalities were noted at 480 mg/cu m (84 ppm). There were no toxic effects observed, at any concentration of Stoddard solvent used in this study, on canine chemical or cellular constituents or tissue sections.

At the termination of the 13-week inhalation experiment, 10 rats from each exposure concentration, including air controls and 20 naive controls were exposed to a challenge concentration of Stoddard solvent at 6,200 mg/cu m (1,100 ppm) for 6 hours [21]. No deaths occurred during this period and the authors concluded that repeated inhalation of solvent vapors did not change subsequent susceptibility to Stoddard solvent.

Since only slight eye irritation was reported by volunteers exposed at 850 mg/cu m but not at 140 mg/cu m and animal studies showed, in the authors' opinion, no signs of solvent-related toxicity, Carpenter et al [21] concluded that there was no reason to reduce the TLV of Stoddard solvent which at the time was 1,150 mg/cu m (200 ppm) [84].

In 1975, Carpenter and associates [56] reported the effects of inhalation of 140 flash aliphatic solvent (a type of Stoddard solvent) on mice, rats, cats, and dogs. Five groups of 16 male rats, weighing 100-150 g, inhaled the solvent at either 270, 450, 790, 1,900, or 2,900 mg/cu m (43, 71, 125, 302, or 461 ppm, respectively, based on a mean molecular weight of 154, calculated by mass spectrometry data and analyzed by gas chromatography) for 8 hours to determine a concentration that caused cellular injury. At concentrations greater than 270 mg/cu m, the solvent

was present in the form of a vapor-aerosol mixture. Two of 16 rats died at the 2,900 mg/cu m solvent concentration. There were no other animal deaths. Gross and microscopic examination showed no abnormalities. The only signs of toxicity were irritation of the skin of the extremities at 1,900 and 2,900 mg/cu m and a slight loss of coordination at 2,900 mg/cu m after 6.5 hours of exposure. Since only 2 of 80 animals died, an LC50 could not be determined.

One female beagle (10.4 kg) was exposed to 140 flash aliphatic solvent at a concentration of 1,700 mg/cu m (270 ppm) of solvent for 8 hours [56]. Transitory lacrimation, starting after 30 minutes of exposure and lasting 1 hour, was apparent. A 0.5-kg loss in body weight occurred during the exposure period and overnight, but body weight increased to 10 kg by the succeeding day. A second beagle (10 kg) was exposed to solvent vapor at a concentration of 210 mg/cu m (33 ppm) for 8 hours with no signs of distress except lacrimation that occurred between 5.5 and 7.5 hours of the exposure. Weight loss occurred during the period following exposure. No microscopic or blood chemistry changes were reported.

Four male cats were exposed to 140 flash aliphatic solvent at 440 mg/cu m (70 ppm) for 6 hours [56]. No effects on the CNS were evident as assessed by righting reflexes, placing reactions, aversion to foot pain, extensory thrust reflex, and pupillary contraction. Microscopically, there were no tissue lesions that were attributed to solvent inhalation. An additional four male cats were subjected to the solvent aerosol at a nominal concentration of 10,000 mg/cu m for 6 hours. No body weight changes or evidence of toxicity were noted.

Ten male rats (107.5 g, mean body weight) were exposed to an aerosol of 140 flash aliphatic solvent (0.5 μm) at a nominal concentration of 10,200 mg/cu m for 340 minutes [56]. Signs of toxicity appeared in the following sequence: wet mouth, sluggish movements by 2 hours, extremities irritated by 4.5 hours, tremors and one death by 5.5 hours, three dead by 5.7 hours, and no deaths thereafter during a recovery period of 7-14 days. Fourteen days after exposure, mean body weight gain was slightly less than the controls (88 versus 105 g, respectively). The daily weight gain changes were not reported by the authors. Two solvent-exposed animals were killed after 7 days and were found to have had pneumonia, but the three rats that died during the exposure period had no evidence of this change. There was no increase in erythrocyte fragility in six male rats that were exposed to "saturated" vapor for 7 hours.

Groups of 25 male rats and 4 male dogs were exposed to 140 flash aliphatic solvent at a concentration of 0, 49, 100, or 230 mg/cu m (0, 7.8, 16, or 37 ppm) for 6 hours/day, 5 days/week, for 72-73 days [56]. Three rats from each exposure concentration were killed for microscopic examination after 14- and 39-day intervals. Body weight was measured, and blood and urine were analyzed. Abdominal and thoracic organs, endocrine glands, bone marrow, and nerve tissue were sectioned and examined microscopically.

No exposure-related effects were found at any of the concentrations tested in rats [56]. Changes in serum alkaline phosphatase, body weight gain, and differential leukocyte counts occurred in some of the exposed groups but, in the authors' opinion, were not related to solvent exposure

because the changes were within normal limits of their animals or were not dose-related.

No toxic effects in dogs were reported to have resulted from solvent exposure [56]. Serum glutamic-pyruvic transaminase values for the dogs exposed to 140 flash aliphatic solvent at a concentration of 49 mg/cu m (7.8 ppm) after 14 weeks of treatment were higher than controls, but, since there was no dose-dependent relationship, the authors felt that this effect was not solvent-related. They [56] concluded that, based on the lack or toxicity results found in the inhalation studies with rats and dogs and on sensory responses of human subjects, a hygienic standard should be 230 mg/cu m (37 ppm).

(f) Kerosene

Deichmann et al [85], in 1944, investigated the effects of kerosene on the skin of rabbits. Kerosene was applied at a dose of 3 ml/kg to the skin of rabbits for 6 consecutive days. Gross examination findings showed hair loss and scaling and cracking of the epidermis but no evidence indicating systemic toxicity.

In 1963, Rebello and Suskind [86] described the effects of kerosene on the dermal reactivity of guinea pigs sensitized to 2,4-dinitrochlorobenzene (DNCB). Seventeen albino guinea pigs, weighing 300-400 g, were sensitized with a single intradermal injection of 0.1 ml of a 0.05% solution of DNCB in 50% alcohol-saline. The backs of the guinea pigs were shaved and 0.5 ml kerosene was applied to one side of the back every 3rd day for 2 weeks; the other side of the back was left untreated. The last kerosene application occurred 24 hours before the challenging procedure, which consisted of the application of 0.1 ml of 0.1, 0.05, and

0.01% DNCB to both the kerosene-treated and untreated skin. Biopsy specimens were taken from the animals at both treated and control sites immediately before testing and from corresponding challenge sites after 24 and 48 hours. The criteria for estimating the degree of reactivity were as follows: 0, no evidence of erythema; 1+, slight erythema; 2+, moderate erythema, 3+, intense erythema or erythema and swelling.

The control sites challenged with 0.01% DNCB were all scored as 0 while the kerosene-treated sites had 15 scores of 0 and 2 of 1+ [86]. Five control sites challenged with 0.05% DNCB were reported as negative, while 11 and 1 were scored as 1+ and 2+, respectively. The kerosene-treated sites challenged with 0.05% DNCB had the following scores: eight skin specimens, 0; three skin specimens, 1+; five specimens, 2+; and one skin specimen, 3+. Four control sites challenged with 0.1% DNCB were reported as negative while nine and four were scored as 1+ and 2+, respectively. The kerosene-treated sites challenged with 0.1% DNCB were scored as follows: four skin sites, 0; three skin sites, 1+; nine skin sites, 2+; and one skin site, 3+. Microscopic examination of the kerosene-treated skin showed an eczematous type of reaction with dermal edema, spongiosis, and vesiculation, as well as dermal infiltrate. Only mild swelling of the epidermis and a lymphocytic dermal infiltrate extending into the epidermis were seen in the untreated skin. The authors concluded that kerosene may increase the reactivity of guinea pig skin to certain sensitizing agents.

In 1946, Carpenter and Smyth [87] examined the effects of deodorized kerosene on the rabbit cornea. The eyes of untreated albino rabbits were checked for preexisting abnormal lesions by instillation of a 5% solution of fluorescein and, 20 seconds later, by distilled water; only rabbits with

healthy eyes were selected for experimentation. Two hours later, 0.5 ml of undiluted deodorized kerosene was applied to the center of the cornea while the eyelids were retracted. The eyelids were then held closed for 1 minute and then released. After 18-24 hours, the eyes were examined in strong diffuse daylight, stained with fluorescein, and the injury graded from 1 to 10. The deodorized kerosene had a 1 rating and was thus rated innocuous to the rabbit eye.

Grant [54], in 1974, reported that kerosene was essentially innocuous to the rabbit eye. No details were given.

In 1967, Narasimhan and Ganla [88] discussed the effects of kerosene given orally to Swiss albino mice and Belgian rabbits and ip to dogs. The composition of the kerosene used in this study was 80% paraffins and naphthenes (no unsaturates), 20% aromatics, 0.25% sulfur (maximum by weight), and 0.005% mercaptans (maximum by weight) and was representative of three different commercial samples of kerosene from Middle-Eastern crude oil. Mice weighing 30 g were given filtered kerosene orally at a dose of 1 ml. Controls for this experiment received 1 ml of distilled water orally. Twenty-four hours after kerosene was initially administered, a second 1-ml dose of kerosene was given to the mice. The mice became drowsy 12-15 minutes later. Difficulty in breathing and rapid respiration also were evident. The drowsiness became very pronounced by the 2nd hour. Neuromuscular strength, as determined by the "inclined plane method," was weaker in the mice treated with kerosene than in the controls. The mice recovered 4 hours after kerosene administration. However, their coats were shaggy and smelled of kerosene and their anogenital regions were stained. The mice gradually became normal in appearance and in feeding habits.

After the second oral 1-ml dose of kerosene, 24 hours after the initial one, animal response was qualitatively the same as after the first dose. Drowsiness was more pronounced, and, at the end of 5 hours, the mice became comatose. All died 8-10 hours after receiving the second dose. On gross examination, the kidneys, including cut surfaces, appeared to be undamaged. Kidney tissue examined microscopically, however, showed cloudy degeneration of the renal tubules and the glomeruli and pelves were congested. The spleen was normal by both gross and microscopic examination. Gross examination findings showed no changes in the lungs, pleurae, trachea, and hilar glands. Cut surfaces of the lungs were hyperemic. The main blood vessels were found to be dilated when examined microscopically and the alveolar walls were hyperemic. A few erythrocytes were found in some alveoli located in the basal lobes. The authors stated that no cellular exudate or inflammatory cell infiltration was found in the lungs or pleurae. The bronchi and bronchioles were normal with an intact mucosa. The livers were enlarged and pale, had yellow patches scattered on their surfaces, and smelled of kerosene. A film of kerosene appeared on the surface of the formalin fixative in which liver tissue was placed before microscopic examination. Microscopic examination showed normal central veins and centrilobular zones, but the intermediate zones showed vacuolation and cloudy degeneration. Vacuolation also occurred in the periportal zone, but to a lesser extent.

Sixteen dogs, weighing 7-8 kg, each were given kerosene ip at a dose of 50 ml/kg [88]. After 1 hour, the adverse effects in dogs resembled those seen in mice in that they appeared sedated and drowsy. They also had rapid respiration, difficulty in breathing, and tachycardia. The dogs'

breath and urine smelled of kerosene. After 6 hours, the tachycardia persisted and the difficulty in breathing had increased. While cornea and conjunctival reflexes were present, the dogs gave no response to painful stimuli such as pinpricks. When forced to stand, the animals staggered. Liver function was affected and eventually severely impaired as shown by the sulfobromophthalein test increasing from an average of 4.6% retention at 0 hours to an average of 48.9% at 4 hours. In 7 or 8 hours, two of the dogs had tremors in their extremities, five had brief convulsions, and the remaining dogs, although not having convulsions, gradually became comatose. In a few hours, all animals were dead. At autopsy, the lungs appeared congested, but no fluid could be removed from the tracheobronchial tree. The bronchi and alveoli appeared to be normal when examined microscopically, although the blood vessels were dilated. No exudate or inflammatory cells were found. Gross examination of the kidneys showed no lesions; however, microscopically, severe cloudy degeneration was observed. The urinary bladder was severely congested and denuded in some areas. Livers appeared congested. Microscopic examination of the liver parenchyma showed cloudy degeneration with intense hyperemia.

Rabbits, weighing 1.5 kg, received kerosene orally at a dose of 70 ml/kg body weight [88]. Three hours later, the animals developed tachycardia and their body temperature was reported to increase to 38.6 C. This is a low temperature for normal rabbits and the authors did not indicate the initial body temperature. The coats were shaggy and stained with kerosene. Rapid respiration persisted throughout the day, and labored breathing occurred 19 hours after the administration of kerosene. Corneal responses were still present as was the response to painful stimuli. At 22

hours, breathing was even more difficult and the animals lost their righting reflexes. The extensor tone appeared to increase as the rabbits' necks became rigid and their extremities were completely extended. The animals went into convulsions and died without going into a coma. Blood glucose tests indicated progressivly decreasing blood glucose. Superficial yellow areas appeared on the liver, and cut sections showed areas of focal necrosis. Where complete tissue destruction had occurred, necrotic parenchyma and inflammatory cells were observed microscopically. At other sites, fatty degeneration was evident. Congestion was the only change seen in the lung parenchyma and bronchioles. The kidney tubules showed cloudy degneration with "frayed" cell margins. The glomeruli were severely congested.

The authors [88] concluded that ingested kerosene severely impaired liver function, which led to low blood glucose and eventual death. They further stated that the lowest value of blood glucose coincided with the onset of convulsions seen in rabbits and dogs and with the onset of coma as seen in dogs. Since only hyperemia of the lungs was observed, and, since there was no possibility of aspiration (because of the choice of animal and route of administration), the authors concluded that the cause of death from kerosene was not primarily the result of pneumonia but rather of acute liver damage.

In 1972, Wolfsdorf and Kundig [89] reported a study in which vervet monkeys were used to determine if the lung effects after kerosene ingestion were the result of absorption and excretion of the solvent by the lungs.

Monkeys, weighing 1.8-2.75 kg, were divided into three test groups of five monkeys each [89]. The test animals were anesthetized and then

weighed. Group I animals were sham tracheostomized, group II animals received a tracheostomy and had a plastic endotracheal tube inserted with the proximal end tied off. Both group I and II animals received kerosene at a dose of 45 ml/kg body weight via a nasogastric tube. Group III was tracheostomized and had cannulas inserted as had group II. Group III then received kerosene at a dose of either 1.0 ml iv or 0.2 ml in 5 ml of normal saline endotracheally. Six to 8 hours after treatment, all the test animals that survived were killed using an iv injection of barbiturate. The lungs were removed and examined macroscopically and microscopically, and the lung weight/body weight and the lung wet weight/dry weight ratios were determined. A control group consisted of 22 healthy monkeys ranging in weight from 1.8 to 5.4 kg. The animals were killed and their lungs were removed; lung weight/body weight and lung wet weight/dry weight ratios were determined.

Both mean ratio values for groups I and III were significantly greater than those of the control group but group II were not significantly different from the controls [89]. The mean lung weight/body weight and lung wet weight/dry weight ratios for Groups I and III were not significantly different. Lung lesions were present in four of five animals in group I. The number of animals with lesions in group III was not stated. Macroscopic and microscopic examination of the lungs from groups I and III showed heavy edematous lungs with patchy hemorrhagic areas. The lungs from group II animals were not distinguishable from the lungs of the control group.

The authors [89] concluded that the adverse pulmonary effects after kerosene ingestion were not the result of absorption and excretion of the

solvent through the lungs but rather the result of aspiration of the kerosene directly into the tracheobronchial tree. They based their conclusions on the fact that both group I and group II animals received kerosene nasogastrically, but, when aspiration was prevented in group II animals by a tracheostomy, no lung lesions were seen nor were the lung weight ratios significantly different from the controls. Group I and group III test animals both showed similar lung damage that had been produced in group III animals by the iv or endotracheal administration of kerosene. Furthermore, the mean lung weight ratios for both groups differed significantly from the controls.

In 1969, Volkova et al [90] described the effects of various types of kerosene on rats, mice, rabbits, and cats. The animals (unknown age and sex) were exposed to either lamp fuel kerosene, lamp fuel export type B, or lamp fuel export type A at aerosol concentrations of 500, 1,200, 2,500, or 12,000 mg/cu m for 2 hours/day for either 1 day or 2-4 weeks. During the experiment, the animals were observed for signs of gross toxicity and breathing rates. At the end of the experiment, the animals were killed and blood samples were taken for various unspecified analyses. Microscopic examination of the organs of the respiratory tract also was performed. The diameter of the aerosol particles was either 7 or 16 μm. The kerosene was combined with a mixture of equal weight of freon 11 and freon 12 so that the overall kerosene content was either 25 or 40% by weight. Lamp fuel kerosene was shown to have the highest aromatic content of the kerosenes and lamp fuel export type A the lowest, although chemical composition data were not reported.

Although very few quantitative data were reported, the authors [90] indicated that exposure to lamp fuel kerosene at 500 mg/cu m (droplet size, 7 μm) caused tracheitis, bronchitis, and an increase in the erythrocyte sedimentation rate. In addition to these effects, concentrations at 2,500 mg/cu m caused peribronchitis. A single exposure at 500 mg/cu m did not cause any signs of toxicity. Lamp fuel kerosene dispersed in particles of 16 μm at 1,200 mg/cu m for 2-4 weeks did not cause toxicity, but, at 12,000 mg/cu m, leukocytosis, a decreased erythrocyte sedimentation rate, and a 15-20% decrease in the respiratory rate were observed. Tracheitis, bronchitis, and pneumonia were also present. In all cases, lamp fuel kerosene caused conjunctivitis.

An aerosol of type B kerosene was found to be less toxic than lamp kerosene [90]. A single inhalation of this kerosene (droplet size, 7 μm) at 500 mg/cu m did not cause any signs of toxicity. Repeated exposure at this concentration and droplet size produced a 15-20% decrease in the respiratory rate and caused inflammation of the respiratory organs. With an aerosol concentration of 500 mg/cu m, no changes in the blood occurred, but, if the kerosene concentration was 2,500 mg/cu m, leukocytosis and monocytosis developed. In addition, pneumonia was seen in most animals. An increase in the diameter of the aerosol particles from 7 to 16 μm with single exposures to type B kerosene at 1,200 mg/cu m did not alter the toxicity. On repeated exposure to the same aerosol concentration, leukocytosis and bronchitis developed. If the aerosol concentration was 12,000 mg/cu m, the animals developed desquamative bronchitis and pneumonia in addition to leukocytosis. Type B kerosene caused conjunctitivits in exposed animals, regardless of dose or particle size.

A 7-μm aerosol of type A kerosene at 500 mg/cu m for either 1 day or 3-4 weeks of exposure had no toxic effects. Concentrations of type A kerosene at 2,500 mg/cu m only caused pulmonary polyemia in mice and rats. Larger particles (16 μm) of type A kerosene, at 1,200 mg/cu m, failed to cause signs of toxicity. If the concentration was increased to 12,000 mg/cu m, pulmonary polyemia and slight irritation of the mucous membranes occurred.

The authors [90] concluded that the toxicity of kerosene aerosols of various types differed, depending on the composition of the kerosene, its dispersion, and the frequency and duration of exposure. Purified kerosene was less toxic than the unpurified type. Although the purification procedure probably reduced the aromatic content, it is not possible to quantitatively correlate aromatic content with toxicity since no chemical composition data were given.

In 1976, Carpenter et al [67] described the effects of inhalation of deodorized kerosene vapors and aerosols on rats, mice, dogs, and cats. Six 90- to 120-g male albino rats were exposed for 8 hours to air "substantially" saturated with deodorized kerosene vapors. The approximate airborne concentration for this exposure was 100 mg/cu m (14 ppm) based on a mean molecular weight of 171 calculated from mass spectrometry data and analyzed by gas chromatography. The exposed rats showed no signs of discomfort or toxicity during the exposure, and the mean weight gain of 60 g during the 14-day observation period was not abnormal. After the 14-day observation period, the rats were killed and examined. No unusual pathologic findings were reported. A second group of six male rats were exposed to an aerosol of deodorized kerosene 6 hours/day for 4 days. The

mean airborne concentrations of the aerosol on the 4 days were 9,600, 6,900, 7,000, and 7,400 mg/cu m. The droplets in the aerosol averaged less than 1 μm in diameter.

After 1.25 hours of exposure on the 1st day, the rats showed a slight loss of coordination and were sluggish after 2.75 hours [67]. On the 2nd day of exposure, the rats were sluggish after 3 hours but showed good coordination. By the end of the second exposure, the extremities of the rats were red. On days 3 and 4, the condition of the rats did not appreciably change. After 1 day of no exposure, the extremities of the rats were dry with flakes forming. The dryness and flaking continued for 3 additional days, at which time one of the six rats showed a slight hair loss. The weights of the animals remained almost unchanged during the exposure and 1 day after exposure. The mean weight gain for the rats over a 14-day observation period was 63 g and was considered by the authors to be within acceptable limits. When six male albino rats inhaled deodorized kerosene at a concentration of 5,900 mg/cu m as an aerosol for 6 hours, no increase in osmotic-erythrocyte fragility was seen as compared with control rats immediately after exposure. Four male cats of mixed breed exposed at 6,400 mg/cu m for 6 hours showed no effect.

Separate groups containing 25 male rats and 4 male beagles each were exposed to deodorized kerosene at mean measured airborne concentrations of 20, 48, or 100, mg/cu m (approximately 2.9, 6.9, or 14 ppm, respectively) or to solvent free air 6 hours/day, 5 days/week, for 67 days [67]. The criteria of response for these exposures were body weight change and blood and urine analyses. Baseline blood values were measured in the dogs before the 1st day of inhalation. The values in rats were compared with a control

group that breathed solvent-free air.

Only two rats died during the 67-day study. One of eight died after 30 days of exposure at 100 mg/cu m. This animal had no weight loss before death [67]. Autopsy indicated pneumonia as the cause of death. The other death occurred after 16 days of exposure at 48 mg/cu m (6.9 ppm). This animal lost 40 g in weight during the 7 days preceding death. Abscess bronchopneumonia was believed to be the cause of death in this rat. The urine pH was increased, and specific gravity of the urine was decreased in the surviving rats after 8 weeks at 100 mg/cu m. There was a slight decrease in the rats' erythrocyte count in the 48 mg/cu m group at 8 weeks, which was not considered abnormal by the authors. Differential blood smears of rats exposed to kerosene at 20 mg/cu m showed a low value for immature neutrophils at 8 weeks and a slight increase in the ratio of neutrophils at 13 weeks. An elevated serum alkaline phosphatase value was reported after exposure at 100 mg/cu m for 8 weeks. This finding was the only abnormality in blood chemistry. The animal was sick when killed, and pleural adhesions and abscess bronchopneumonia were found at necropsy. Microscopic examination of tissues removed from the rats exposed at all three exposure concentrations showed no dose-related changes. The incidence of tubular regeneration was neither dose-related nor higher than that of controls with one exception. After 13 weeks, seven of nine rats exposed at 20 mg/cu m were reported to have had slight tubular regeneration as compared with two of eight rats in each of the higher exposure concentrations and with three of nine rats in the control group. In dogs exposed at 20 mg/cu m, there was a slight but significant increase in the body weight after 13 weeks. Occasional lesions were seen in the organs of

exposed and control dogs, but they were not considered to be related to the deodorized kerosene exposure.

From the results of these animal studies which showed a lack of toxicity at 100 mg/cu m and human sensory irritation studies which indicated that 140 mg/cu m was tolerable, Carpenter et al [67] suggested a hygienic standard of 100 mg/cu m (14 ppm) for deodorized kerosene.

Light petroleum hydrocarbons, such as kerosene, have a low toxicity when ingested and retained in the stomach, but, if the solvent reaches the lungs, extensive lung damage and death can occur [91]. In 1963, in an article in the Industrial Hygiene News Report [91], Gerarde and Eckardt were reported to have studied the aspiration hazard of kerosene. These investigators administered kerosene at 40 doses of 5 ml each by stomach tube to two rats. The animals appeared healthy and had normal lungs. Only minor losses of skin around the anus were noticed. After an administration of kerosene at 0.1 ml directly into the trachea of both rats, the animals developed hepatization of the lungs and acute cardiopulmonary congestion and subsequently died. Similar experiments were performed with chickens and rabbits with comparable results.

Gerarde [92], in 1963, reported the effect of increasing doses of kerosene given by tracheal insufflation, on the mortality of male rats (200-275 g). The animals that received 0.05, 0.10, 0.15, 0.20, or 0.25 ml had mortality ratios, 72 hours after administration, of 0/10, 4/10, 9/10, 9/10, and 10/10, respectively. The authors also reported that hydrocarbons having low viscosity, not exceeding 45 Saybolt Seconds Universal (SSU) at 100 F, would be readily aspirated. Kerosene has a viscosity of 32 SSU at 100 F.

Gross et al [93], in 1963, reported that an intratracheal injection of kerosene at sublethal doses of 0.05 ml and 0.02 ml produced either an acute exudative reaction or a chronic proliferative inflammation. The acute reaction was mainly of a leukocytic character and involved scattered, small clusters of alveoli. Other alveoli contained exudates consisting mainly of serous fluid or fibrin. In general, the acute inflammatory response was of mesodermal origin. The chronic inflammation was characterized by the enlargement of visible alveolar cells and an increase in their number. Many of the cells had large, excessively dark, round nuclei and basophilic, lacy cytoplasm. The vascular periadventitial tissue was usually edematous and infiltrated by sparsely distributed monocytes. In general, the chronic inflammation was of endodermal origin. The acute response reached its apex after 3 days while the chronic inflammation reached its peak in 10 days, gradually declining with remnants of the inflammation still demonstrable more than 1 month after the kerosene administration.

In 1965, Schwartz and coworkers [94] found that intratracheal administration of kerosene to rats at a dose of 0.2 ml was followed within minutes by development of noisy, labored ventilation. There was frequently a frothy nasal discharge which had a serosanguinous appearance. The gross adverse effect was that of a hyperemic and hemorrhagic pulmonary parenchyma. Microscopic examination of the tissue showed marked diffuse capillary engorgement, venous congestion, intraalveolar edema and a frequent occurrence of subepithelial vacuolation with separation of the bronchial lining.

In 1972, Steele et al [95] reported the effects of kerosene insufflation by studies in rats and dogs. Eighty white rats were used to determine the LD50 of intratracheally administered kerosene. This dose was subsequently used in a study to assess the value of corticosteroid and antibiotic treatment in hydrocarbon-induced pneumonitis in dogs. The intratracheal LD50 was determined to be 0.6 ml/kg, and this dose was administered with a catheter into the upper portion of the trachea of 20 dogs (3.8-32.3 kg), half of which received dexamethasone im at a dose of 2 mg immediately after kerosene instillation and 1 mg every 6 hours for 48 hours and ampicillin im at a dose of 25 mg/kg every 6 hours for 10 days. There were no significant differences between treated and control animals with respect to mortality, blood pH, pO2, pCO2, leukocyte count, and clinical appearance. Roentgenographic examination showed the presence of pneumonia within 24 hours after kerosene aspiration. The animals that died within a short time had lungs that were heavy and had massive confluent hemorrhages. No areas of crepitation were found, and all lobes were equally affected in both lungs. The cut surfaces showed extensive hemorrhage throughout the parenchyma and copious amounts of bloody fluid exudate. Microscopic examination revealed hemorrhage and epithelial destruction in the medium and small bronchi. The lung parenchyma showed extensive destruction with alveoli filled with bloody exudate, cell debris, and large numbers of inflammatory cells. Upon gross examination of the lungs of the animals that survived a 21-day observation period, the authors found patchy areas of normal-appearing parenchyma with normal crepitation. There were large areas of hyperemic edematous parenchyma with

focal areas of necrosis and abscess formation. Microscopic examination showed extensive areas of inflammation with microabscess formation.

Correlation of Exposure and Effect

(a) Petroleum Ether

Spruit et al [38], in 1970, reported that dermal exposure to petroleum ether caused disruption of the horny layer of the skin in humans. The average time of exposure before the appearance of irritation was about 20 minutes. No other reports have been found concerning the dermal toxicity of petroleum ether, but Oettel [39] conducted a study using pentane and hexane, the major constituents of petroleum ether, to evaluate the toxicity of these compounds and reported in 1936 that dermal exposure to pentane or hexane for up to 1 hour resulted in the development of irritation in humans characterized by erythema, hyperemia, swelling, and pigmentation. After 5 hours of exposure, these alkanes produced skin blisters.

Several studies have related industrial exposure to hexane with the development of polyneuropathy [40-43]. Yamamura [42], in 1969, reported the effects on workers after exposure to hexane, a constituent of the glue used in the production of sandals. The concentration of hexane in the air ranged from 1,759 to 8,793 mg/cu m. The initial symptoms included sensory impairment in the distal portion of the extremities. Inoue et al [44], in a followup study on the sandal workers, indicated that polyneuropathy could have developed as a result of exposure at concentrations of n-hexane below 1,759 mg/cu m. In 1971, Herskowitz et al [40] examined employees working in a furniture factory who were exposed to n-hexane. Air samples of hexane

were found to average 2,286 mg/cu m and peaked at 4,573 mg/cu m. The patients complained of one or more of the following symptoms: abdominal cramps, burning sensations, numbness and weakness of the distal extremities, and paresthesia. In 1972, Yamada [41] investigated 17 workers reporting symptoms of intoxication from exposure to hexane vapor. Six worked in polyethylene laminating plants where airborne hexane concentrations ranged from 3,517 to 8,793 mg/cu m. The 11 other workers were employed by a pharmaceutical company and used a 95% hexane solution to remove oil from the surface of tablets. The airborne hexane concentration in the center of the workroom was 1,759 mg/cu m, but, in the immediate work area, the concentration was 3,517 mg/cu m. The initial worker complaints were fatigue and loss of appetite, followed by paresthesia in distal parts of the extremities and difficulty in walking. In 1975, Takeuchi et al [43] reported on four persons exposed to petroleum benzine who worked in a brocade sash cleaning shop in a poorly ventilated workroom. In general, within 1-9 months the workers experienced fatigue, loss of appetite, difficulties in walking, muscle weakness, paresthesia, irritability, insomnia, and weight loss. Although determination of the air concentrations of petroleum benzine were not made at the time the workers developed their illness, analysis of the concentrations of petroleum benzine and its major constituents in the workroom air was subsequently made. The concentration of petroleum benzine and n-hexane did not exceed 4,400 and 844 mg/cu m, respectively. The authors [43] indicated that, if the concentration of petroleum benzine rose higher than 4,400 mg/cu m, irritation of the mucous membranes would have become unbearable and a narcotic effect would have occurred. The effects of dermal exposure,

although not measured, could not be disregarded as a potential route of intoxication. In all the above cases, the authors [40-44] concluded that the workers had signs and symptoms of polyneuropathy. Gaultier et al [45] stated that other alkanes other than n-hexane may also cause polyneuropathy.

In 1967, Miyagaki [79] reported the neurotoxic effects of n-hexane exposure in mice. The animals exposed at n-hexane concentrations greater than 879 mg/cu m for 24 hours/day, 6 days/week, for 1 year developed signs of neurotoxicity while mice similarly exposed at 352 mg/cu m of hexane showed no abnormalities.

Truhaut et al [80] exposed rats to a technical grade hexane at a concentration of 2,000 ppm, 5 hours/day, 5 days/week, for 1-6 months. The hexane contained 0.3% n-pentane, 25.1% 2-methylpentane plus cyclopentane, 18.4% 3-methylpentane, 48.8% n-hexane, 8% methylcyclopentane, 1.2% methylhexane, and 1.2% benzene. Studies on the sciatic and saphenous nerves indicated that this solvent caused a decrease in the conduction rate, an increase in the refractory period, and a decrease in the excitability of the nerves.

(b) Rubber Solvent

Carpenter et al [9] exposed volunteers for about 10 seconds to rubber solvent vapor to determine its odor threshold. The authors concluded that the most probable threshold concentration was about 40 mg/cu m (10 ppm) given the determined range of 6.4-64 mg/cu m (1.6-16 ppm). Volunteers were also exposed to rubber solvent vapor at one of a series of concentrations from 1,700 to 8,100 mg/cu m (430-2,000 ppm) for one 15-minute period/day. Slight transitory eye, nose, and throat irritation responses were noted at

concentrations of 3,100 mg/cu m (780 ppm) and above, as well as four cases of lightheadedness and one of headache at the 8,100 mg/cu m concentration, both of which were reported to have subsided within 10 minutes after exposure. At the 3,100 mg/cu m concentration, one volunteer reported eye irritation and two others throat irritation. One of six exposed to rubber solvent at 8,100 mg/cu m reported eye and throat irritation.

The authors [9] also reported the toxic effects of rubber solvent inhalation in animal toxicity studies. Groups of rats were each exposed at 11,000, 21,000, 39,000, or 96,000 mg/cu m (2,800, 5,300, 9,800, or 24,200 ppm) for a single 4-hour period. Impairment of coordination and eye irritation were observed at concentrations greater than 11,000 mg/cu m. Convulsions and death occurred at 96,000 mg/cu m. The calculated 4-hour LC50 was reported to be 61,000 mg/cu m (15,000 ppm). Female beagles were exposed to rubber solvent vapors at concentrations of 5,900, 13,000, or 25,000 mg/cu m (1,500, 3,300, or 6,300 ppm) for a single 4-hour period. Loss of coordination was observed at concentrations of 13,000 and 25,000 mg/cu m. No observable effects occurred at 5,900 mg/cu m.

The acute CNS effects of a 4-hour exposure to rubber solvent vapors at 49,000 mg/cu m (12,400 ppm) were examined in male cats [9]. A time-related and sequential pattern of events occurred which included ataxia, loss of proprioception, salivation, relaxation of the nictitating membrane, unconsciousness, tremors, and convulsions. Gross and microscopic examination of tissues showed no lesions related to solvent exposure.

Male rats and beagles were exposed to either 0, 1,900, 3,700, or 7,900 mg/cu m (0, 480, 930, or 2,000 ppm) of rubber solvent, 6 hours/day, 5 days/week, for up to 62-63 days [9]. There were no animal deaths

attributed to rubber solvent. There were no changes in body weight gain, blood chemistry, or hematology that resulted from solvent exposure. Serum alkaline phosphatase was higher after 62 days in all rats exposed to rubber solvent, but the authors suggested that this finding was an artifact which resulted from very low control alkaline phosphatase levels. Microscopic examination of various organ sections showed no tissue damage that could be attributed to the solvent vapors. There was a significant increase in the specific gravity of the urine of dogs exposed at 7,900 mg/cu m for 62 days. The significance was not reported by the investigators.

(c) Varnish Makers' and Painters' Naphtha

Carpenter et al [17] reported the effects of exposure to VM and P naphtha on human odor and sensory responses. The authors concluded that the odor threshold was about 4 mg/cu m (0.86 ppm). In assessing the sensory responses to VM and P naphtha, Carpenter et al subjected volunteers to 15-minute exposures to the naphtha at concentrations ranging from 660 to 4,100 mg/cu m (140 to 880 ppm). Olfactory fatigue was noted at all concentrations. Solvent concentrations up to 2,100 mg/cu m (450 ppm) caused only slight or transitory eye and throat irritation in two of seven subjects which the authors considered "sporadic sensory responses." At the highest concentration tested, 4,100 mg/cu m (880 ppm), definite throat and eye irritation was produced.

In an acute inhalation study, rats were exposed to VM and P naphtha at 4,400, 9,800, or 26,000 mg/cu m (940, 2,100, or 5,600 ppm) for 4 hours [17]. Animals exposed to 4,400 mg/cu m of VM and P naphtha were reported to be free from distress during and after exposure. All animals exposed at 26,000 mg/cu m died. Responses of the rats at the highest concentration

were eye irritation and CNS depression characterized by poor coordination followed by convulsions and death. The authors estimated an approximate 4-hour LC50 of 16,000 mg/cu m (3,400 ppm) for VM and P naphtha.

Two dogs were exposed to VM and P naphtha at a nominal concentration of 16,000 mg/cu m (3,400 ppm) for 2 hours [17]. Eye irritation, tremors, mild ataxia, and mydriasis were evident. One animal became prostrate after 1.5 hours but recovered after cessation of solvent exposure. A third dog was exposed to VM and P naphtha at 8,000 mg/cu m (1,700 ppm) for 4 hours and appeared normal during and after solvent exposure.

Cats inhaling VM and P naphtha at 19,000 mg/cu m for 4 hours exhibited progressive symptoms usually indicative of CNS depression: salivation, mydriasis, body tremors, prolapse of the nictitating membrane, poor coordination, vomiting, convulsions, and prostration [17]. All of the animals survived the exposure, but one became moribund shortly thereafter and was killed. Autopsy showed suppurative pneumonia.

In short-term inhalation studies, Carpenter et al [17] subjected rats and dogs to repeated daily inhalation of VM and P naphtha for 6 hours/day, 5 days/week, for 65 days. The concentrations of solvent used were 0, 1,300, 2,800, or 5,800 mg/cu m. No outward signs of distress were observed in either species during the study. Rats exposed to VM and P naphtha at 5,800 mg/cu m showed a significant decrease in erythrocyte count after 65 days of exposure. The following statistically significant differences were noted in the dogs exposed for 65 days to VM and P naphtha: an increase in serum alkaline phosphatase at the 5,800 mg/cu m concentration, an increase in the ratio of liver weight to body weight and a decrease in the reticulocyte count at the 2,800 mg/cu m concentration, and increases in

reticulocyte counts at the 5,800 and 1,300 mg/cu m concentrations. The authors felt that the above changes were unimportant and could possibly be experimental artifacts rather than serious deleterious effects.

(d) Mineral Spirits

In 1975, Astrand et al [48] reported on the effects of white spirits (mineral spirits) on human alveolar air and blood solvent concentrations during rest and exercise. The white spirits used in the study consisted of 83% aliphatic and 17% aromatic components. In the initial trials, men were exposed at 2,500 or 5,000 mg/cu m for an unspecified period of time. Nausea and vertigo were apparent at both concentrations. No differences were noted in heart rate, alveolar ventilation, or oxygen uptake either at rest or during exercise at an intensity of 50 watts during exposure at 1,250 and 2,500 mg/cu m of white spirits. In addition, their studies [48] indicated that more solvent reaches the blood during exercise than during rest. This finding, in the absence of changes in alveolar ventilation, suggests changes in the respiratory transport.

In 1975, Gamberale et al [50] reported the effects of exposure to white spirits (mineral spirits) on humans. Performance tests were conducted in perceptual speed, reaction time, short-term memory, numerical ability, and manual dexterity. Men exposed to white spirits at 625, 1,250, 1,875, and 2,500 mg/cu m for four continuous 30-minute periods showed no impairment of the five performance tests. Exposure to 4,000 mg/cu m of white spirits for 50 minutes had no effect on perceptual speed, numerical ability, and manual dexterity. There was, however, a definite prolongation of reaction time and a possible impairment of short-term memory as a result of exposure at 4,000 mg/cu m. The authors concluded that there was a risk

of subjective distress and adverse effects on psychomotor and intellectual functions in a worker exposed to 2,500 mg/cu m who is doing light industrial work, since the alveolar air concentrations of white spirits in workers at rest exposed at 4,000 mg/cu m was similar to the white spirits alveolar air concentration of workers exposed at 2,500 mg/cu m doing light physical activity [48,50].

Rector et al [82], in 1966, described the effects of mineral spirits on five species of animals exposed continuously for 60-90 days or exposed intermittently, 8 hours/day, 5 days/week, for a total of 30-60 exposure periods. In continuous 90-day exposure experiments, rats, guinea pigs, rabbits, dogs, and monkeys were exposed to mineral spirits of concentrations ranging from 114 to 1,271 mg/cu m (18-200 ppm, assuming a molecular weight of 156). Exposure of the dogs, monkeys, and rabbits to the mineral spirits at all concentrations tested failed to induce mortality. An occasional death was noted in the rats at all concentrations, but the number of deaths was similar to that of the controls. In contrast, the guinea pigs were very susceptible to the mineral spirits with deaths occurring in all groups subjected at a concentration of 363 mg/cu m (60 ppm) or greater. No deaths occurred in the guinea pigs exposed at 114 or 238 mg/cu m (18 or 37 ppm). The rate of body weight gain generally was similar in test animals and in controls except in guinea pigs and monkeys exposed at the highest concentration of 1,271 mg/cu m. In the overall study, no consistent pattern of dose-response hematologic realtionships was found, and, therefore, some of the alterations seen in preexposure and terminal leukocyte counts could not be attributed to solvent exposure. Although no remarkable changes were noted

on gross examination of all animals, lung irritation and congestion were observed in all species. In general, the observations of congested lungs were substantiated microscopically in only those animals exposed to mineral spirits at 1,271 mg/cu m, where lung tissue showed evidence of bronchitis and mixed inflammatory cell infiltration. Microscopic examination of the heart, spleen, and kidneys did not show adverse findings that could be attributed to solvent exposure.

Rector et al [82] also conducted three intermittent exposure studies in which the same five species were exposed 8 hours/day, 5 days/week, for 30-60 exposures to mineral spirits at concentrations of 593-596 or 1,353 mg/cu m (93-94 or 212 ppm). The animals exposed at 1,353 mg/cu m for 6 weeks showed no toxic signs and body weight patterns and hematologic values were similar to those of the controls. No consistent microscopic changes were found except for possible lung irritation and liver damage in guinea pigs exposed at 1,353 mg/cu m. Animals exposed at 596 mg/cu m for 6 weeks showed no signs of toxicity and body weight gains and hematologic parameters were all within normal limits. No noteworthy microscopic tissue changes were reported. After a 2-week recovery interval, several rats and guinea pigs who were exposed previously to 596 mg/cu m were reexposed for a second series of 30 exposures at 593 mg/cu m. There were no noticeable signs of toxicity during this second reexposure and hematologic parameters were within normal limits. After a 17-day observation period, the animals were killed and autopsied. The only noteworthy microscopic finding was focal lymphocytic involvement in the lungs of some exposed guinea pigs.

(e) Stoddard Solvent

Braunstein [51] reported follicular dermatitis on the hands and arms of a worker after 2 weeks of dermal exposure to liquid Stoddard solvent. He also complained of nausea when initially inhaling the solvent. Eventually, this worker developed obstructive jaundice and subacute yellow liver atrophy.

Scott et al [52] observed four cases and Prager and Peters [53] one case of aplastic anemia after dermal exposure to liquid Stoddard solvent.

Markel and Shmunes [74], in 1974, cited the results of a Stoddard solvent hazard evaluation of a greeting-card company. Workers were exposed to Stoddard solvent at 99-1,906 mg/cu m (average 438 mg/cu m) in their working environment and the authors [74] concluded that, under the conditions found at the time of the survey, Stoddard solvent was not toxic and did not constitute a hazard to health.

In 1974, Larsen and Shmunes [75] found that Stoddard solvent used to clean polishing machines was probably the cause of dermatitis in several industrial workers. These workers also complained of headache and eye and nose irritation. Although Stoddard solvent concentrations of less than 20 ppm (115 mg/cu m) were detected, the authors felt that higher concentrations could have occurred immediately after the polishing machines were cleaned with Stoddard solvent and could have been the cause of the headache and eye and throat irritation.

Carpenter et al [21] determined both the odor and the sensory thresholds for Stoddard solvent. The odor threshold was found to be between 0.5 and 5 mg/cu m (0.09 and 0.9 ppm). The sensory threshold was found to be between 850 and 2,700 mg/cu m (150 and 470 ppm) for a 15-minute

exposure. No irritation was noted at 140 mg/cu m (24 ppm), while slight, transient eye irritation occurred in one volunteer at 850 mg/cu m and in all at 2,700 mg/cu m, some with tearing. Slight dizziness also was reported at 2,700 mg/cu m by some of the subjects. The volunteers experienced olfactory fatigue at all of the concentrations tested, but recovered fully within 10 minutes after exposure ended.

Nelson et al [55] similarly observed that volunteers exposed to Stoddard solvent for 3-5 minutes at air concentrations in excess of 400 ppm (2,290 mg/cu m) suffered irritation of the eyes, nose, and throat.

Carpenter et al [56] described odor threshold sensory irritation in humans exposed to 140 flash aliphatic solvent. The odor threshold was about 4 mg/cu m (0.6 ppm). Minor eye irritation was the only discomfort noted by subjects exposed to 140 flash aliphatic solvent at either 110 or 310 mg/cu m (17 or 49 ppm) for 15 minutes. This response was expressed by the same subject during each inhalation period and did not persist after exposure. All subjects reported olfactory fatigue at both concentrations. The subjects felt that 310 mg/cu m (49 ppm) could be an acceptable concentration for an 8-hour day.

In 1975, Carpenter et al [21] examined the effects of Stoddard solvent inhalation in rats, mice, cats, and dogs. Rats inhaled Stoddard solvent at 0, 2,400, 4,800, or 8,200 mg/cu m (0, 420, 800, or 1,400 ppm) for 8 hours. The highest concentration, 8,200 mg/cu m, was not lethal to the rats during the exposure period, but one rat died while being removed from the exposure chamber. No other animal deaths occurred. Loss of coordination, eye irritation, and bloody nasal exudate were reported to have occurred in the animals exposed at 8,200 mg/cu m. When rats inhaled

4,600 mg/cu m, they showed similar symptoms but no loss of coordination. Inhalation at 2,400 mg/cu m failed to cause any response during or after solvent exposure. A beagle exposed at 8,000 mg/cu m (1,400 ppm) for 8 hours developed eye irritation, salivation, tremors, and clonic spasms but did not die. There were no toxic effects seen in a dog exposed at 4,000 mg/cu m (700 ppm) of Stoddard solvent for 8 hours. Cats were exposed to Stoddard solvent at a nominal concentration of 10,000 mg/cu m (1,700 ppm) until death ensued between 2.5 and 7.5 hours of exposure after showing signs of CNS depression. In short-term inhalation experiments, Carpenter et al subjected rats and dogs to repeated daily inhalations of Stoddard solvent for 6 hours/day, 5 days/week, for 13 weeks. The concentrations of solvent used in the study were 0, 480, 1,100, or 1,900 mg/cu m (0, 84, 190, or 330 ppm). No animals died as a result of solvent exposure. The authors did not consider that the solvent exposure caused changes in blood chemistry or hematology except for blood urea nitrogen levels in rats after 13 weeks of exposure at 1,900 mg/cu m since the changes were not dose related. Marked tubular regeneration in the kidneys and dilation of the loops of Henle were evident in rats exposed to Stoddard solvent vapor at 1,900 mg/cu m for either 8 or 13 weeks. Similar renal changes were seen following 8 and 13 weeks' exposure to Stoddard solvent at 1,100 mg/cu m. The authors [21] reported that the loop of Henle dilation seen after 13 weeks was not statistically significant.

Carpenter et al [56] exposed rats, cats, mice, and dogs in a series of experiments to 140 flash aliphatic solvent. Rats were exposed to the solvent at concentrations of either 0, 270, 450, 790, 1,900, or 2,900 mg/cu m (0, 43, 71, 125, 302, or 461 ppm) for 8 hours. Two of 16 rats died at

the 2,900 mg/cu m concentration. There were no other animal deaths. The only signs of toxicity were skin irritation at 1,900 and 2,900 mg/cu m and minor loss of coordination at 2,900 mg/cu m of 140 flash aliphatic solvent. A beagle was exposed at either 210 or 1,700 mg/cu m (33 or 270 ppm) of solvent for 8 hours. Both concentrations caused transitory tearing and weight loss. Cats exposed at 440 mg/cu m or 10,000 mg/cu m of solvent for 6 hours showed no signs of CNS disturbance. Rats exposed at 10,200 mg/cu m of solvent aerosol for 340 minutes showed signs of toxicity: wet mouth, sluggish movement, irritated extremities, tremors, and death. Groups of rats and dogs were exposed to either 0, 49, 100, or 230 mg/cu m (0, 7.8, 16, or 37 ppm) of 140 flash aliphatic solvent for 6 hours/day, 5 days/week, for 72-73 days. In the authors' opinion, there were no treatment-related effects of solvent inhalation at any of the concentrations tested in rats or dogs.

(f) Kerosene

Several investigators have shown that kerosene can cause dermatitis [61,85,94]. In addition, several studies have examined the mechanism of action of the kerosene-induced skin irritation [62-64].

In 1963, Rebello and Suskind [86] found that kerosene increased the reactivity of guinea pig skin to 2,4-dinitrochlorobenzene (DNCB), a sensitizing agent. Dermal administration of kerosene increased the dermal irritation caused by DNCB. Based on the results of this study, it is possible to speculate that other sensitizing agents, such as pollen or certain drugs, may heighten the response to dermal kerosene exposure and result in augmented toxicity. Several theories have been postulated to explain the increased dermal reactivity to sensitizers after pretreatment

with chemical agents. The chemically treated skin may provide a larger quantity of appropriate protein for conjugation and consequent conversion of a particular chemical into an antigen. The chemicals may enhance the rate of formation of a complete antigen by increasing the permeability of the skin to substances such as DNCB. Finally, the mononuclear cells and macrophages may be increased as a result of chemical treatment and therefore increase the degree of sensitization. The results from the studies by Lupulescu et al [62,63] tend to support the latter two theories with respect to dermal kerosene treatment.

In 1939, Cavanagh and Wilner [57] described a fatal case of aplastic anemia that resulted from dermal exposure to kerosene where the patient had rubbed kerosene on her legs daily for several months. The authors concluded that the aplastic anemia seen in the patient may have been the result of the aromatic hydrocarbon content of the kerosene.

In 1955, Johnson [58] investigated a presumable sensitivity of a person to kerosene. The patient developed hypoplastic anemia with a deficiency of all cell elements and hypoplastic marrow after recurrent exposure to kerosene for a 3-year period. The author [58] suggested, however, that aromatic hydrocarbons of the benzol series present in kerosene may have been responsible for the myelotoxicity in this individual.

Hiebel et al [59] observed bone marrow depression after dermal exposure to kerosene in one patient and by a combination of dermal and oral routes in two patients.

In 1946, Carpenter and Smyth [87] related that the application of 0.5 ml of deodorized kerosene into the eye of rabbits produced no adverse

effects. However, Volkova et al [90] found that animals exposed to unpurified kerosene in an aerosol developed conjunctivitis.

In 1969, Volkova et al [90] noted that aerosols of purified kerosene were less toxic than aerosols of unpurified kerosene. Exposure to unpurified kerosene at 500 mg/cu m caused respiratory irritation and leukocytosis.

In 1976, Carpenter et al [67] determined the odor and sensory thresholds for deodorized kerosene determined in a group of volunteers. The odor threshold was approximately 0.6 mg/cu m (0.09 ppm). Fifteen-minute exposures to kerosene at a mean measured vapor concentration of 140 mg/cu m (20 ppm) were easily tolerated without sensory irritation. A slight decrease in olfactory acuity, but not total fatigue, was noted in two subjects. The 140 mg/cu m concentration of deodorized kerosene was deemed by the subjects to be acceptable for an 8-hour workday, based on the 15-minute exposure.

In 1976, Carpenter et al [67] examined the effects of inhalation of deodorized kerosene vapors and aerosols on rats, mice, dogs, and cats. Male rats were exposed for 8 hours to air "substantially" saturated with deodorized kerosene vapors. The approximate air concentration for this exposure was 100 mg/cu m (14 ppm). The exposed rats showed no signs of discomfort or toxicity during the exposure. After the 14-day observation period, the rats were killed, examined, and found to have no unusual or exposure-related findings. A second group of male rats were exposed to an aerosol of deodorized kerosene for 6 hours/day for 4 days. The mean air concentrations of the aerosol on the 4 days were 9,600, 6,900 7,000, and 7,400 mg/cu m. After 1.25 hours of exposure on the 1st day, the rats

showed a slight loss of coordination and were sluggish after 2.75 hours. On the 2nd day of exposure, the rats were sluggish but showed good coordination. By the end of the second exposure, the extremities of the rats were red. On days 3 and 4, the condition did not appreciably change. After 1 day of no exposure, the extremities of the rats were dry with flakes forming. The dryness and flaking continued for 3 additional days at which time one rat showed a slight hair loss. The weights of the animals remained almost unchanged during the exposure and at 1 day postexposure. Four male cats of mixed breed exposed to deodorized kerosene at 6,400 mg/cu m as an aerosol for 6 hours showed no toxic effects. Separate groups of 25 male rats and 4 male beagle dogs were exposed to deodorized kerosene at mean measured air concentrations 20, 48, or 100 mg/cu m (approximately 2.9, 6.9, or 14 ppm, respectively) or to solvent-free air for 6 hours/day, 5 days/week, for 67 days. The criteria of response for these exposures were body weight change and blood and urine analyses. Only two rats died during the 67-day study. One died after 30 days of exposure at 100 mg/cu m. This animal had no weight loss prior to death. Autopsy showed that death might have been from pneumonia. The other death occurred after 16 days in rats exposed at 48 mg/cu m. This animal lost 40 g of weight during the 7 days before death. Abscess bronchopneumonia was believed to be the cause of death in this rat. The urine pH was increased and specific gravity of the urine was decreased after 8 weeks, which were not considered abnormal by the authors. Differential blood smears of rats exposed at 20 mg/cu m showed a low value for immature neutrophils at 13 weeks. An elevated serum alkaline phosphatase value was reported after exposure at 100 mg/cu m for 8 weeks in a single rat. This finding was the only

abnormality in blood chemistry. The animal was sick when killed and pleural adhesions and abscess bronchopneumonia were found at autopsy. Microscopic examination of tissues removed from the rats exposed at all three concentrations showed no dose-related changes. The incidence of tubular regeneration was neither dose related nor higher than controls with one exception. After 13 weeks, seven of nine rats exposed at 20 mg/cu m had slight tubular regeneration as compared with two of eight rats at each of the higher exposure concentrations and three of nine rats in the control group. In dogs exposed at 20 mg/cu m, a slight increase in the body weight of dogs was reported after 13 weeks. Occasional lesions were seen in the organs of the dogs in the exposed and control groups. The lesions were not considered by the authors to be related to the deodorized kerosene.

Light petroleum hydrocarbons, such as kerosene, have a low toxicity when ingested and retained in the stomach, but, if the solvent is aspirated directly into the lungs, extensive lung damage and death can occur [91]. Several investigators [91,92,94,95] have reported that 0.1-0.2 ml of kerosene administered into the trachea can cause death. In addition, there are numerous cases of kerosene poisoning in humans by aspiration or ingestion of the liquid [68-70].

Carcinogenicity, Mutagenicity, Teratogenicity, and Effects on Reproduction

There is no present reason for suggesting that these solvents, if they are free of carcinogenic aromatics such as benzene, would cause cancer, birth defects, or germinal mutations. McMichael et al [76], in 1975, demonstrated an association between leukemia and jobs entailing exposure to solvents but did not identify the exact etiologic agent.

Benzene, a known myelotoxic agent, was used by these workers and it may have been the causative agent. Downing [65], in 1952, related that a man exposed to various solvents and greases including kerosene developed a epidermoid carcinoma. The etiologic agent responsible for the carcinoma was unknown since the worker was exposed to a wide variety of substances.

TABLE III-3

EFFECTS OF PETROLEUM ETHER EXPOSURE ON HUMANS

Number of Subjects	Route of Exposure	Duration of Exposure	Observed Effects	Reference
1	Respiratory	-	Severe clonic convulsions	37
-	Dermal*	10-30 min	Skin irritation, peeling of skin, water vapor loss from injured skin	38

*1 ml

TABLE III-4

EFFECTS OF RESPIRATORY EXPOSURE TO RUBBER SOLVENT ON HUMANS

Number of Subjects	Exposure Concentration	Duration of Exposure	Observed Effects
7	8,100 mg/cu m (2,000 ppm)	15 min	Olfactory fatigue in 6/7, light-headedness in 4/7, reddening of sclera in 2/7, eye, nose, and throat irritation in 1/7
7	6,700 mg/cu m (1,700 ppm)	"	Olfactory fatigue in 7/7, eye and throat irritation and reddening of sclera in 2/7, light-headedness and nose irritation in 1/7
7	3,100 mg/cu m (780 ppm)	"	Olfactory fatigue in 5/7, throat irritation in 2/7, eye and nose irritation in 1/7
7	1,700 mg/cu m (430 ppm)	"	Olfactory fatigue in 7/7, eye and nose irritation in 1/7
6 (two trials)	640 mg/cu m (160 ppm)	10 sec	All detected odor
6 (two trials)	64 mg/cu m (16 ppm)	"	Odor detected by 9/12
6 (two trials)	6.4 mg/cu m (1.6 ppm)	"	Odor detected by 2/12

Adapted from reference 9

TABLE III-5

EFFECTS OF RESPIRATORY EXPOSURE TO
VARNISH MAKERS' AND PAINTERS' NAPHTHA

Number of Subjects	Exposure Concentration	Duration of Exposure	Observed Effects
7	4,100 mg/cu m (880 ppm)	15 min	Olfactory fatigue in 6/7, eye irritation in 3/7, throat irritation in 4/7
7	2,100 mg/cu m (450 ppm)	"	Olfactory fatigue in 5/7, eye and throat irritation in 2/7
7	1,400 mg/cu m (300 ppm)	"	Olfactory fatigue in 3/7, throat irritation in 2/7, eye irritation in 1/7
7	660 mg/cu m (140 ppm)	"	Olfactory fatigue in 6/7, eye irritation in 2/7, throat irritation in 1/7
6 (two trials)	70 mg/cu m (15 ppm)	10 sec	All detected odor
6 (two trials)	7 mg/cu m (1.5 ppm)	"	Odor detected by 11/12
6 (two trials)	0.7 mg/cu m 0.15 mg/cu m		Odor detected by 2/12

Adapted from reference 17

TABLE III-6

EFFECTS OF RESPIRATORY EXPOSURE TO MINERAL SPIRITS ON HUMANS

Number of Subjects	Exposure Concentration	Duration of Exposure	Observed Effects	Reference
-	500 mg/cu m	-	Severe nausea, vertigo	48
-	2,500 mg/cu m	-	"	48
14	625-2,500 mg/cu m	Up to 2 hr	No effects on perceptual speed, reaction time, short-term memory, numerical ability, and manual dexterity	50
8	4,000 mg/cu m	50 min	Prolonged reaction time, probable impaired short-term memory	50

TABLE III-7

EFFECTS OF RESPIRATORY EXPOSURE TO STODDARD SOLVENTS ON HUMANS

Number of Subjects	Exposure Concentration	Duration of Exposure	Observed Effects
6	2,700 mg/cu m (470 ppm)	15 min	Eye irritation in 6/6, olfactory fatigue in 5/6, dizziness in 2/6, throat irritation in 1/6
6	850 mg/cu m (150 ppm)	"	Olfactory fatigue in 6/6, eye irritation in 1/6
6	140 mg/cu m (24 ppm)	"	Olfactory fatigue in all
6 (two trials)	5 -50 mg/cu m (1 - 9 ppm)	10 sec	Odor detected by 11/12
"	0.5 mg/cu m (0.1 ppm)	"	None detected odor

Adapted from reference 21

TABLE III-8

EFFECTS OF STODDARD SOLVENTS ON HUMANS AT UNKNOWN CONCENTRATIONS

Number of Subjects	Route of Exposure	Duration of Exposure	Observed Effects	Reference
1	Dermal and possibly respiratory	10 wk	Follicular dermatitis, jaundice	51
1*	"	2/mon 2 yr	Excessive uterine bleeding, purplish discolorations of skin, moderate marrow hypoplasia, death	52
1**		4-5/wk 6 mon	Fatigue, moderate marrow hypoplasia, death	52
1	"	2 yr	Purplish discolorations of skin, fatigue, pallor, marked marrow hypoplasia, death	52
1	"	20 yr	Slight reduction of all formed elements in blood	52
10	Respiratory	3-5 min***	Eye, nose, and throat irritation	55

*Carbon tetrachloride exposure also occurred.
**Tripelennamine and diphenhydramine were taken by patient for seasonal allergy.
***Greater than 2,290 mg/cu m

TABLE III-9

EFFECTS OF RESPIRATORY EXPOSURE TO 140 FLASH ALIPHATIC SOLVENT ON HUMANS

Number of Subjects	Exposure Concentration	Duration of Exposure	Observed Effects
6	110-310 mg/cu m (17- 49 ppm)	15 min/d 2 d	Olfactory fatigue in 6/6, eye irritation in 1/6
6 (two trials)	40 mg/cu m (6 ppm)	10 sec/d 2 d	Odor detected by all 12
"	4 mg/cu m (0.6 ppm)	"	Odor detected by 7/12
"	0.4 mg/cu m (0.06 ppm)	"	None detected odor

Adapted from reference 56

TABLE III-10

EFFECTS OF RESPIRATORY EXPOSURE TO DEODORIZED KEROSENE ON HUMANS

Number of Subjects	Exposure Concentration	Duration of Exposure	Observed Effects
6	140 mg/cu m (20 ppm)	15 min	Slight olfactory fatigue in 3/6
6 (two trials)	100 mg/cu m (3 ppm)	10 sec/d 2 d	Odor detected by all 12

Adapted from reference 67

TABLE III-11

EFFECTS OF EXPOSURE TO KEROSENE ON HUMANS

Number of Subjects	Route of Exposure	Amount	Duration of Exposure	Observed Effects	Reference
6	Dermal	1 ml	30-90 min	Cellular damage of skin	62
6	"	"	90 min	"	64
1	"	-	3 yr	Fever, chills, cough, pleuritic pain, marrow hypoplasia, reduction of all formed elements of blood, death	58
4	"	-	-	Dermatitis, erythema, blisters, burning sensations	61
1	"	-	24 hr	Burning sensations at 1 hr, slight erythema at 2 hr, erythema and tenderness at 7 hr, blister formation at 12 hr, pus-filled blisters at 24 hr	61
34	"	85% kerosene	"	Dermatitis in all	61
34	"	70% kerosene	"	Dermatitis in 85%	61
34	"	55% kerosene	"	Dermatitis in 24%	61
34	"	40% kerosene	"	No dermatitis	61
1	Dermal and oral	2-3 doses/yr	25 yr	Reduction of erythrocytes, slight marrow hypoplasia	59
1	Dermal	"	3 yr	Marrow hypoplasia, reduction of neutrophils	59
1	-	3 doses/yr	45 yr	Marrow hypoplasia, changes in formed elements of blood	59

TABLE III-11 (CONTINUED)

EFFECTS OF EXPOSURE TO KEROSENE ON HUMANS

Number of Subjects	Route of Exposure	Amount	Duration of Exposure	Observed Effects	Reference
1	Oral	-	-	Headache, intense labored breathing, vomiting, epigastric pain, moderate fever, jaundice, pulmonary lesions	70
-*	Oral and aspiration	-	-	Upper respiratory tract infections, pneumonia and stupor in some	69
-**	"	-	-	Rapid and shallow respiration, sounds of rales, cyanosis, pneumonia	68
-	Respiratory	-	7 min	Grogginess, slurring of speech, slight staggering on walking, possitive Romberg's sign, mild muscular weakness	66

*204 incidents of kerosene ingestion in children
**65 incidents of kerosene ingestion in children

TABLE III-12

EFFECTS OF RESPIRATORY EXPOSURE TO RUBBER SOLVENTS ON ANIMALS

Species	Exposure Concentration	Duration	Observed Effects
Rats	180,000 mg/cu m (45,000 ppm)	2-8 min	Convulsions by 2 min of exposure, death of 50% of the rats by 4.3 min
"	96,000 mg/cu m (24,000 ppm)	4 hr	Loss of motor coordination, convulsions followed by death
"	61,000 mg/cu m (15,000 ppm)	"	LC50
"	39,000 mg/cu m (9,800 ppm)	"	Loss of motor coordination, eye irritation
"	11,000 mg/cu m (2,800 ppm)	"	No effects
"	1,900 - 7,900 mg/cu m (480 - 2,000 ppm)	6 hr/d 5 d/wk 13 wk	No significant effects
Mice	250,000 mg/cu m (63,000 ppm)	1 min	Respiratory tract irritation
"	130,000 mg/cu m (33,000 ppm)	"	No effects
Cats	49,000 mg/cu m (12,400 ppm)	4 hr	CNS depressant effects
Dogs	13,000 -25,000 mg/cu m (3,300 - 6,300 ppm)	"	Loss of motor coordination, eye irritation
"	5,900 mg/cu m (1,500 ppm)	"	No effects
"	1,900 - 7,900 mg/cu m (480 - 2,000 ppm)	6 hr/d 5 d/wk 13 wk	No significant effects

Adapted from reference 9

TABLE III-13

EFFECTS OF RESPIRATORY EXPOSURE TO
VARNISH MAKERS' AND PAINTERS' NAPHTHA ON ANIMALS

Species	Exposure Concentration	Duration	Observed Effects
Rats	71,000 mg/cu m (15,000 ppm)	-	Loss of motor coordination, convulsions followed by death of 50% of the rats by 37 min
"	25,000 mg/cu m (5,460 ppm)	4 hr	Death in 10/10
"	16,000 mg/cu m (3,400 ppm)	"	LC50
"	4,400-9,800 mg/cu m (920-2,060 ppm)	"	No significant effects
"	1,300-5,800 mg/cu m (273-1,200 ppm)	6 hr/d 5 d/wk 65 wk	"
Mice	36,000 mg/cu m (7,700 ppm)	1 min	Decreased respiration rate in 5/6
"	12,000 mg/cu m (2,600 ppm)	"	Slightly decreased respiration rate
Cats	19,000 mg/cu m (4,100 ppm)	4 hr	CNS depressant effects
Dogs	16,000 mg/cu m (3,400 ppm)	2 hr	Eye irritation, tremors, poor coordination, dilatation of pupils, prostration in a male dog with 1.5 hr of exposure
"	8,000 mg/cu m (1,700 ppm)	4 hr	No significant effects
"	1,300-5,800 mg/cu m (273-1,200 ppm)	6 hr/d 5 d/wk 65 wk	"

Adapted from reference 17

TABLE III-14

EFFECTS OF RESPIRATORY EXPOSURE TO MINERAL SPIRITS ON ANIMALS

Species	Exposure Concentration	Effects
Guinea pigs	1,353 mg/cu m*	Emphysema and lung congestion exhibited in some
"	596 mg/cu m*	No effects
"	1,271 mg/cu m**	Body weight loss of 4%
"	550 mg/cu m**	Death in 16/51
"	513 mg/cu m**	Death in 12/59
"	363 mg/cu m**	Death in 4/15
"	238 mg/cu m**	Death in 0/15
Monkeys	1,271 mg/cu m**	Body weight loss of 9%
"	619 mg/cu m**	Body weight loss of 6.4%
"	555 mg/cu m**	Body weight loss of 7.7%
"	504 mg/cu m**	Body weight gain of 1%
"	Controls	Body weight gain of 0.8%

*30 doses, 8 hr/d, 5 d/wk
**90-d continuous exposure

Adapted from reference 82

TABLE III-15

EFFECTS OF RESPIRATORY EXPOSURE TO STODDARD SOLVENTS ON ANIMALS

Species	Exposure Concentration	Duration	Observed Effects
Rats	8,200 mg/cu m (1,400 ppm)	8 hr	Eye irritation, blood exudate around nostrils, slight loss of coordination
"	4,600 mg/cu m (800 ppm)	"	Eye irritation, bloody exudate around nostrils
"	2,400 mg/cu m (420 ppm)	"	No effects
"	1,100-1,900 mg/cu m (190- 330 ppm)	6 hr/d 5 d/wk 13 wk	Marked tubular regeneration of kidneys
"	480 mg/cu m (84 ppm)	"	No effects
Mice	10,000 mg/cu m (1,700 ppm)	1 min	Decreased respiration rate
"	4,400 mg/cu m (770 ppm)	"	No effects
Cats	10,000 mg/cu m (1,700 ppm)	-	CNS depressant effects
Dogs	8,000 mg/cu m (1,400 ppm)	8 hr	"
"	4,000 mg/cu m (700 ppm)	"	No significant effects
"	480-1,900 mg/cu m (84- 330 ppm)	6 hr/d 5 d/wk 13 wk	"

Adapted from reference 21

TABLE III-16

EFFECTS OF RESPIRATORY EXPOSURE TO
140 FLASH ALIPHATIC SOLVENT ON ANIMALS

Species	Exposure Concentration	Duration	Observed Effects
Rats	10,200 mg/cu m* (1,620 ppm)	340 min	Wet mouth, sluggish movement, irritation of extremities, tremor, death in 3/10
"	2,900 mg/cu m* (461 ppm)	8 hr	Skin irritation of extremities, slight loss of coordination, death in 2/16
"	1,900 mg/cu m** (302 ppm)	"	Skin irritation of extremities
"	270 - 790 mg/cu m** (43 - 125 ppm)	"	No effects
"	49 - 230 mg/cu m (8 - 37 ppm)	6 hr/d 5 d/wk 72 wk	"
Mice	350 mg/cu m (56 ppm)	-	No respiratory tract irritation
"	12,000 mg/cu m* (1,906 ppm)	-	"
Cats	440 mg/cu m** (70 ppm)	6 hr	No significant effects
"	10,000 mg/cu m* (1,588 ppm)	-	No CNS depressant effects
Dogs	210 -1,700 mg/cu m* (33 - 280 ppm)	8 hr	Transitory lacrimation

TABLE III-16 (CONTINUED)

EFFECTS OF RESPIRATORY EXPOSURE TO
140 FLASH ALIPHATIC SOLVENT ON ANIMALS

Species	Exposure Concentration	Duration	Observed Effects
Dogs	49 - 230 mg/cu m (8 - 37 ppm)	6 hr/d 5 d/wk 73 wk	No significant effects

*Nominal concentration
**At concentrations exceeding 270 mg/cu m (43 ppm), the solvent was in the form of a vapor-aerosol mixture.

Adapted from reference 56

TABLE III-17

EFFECTS OF RESPIRATORY EXPOSURE TO
DEODORIZED KEROSENE ON ANIMALS

Species	Exposure Concentration	Duration	Observed Effects
Rats	6,000-9,600 mg/cu m* (840-1,344 ppm)	6 hr/d 4 d	Slight loss of coordination, sluggishness, irritation of extremities
"	5,900 mg/cu m* (826 ppm)	6 hr	No effects
"	100 mg/cu m (14 ppm)	8 hr	"
"	100 mg/cu m (14 ppm)	6 hr/d 5 d/wk 67 d	Death of 1 from pneumonia
"	48 mg/cu m (7 ppm)	"	Death of 1 from abscess bronchopneumonia
Mice	6,900 mg/cu m* (966 ppm)	-	No effects on upper respiratory tract
Cats	6,400 mg/cu m* (896 ppm)	6 hr	No effects
Dogs	20 - 100 mg/cu m (3 - 14 ppm)	6 hr/d 5 d/wk 67 d	"

*The droplets in the aerosol averaged less than 1 μm in diameter.

Adapted from reference 67

TABLE III-18

EFFECTS OF KEROSENE EXPOSURE ON ANIMALS

Route of Exposure	Species	Exposure Concentration	Effects	Reference
Oral	Rats	5 ml*	Appeared normal, excoriations around anus	91
"	Mice	1 ml/d**	Abnormal and rapid respiration, neuromuscular strength weakening, death after 2nd dose	88
"	Rabbits	70 ml/kg	Tachycardia, high body temperature, rapid respiration, convulsions, death	88
ip	Dogs	50 ml/kg	Tachycardia, rapid respiration, drowsiness, convulsions, tremor, coma, death	88

*40 doses
**2 d

IV. ENVIRONMENTAL DATA AND ENGINEERING CONTROLS

Sampling and Analysis

There are several instrumental methods suitable for the evaluation of airborne concentrations of refined petroleum solvents.

A direct reading instrument such as a combustible gas meter may be used to determine concentrations of refined petroleum solvent vapor [96]. While this type of instrument is not specific, certain calibration procedures can be used to increase the instrument's accuracy. Examples of such procedures would be: (1) calibrating the instrument with the solvent which is actually in use at the sampling site, (2) simulating temperature conditions during the calibration procedure to duplicate conditions expected to exist at the sampling site, and (3) doing the actual calibration at the sampling site.

In 1974, nine commercially available portable combustible gas meters, weight range 1.1-6.8 lb, were evaluated by NIOSH [97]. On the basis of 11 separate operation manual criteria, the total weighted scores for the tested instruments ranged from 15 to 63 out of a possible 72; the basic cost of the instruments ranged from 175 to 535 dollars.

In 1976, NIOSH [98] published the results of a study in which three types of commercial available hydrocarbon meters were evaluated: four instruments using flame ionization, one infrared analyzer, and one using photo-ionization. The test criteria were similar to those of the above study. The results of these tests were used by NIOSH to recommend construction and performance standards for these instruments.

An interferometer has been used to evaluate concentrations of solvent vapor [99]. The sensitivity of this instrument varies with the relative densities of the air and of the solvent vapor being measured: the closer the relative densities are to being equal, the less sensitive the instrument is for the particular, considered solvent.

The combustible gas meter, hydrocarbon meter, and the interferometer can be used to detect vapors of a large number of solvents, but both are subject to interferences from other chemicals, none are convenient for personal zone sampling, all require grab samples, and none are readily adaptable to TWA sampling and analysis unless many readings are taken and integrated.

Smith and Pierce [100] used nonreactive metalized polyester bags to sample for benzene, methyl alcohol, dichloromethane, and methyl isobutyl ketone. While reports of these bags being used specifically for the sampling of refined petroleum solvents have not been found, they could possibly be used successfully. This particular sampling method may be used for TWA determinations if many samples are taken at a slow sampling rate.

Ray [101] reported that petroleum distillate vapors could be collected in a midget bubbler containing chloroform or on silica gel. An unspecified lacquer thinner was injected into a polyester bag with a tared microimpinger to prepare a test concentration of 3,850 μg/liter of the lacquer. When the sampling rate of the bubbler was 1 liter/minute, 26% of the test concentration, 1,000 μg/liter, was recovered. When the sampling rate was reduced to 100 ml/minute for two consecutive tests, the recovered solvent concentrations were 3,910 and 3,700 μg/liter or 102 and 95%, respectively. Silica gel was tested using a known lacquer solvent vapor at

a concentration of 9,000 μg/liter. When two consecutive samples were taken at a sampling rate of 100 ml/minute, concentrations of 8,670 and 8,500 μg/liter or 96 and 95%, respectively, were recovered. While the sampling method using chloroform can be used for solvents that can exist in both mist and vapor forms, the collection medium is a very volatile liquid which may leak or evaporate in transport without proper handling. Furthermore, the sampling rate is limited to about 100 ml/minute.

Feldstein et al [102] reported using silica gel for collecting the vapors of numerous organic substances, one of which was Stoddard solvent. Three silica gel tubes in series, each containing 20 g of silica gel, were used for sampling. Test atmospheres were described by the total amount injected rather than in terms of concentration. When 100 μl of Stoddard solvent was injected into a heated test chamber, 98 μl or 98%, was recovered, and when 210 μl was injected, 204 μl or 97%, was recovered. The air flowrate through the system, which is the same as the sampling rate in this system, was 0.25 cu ft/minute (7.1 liters/minute) for 1 hour. Several of the solvents, eg, isopropyl alcohol, butyl cellosolve, ethyl acetate, and perchloroethylene, were tested in air having a high relative humidity. Only the sampling of perchloroethylene was affected, the collection efficiency was reduced. In dry air, 95-100% of the sampled perchloroethylene was collected in the first tube. In three consecutive tests with wet air, the amount collected in the first tube was reduced to 15, 14, and 5%. Stoddard solvent was not sampled at high experimental relative humidities, however, the ambient relative humidity was 40-55% when Stoddard solvent was tested. The authors also stated that, for field studies, where sampling times may be longer than 1 hour and greater

humidity may be present, the efficiency of adsorption of organic compounds is decreased. While the three silica gel tubes in series might be cumbersome for breathing zone samples, a large single silica gel tube could possibly be adapted for this purpose.

In 1936, Cook and Coleman [99] reported using activated charcoal for sampling solvent vapors. The sampling system consisted of a tube containing 8-mesh Ascarite and 20-mesh calcium chloride to remove acid vapors and moisture, attached to an activated charcoal tube to collect solvent vapors. This system was used by the authors in sampling for trichlorethylene, dichlorethylene, benzene, carbon tetrachloride, and petroleum distillates in textile cleaning and rubber goods manufacturing plants.

Charcoal tubes without the Ascarite and calcium chloride front sections have been recommended by the Physical and Chemical Analysis Branch of NIOSH for sampling for Stoddard solvent [103] and petroleum distillates [104]. Ascarite and calcium chloride sections in front of the charcoal tubes were used by Cook and Coleman [99] in conjunction with a gravimetric analytical procedure. The NIOSH-recommended analytical procedure is gas chromatography which does not require the use of Ascarite and calcium chloride as presection to the charcoal sampling tube.

In 1971, Olkhovskaya [105] reported on a colorimetric method for collecting air samples of benzene, kerosene, and white spirits. The principle of the method involves the reaction of either benzene, kerosene, or white spirits with a solution of 0.01% potassium bichromate in concentrated sulfuric acid (specific gravity 1.84). The resultant oxidation leads to the formation of soluble substances ranging in color

from light yellow to a dark cinnamon. The intensity of the color depends on the concentration of either benzene, kerosene, or white spirits. The concentration is then determined by the degree of color change of the sample as compared with the color of standard solutions. The sensitivity of the method for benzene, kerosene, and white spirits is 0.05 mg/3 ml, 0.02 mg/3 ml, and 0.025 mg/3 ml, respectively.

Airborne samples for the above [105] method are collected in two small absorbers each containing 3 ml of 0.01% potassium bichromate in concentrated sulfuric acid. The recommended sample size is 1.5 liters collected at a sampling rate of 5-6 liters/hour. The author [105] did not state the collection efficiency of the absorbers. This method [105] might be convenient for the in-plant monitoring of air concentration of one of these three solvents, as it does not require elaborate and costly equipment.

In a report by Feldstein et al [102] on silica gel source testing, the use of infrared light for analyzing complex materials such as Stoddard solvent and varnish makers' and painters' (VM and P) naphtha was described. Carbon disulfide was used to desorb the silica gel tubes. For Stoddard-type solvents, absorption at 3.4 μm was found by the authors to be proportional to the solvent concentration. No information about the range of this analytical procedure was reported.

A commercially available portable infrared analyzer can be used for the analysis of many air contaminants [106]. It was reported that, at a wavelength of 3.4 μm, the lower detectable limit for Stoddard solvent measured with this instrument was 0.01 ppm.

Gas-chromatographic techniques have been used in the analyses of Stoddard solvent [103], petroleum distillates [104], and organic solvents [107] in air. In recent years, gas chromatography has become one of the most prevalent methods of analysis for organic solvents [108-112]. This type of analysis can be used for the qualitative and quantitative analyses of refined petroleum solvents; however, when complex mixtures, such as many types of these solvents, are analyzed, changes in the chromatographic conditions or columns may be necessary to achieve the desired separation. In conjunction with this method, mass spectrometry can be used for the qualitative determination of complex mixtures.

In 1971, Narayanaswami and Bami [108] reported on the use of gas chromatography in India for forensic studies in the detection of kerosene residues. Both the isothermal and the temperature-programmed modes of gas chromatographic-operating conditions were used. The former mode was used when the volatile constituents of kerosene were considered to be absent, eg, residue samples collected following arson. In the isothermal mode, the gas-chromatographic conditions used were: temperature of 220 C, nitrogen as the carrier gas, with an exit of 42 ml/minute; the column was a 1/8-inch x 6.4-feet Apeizon L on chromosorb 80 mesh. Adequate resolution occurred in 24 minutes with a flame ionization detector. When the more volatile components were also present, samples of kerosene were analyzed by the temperature programmed mode using an AMIL vapor phase chromatograph, a 1/4-inch x 6.4-feet Apeizon L on celite column with a flame ionization detector. The initial temperature of 120 C was increased at a rate of 5 C/minute up to 150 C, 8 C/minute up to 200 C, and 16 C/minute up to 280 C. Using nitrogen as a carrier gas, separation of the sample took 17 minutes.

With both modes, sufficient peak resolution occurred to enable the matching of the kerosene residue samples with the known kerosene bulk samples.

Direct reading indicator tubes can measure hydrocarbons from 2 to 25 mg/liter (2,000 to 25,000 mg/cu m) [113]. These tubes will indicate total hydrocarbons, beginning with hexane (C6 homolog). The reaction of the hydrocarbon with the tube contents causes a brown color. The presence of aromatics such as benzene or toluene changes the color from brown to reddish. These tubes may also be used to test for kerosene vapor [113,114]. Direct reading indicator tubes may be used for worksite surveys but should not be used when precise measurements are needed. The recommended method for the sampling and analysis of the refined petroleum solvents [15,103] are presented in Appendices II and III.

The refined petroleum solvents covered in this document are primarily composed of saturated hydrocarbons, olefins, and aromatics. Many of the individual chemical components of these groups, such as benzene, naphthalene, pentane, hexane, heptane, and octane, have existing federal airborne standards or currently recommended airborne standards. The combined sampling and analytical procedure should have the capability to permit the evaluation of the air concentration of a particular refined petroleum solvent, as well as one or more of the particular substituent compounds of that particular solvent. After evaluating the above sampling and analytical procedures, the combination best suited to these criteria would be sampling with activated charcoal tubes followed by analysis of the sample using gas chromatography, possibly in combination with mass spectrometry.

The preferred and reliable sampling device consists of a glass tube with two sections, each filled with activated charcoal, separated by a section of urethane foam. These tubes are capable of collecting all of the refined petroleum solvent vapors discussed in this document. Moreover, the sampler is light, contains no liquids, and is readily adaptable to personal, TWA, and ceiling sampling. The only interference of any consequence is very high humidity, evident by the visible condensation within the charcoal tube, which will seriously reduce the collection efficiency of the sampling tube. The difficulty may be circumvented by calibration of the sampling tubes prior to field sampling, to estimate the degree to which humidity will affect the collection efficiency.

Gas-chromatographic techniques can be used in the evaluation of both the total concentration of airborne refined petroleum solvents and the concentration of certain individual constituents of the solvent, such as benzene. When using a gas chromatograph in the analysis of refined petroleum solvents, it is imperative that the analyst be supplied with a bulk sample of the solvent in question in order to prepare the standard solutions, determine desorption efficiencies, and check for interferences. The gas-chromatographic patterns of the field samples and bulk or head space samples should be compared to identify any possible interferences. Gas chromatograph-operating conditions stated in Appendix IV have been tested for Stoddard solvent [103] and varnish makers'and painters' naphtha [104] and modifications of these operating conditions may be necessary for the determination of other refined petroleum solvents.

NIOSH recommends that the sampling and analysis be performed using charcoal tubes and gas chromatography. The method has been tested by NIOSH

for Stoddard solvent [103] and varnish makers' and painter's naphtha [104] as part of the Standards Completion Project. Using a 3-liter air sample of Stoddard solvent, this method [103] was validated for concentrations of airborne Stoddard solvent from 1,417 to 5,940 mg/cu m. The probable useful range of the method, using a 3-liter air sample, was stated to be 295-8,850 mg/cu m for Stoddard solvent. Using a 4-liter air sample for varnish makers' and painters' naphtha, a similar method [104] was validated for concentrations of this refined petroleum solvent from 937 to 3,930 mg/cu m, with a probable useful range of 200 to 6,000 mg/cu m. By increasing the air sample size to 10 liters or more (depending on the suspected airborne concentrations) and using a slower sampling rate, the methods should be capable of being extended to the range of concentrations considered in this document.

The above sampling and analytical procedures do not work well for refined petroleum solvents comprised of C5-C8 hydrocarbons, such as petroleum ether which is composed of pentane and isohexane, 80 and 20% respectively, because carbon disulfide which is used as a desorbent, has a boiling point of 46.3 C, and interferes in the elution pattern of the sample. This difficulty can be resolved by the selection of a desorbent with a boiling point above that of the C5-C8 range, such as toluene. A different column packing and gas chromatograph conditions can further refine the method. These modifications however, have not yet been tested by NIOSH. An example of a sampling and analysis procedure using a combustible gas meter is given in Appendix II. A more detailed procedure for the use of charcoal tubes and gas chromatograph are presented in Appendix III and IV.

Environmental Levels

Little information has been found about the air concentrations of petroleum naphtha, mineral spirits, Stoddard solvent, and kerosene encountered in industry. Four studies [74,75,115,116] concerning Stoddard solvent illustrate contemporary uses and possible air concentrations representative of environmental levels of Stoddard solvent.

In 1968, Oberg [115] reported a survey of 30 of 140 randomly selected drycleaning plants in Detroit, Michigan. Twelve plants used Stoddard 105, a Stoddard solvent with a closed-cup flashpoint of 41 C (105 F); nine used 120, a solvent with a closed-cup flashpoint of 49 C (120 F); and nine used Stoddard 140, a solvent with a closed-cup flashpoint of 60 C (140 F). Air concentrations were measured with a Davis Model 6 Vapo Tester, Davis Model 11-650 Flame Ionization Meters, and a J and W Model SS Aromatic Hydrocarbon Indicator. TWA exposures were calculated for each of the three solvents for the entire drycleaning cycle. The actual drycleaning operation was observed by the author to be about one-half of the total 8-hour work shift. The following are 4- and 8-hour time-weighted exposures for each of the three solvents: Stoddard 105, 65 and 35 ppm; Stoddard 120, 47 and 25 ppm; and Stoddard 140, 25 and 15 ppm. Two plants, one using Stoddard 105 and the other using Stoddard 140, had air samples taken at 1-minute intervals during the entire drycleaning cycle, approximately 40 minutes. Higher than average airborne solvent concentrations were found during the washing and extraction cycles. The author gave the following reasons for these above-average air concentrations: (1) the improper placement of air inlets and exhaust ventilation, (2) interruptions in the washing cycle to add additional clothes released high concentrations of the solvents into the

workroom environment, and (3) the placement of extractors at long distances from the washing equipment permitted clothes wet with Stoddard solvent to remain in contact with the atmosphere for longer than normal periods of time.

In 1974, Larsen and Shmunes [75] reported a hazard evaluation in a metals-manufacturing plant. Nine machines, five with a 2-inch belt and four with a 3-inch belt, were used to polish aircraft engine blades. Each polisher had six heads and five polishing stations composed of aluminum oxide and silicon carbide. The blades passed automatically from one polishing station to the next. The only operator who changed the blades was located at the sixth head. About 500 large blades were changed each day; a greater number of smaller blades were polished. Coolant oil was automatically fed in a small stream at the top and bottom of the blades. No visible mist was produced, and, if the blades were adequately cooled, no visible "smoke" was produced. Stoddard solvent was used to clean the machines about once a week.

About 10 workers were involved in this operation; however, Larsen and Shumnes [75] did not specify whether all 10 workers were involved in the operation at the same time. Workers complained of eye, nose, and throat irritation, sinus problems, headache, and nausea. There was no warning label on the storage container of the coolant. The employees also indicated that a coolant which had been used for about 2 years was causing more problems than the one used previously, although analysis of samples from the old and new coolants showed that they were essentially the same. Stoddard solvent was the only component that would have been volatile at room temperature.

On March 25, 1972, breathing-zone sample findings showed concentrations of oil mist that ranged from 0 to 0.55 mg/cu m [75]. The oil mist was generated during the polishing operation when the coolant was placed on the blades and came in contact with the polishers. Oil mist samples were collected on 37-mm vinyl metricel filters [75]. The oil mist was analyzed by an undescribed fluorescence procedure. No Stoddard solvent was found in breathing-zone samples taken using charcoal tubes. No analytical procedure for Stoddard solvent was reported by the authors. On May 8, 1972, sampling was performed again, and airborne concentrations of Stoddard solvent were found to be less than 20 ppm. The sampling performed on March 25 occurred several days after the machines were cleaned with Stoddard solvent, and the May 8 sampling occurred immediately after the machines had been cleaned with Stoddard solvent and put back into operation. The authors concluded that concentrations of airborne Stoddard solvent could at certain times, eg, during startup after cleaning, be higher than those found during the survey unless the Stoddard solvent was thoroughly removed from the system after it was cleaned.

In 1974, Markel and Shmunes [74] reported a health hazard evaluation by NIOSH at a greeting card company in Cincinnati, Ohio, where six people were involved in a flocking operation. The evaluated operation involved insertion of flattened greeting cards under silk screens containing a preselected pattern mesh. An appropriate colored glue was squeezed through the silk screen onto the card which was then dipped into the matching color flocking compound (dyed rayon tow). The glues contained a type of Stoddard solvent. No specific information, such as boiling range or flashpoint, about the Stoddard-type solvent component of the glue was given by the

authors. The persons involved in the flocking operation also cleaned the silk screens with a mineral spirits solution for about 5 minutes/day. The Stoddard-type solvent was sampled with a charcoal tube at a sampling rate of 1 liter/minute. The analysis was with gas chromatography at a sensitivity of 0.05 mg/tube. Twelve general area samples were taken, one of which became contaminated and was discarded. For the remaining 11 samples, the minimum, average, and maximum air concentrations were 99, 438, and 1,906 mg/cu m, respectively.

In 1976, the Research and Development Committee of the Institute of Industrial Launderers [116] conducted a survey to determine the concentrations of petroleum solvents vapors in laundering plants with petroleum solvent cleaning systems. In this survey, concentrations of airborne Stoddard solvent were determined at two representative industrial laundry plants. Air samples were taken by a consultant industrial hygienist to determine an 8-hour average worker exposure and excursion spot tests. The excursion spot tests were taken when the concentrations of airborne Stoddard solvent were believed to be the greatest.

At the first plant [116], a drycleaning machine was used an average of 4 hours/day. Two-hour samples were taken from the breathing zones of the two workers operating the machine. During this period, four loads of clothes were cleaned. The Stoddard solvent concentration in the breathing zone of one worker (designated as a cleaner) was reported to be 50.3 ppm, and, for another worker (designated as a helper), the reported breathing zone concentration was 65.3 ppm. These two concentrations were reported by the consultant industrial hygienist to be an 8-hour average exposure to Stoddard solvent. However, what the two workers did during the remaining 4

hours of their work shift was not mentioned. The excursion spot tests were collected at the breathing level of the two workers while they were (1) removing cotton work gloves and trousers from the machine, (2) removing fender covers from the machine, and (3) removing cotton work gloves from the machine. The concentrations of airborne Stoddard solvent found during these operations were reported as: 67, 68, and 60 ppm, respectively.

At the second plant, similar sampling was performed. However, in addition to breathing zone and excursion spot-test samples, area samples were taken. A breathing-zone sample of approximately 3.5 hours' duration was taken on one worker who operated a drycleaning machine. An area sample was also taken in the immediate vicinity. The drycleaning machine was used on an average of 10 hours/day. The results of the breathing-zone and area samples were 242 and 66 ppm of Stoddard solvent, respectively, and were considered to be representative of an 8-hour exposure. Three excursion spot tests were performed. Two were conducted at the breathing zone level while the worker removed shirts first, and then coveralls from the cleaning machine. The third sample was taken near the extractor, 5 feet above the floor. The Stoddard solvent concentrations during these three spot tests were 60, 57, and 70 ppm, respectively. The 242-ppm value for the breathing-zone sample is higher than the ACGIH recommended level of 100 ppm for Stoddard solvent [117]. The author did not explain the disparity between the TWA breathing-zone sample and the excursion samples. It was recommended that other sampling be performed. Approximately 2 months later, the breathing-zone and area samples were repeated for the same worker and the airborne Stoddard solvent concentrations were reported to be 20.0 and 28.0 ppm. Excursion spot tests were performed for operations

similar to those checked earlier and Stoddard solvent concentrations of 68, 63, and 62 ppm were reported.

Engineering Controls

Engineering controls and work practices for operations using petroleum solvents should have as their objectives: control of vapor concentrations, minimizing of skin contact, prevention of eye contact, and the prevention of fire and explosion.

Where practicable, closed systems should be designed, properly operated, and maintained to achieve these major objectives and should be periodically checked for performance. Where closed systems are not feasible, other control measures, such as local exhaust systems and temperature control, may be used to control petroleum solvent exposures. Specific operations such as spray painting and metal degreasing may require additional precautions such as the placement and design of specialized exhaust hoods, an increase in the capture velocity of the hood, and installation of air movers with designed capabilities to produce a negative pressure relative to the surroundings.

Where mechanical ventilation is used to control concentrations of airborne petroleum solvents, it should be designed and maintained to prevent the accumulation or recirculation of the solvent vapors into the workroom. Exhaust systems discharging into outside air must conform with applicable local, state, and federal air pollution regulations. Measurements to determine the efficiency of ventilation systems used to control exposure should be taken at least every 3 months, and within 5 working days of any change in production, process, or control that might

result in any increase in air concentrations. Air velocity, static pressure, and air volume [118] can be used in the evaluation.

When a fan is located in duct work and the solvent may exceed an air concentration of one-fourth of the lower flammable limit, the rotating element should be nonsparking material or the casting should be coated with or consist of a nonsparking material. The ventilation system should contain devices along its length intended to prevent the propagation of possible flashbacks. Additional information regarding ventilation systems can be found in Industrial Ventilation--A Manual of Recommended Practice [119], Fundamentals Governing the Design and Operation of Local Exhaust Systems Z9.2-1971 [120], and Recommended Industrial Ventilation Guidelines [121].

Drycleaning operations should be provided with general ventilation systems. The system should be designed so that exhaust air is replaced with clean, tempered, makeup air. All connections of this system should be well-sealed and periodically checked for leakage. Drycleaning equipment should be operated at negative pressure so that, when the loading door is opened, air from the room will be drawn into the machine, preventing the escape of contaminants into the workroom [122]. Although respiratory protective equipment is not an acceptable substitute for proper engineering controls, it should be available for emergencies and for nonroutine maintenance and repair.

For additional information on specific operations, pertinent federal regulations should be followed. For example, the design of open surface tank ventilation is dealt with in 29 CFR 1910.94(d). Open surface tanks are used in operations involving the immersion of materials in liquids or

in the vapors of such liquids to clean or impart a finish to a material. There are 16 classes of open surface tanks. The class into which a particular tank operation would be categorized is determined by two factors: specific toxicity and the rate at which gas, vapor, or mist is given off by the system. Dip-tank operations are considered in 29 CFR 1910.108 and in 1910.94(d), and 29 CFR 1910.107 and 1910.94(c) deal with spray finishing.

Emission control of solvent vapors into the atmosphere can be accomplished by several methods. These methods include direct or catalytic combustion, activated carbon adsorption, and condensation [123].

V. WORK PRACTICES

Engineering controls and work practices should be designed and implemented primarily to maintain airborne solvent concentrations below prescribed limits, minimize excursions, prevent skin and eye contact, and reduce fire and explosion hazards. Since the types of solvents discussed in this document have many different industrial uses, the work practices recommended are applicable to many solvents.

Table XIV-1 [1,3-14,17-19,21,27,56,67,82,124-129] gives the chemical and physical properties for six refined petroleum solvents. These solvents are designated as combustible and flammable liquids of Classes IA, IB, IC, II, and IIIA based on the criteria in 29 CFR 1910.106 (a)(18)(i), (a)(18)(ii), (a)(19)(i), (a)(19)(ii), and (a)(19)(iii). These classifications for these refined petroleum solvents are determined primarily on the basis of boiling point and flashpoint or flashpoint range. A particular solvent may belong to different OSHA classifications depending on the properties of the product in use. Petroleum ether is designated as a Class IA flammable liquid if its boiling point is below 37.8 C (100 F) (29 CFR 1910.106 (a)(19)(i)) and as Class IB flammable liquid if its boiling point is at or above 37.8 C (100 F) (29 CFR 1910.106 (a)(19)(ii)). Rubber solvent and varnish makers' and painters' naphtha are flammable liquids of Class IB (29 CFR 1910.106 (a)(19)(ii)). Mineral spirits is handled as a Class IC flammable liquid if its flashpoint is below 37.8 C (100 F) (29 CFR 1910.106 (a)(19)(iii)) and as a Class II combustible liquid if its flashpoint is at or above 37.8 C (100 F) (29 CFR 1910.106 (a)(18)(i)). Stoddard solvents and kerosene are designated as Class II

combustible liquids if their flashpoints are below 60 C (140 F) (29 CFR 1910.106 (a)(18)(i)) and as Class IIIA combustible liquids if their flashpoints are at or above 60 C (140 F) (29 CFR 1910.106 (a)(18)(ii)). When a combustible liquid is heated for use to within 16.7 C (30 F) of its flashpoint, it should be handled in accordance with the requirements for the next lower class of liquids (29 CFR 1910.106 (a)(18)(iii)). The National Fire Protection Association NFPA No. 30 Flammable and Combustible Liquids Code [130] should be strictly adhered to when handling refined petroleum solvents; NFPA No. 70 Electrical Code [131] NFPA No. 36 Solvent Extraction Plants Code [132], and NFPA No. 32 standard for drycleaning plants [26] should be complied with where applicable.

Two articles have been reported in the literature concerning the flashpoint of a redistilled Stoddard solvent [133,134]. The National Association of Dyeing and Cleaning, Inc [133] reported that, when new (unused) Stoddard solvent was continuously distilled from 3 to 8 hours at a time for a total of 50 hours, the distillate had the same flashpoint as the original Stoddard solvent. In the second article, Howanitz [134], reported that, when used Stoddard solvent was redistilled, the flashpoint of the distillate was lower than that of the original material. The reduction in flashpoint after the first recovery was 5-10 F. The actual test data were not reported. In a written communication to NIOSH from the International Fabricare Institute (AC Lloyd, January 1977), data were presented regarding changes in the flashpoint of redistilled (used) regular 100 flash Stoddard solvent. In plant I, the mean and standard deviations for the flashpoint were 104.32 and 1.20 F, respectively, for 20 consecutive flashpoint determinations after the redistillation of used regular Stoddard solvent.

The mean and standard deviations for the flashpoint after 7-14 consecutive distillations in plants II-IV were similar. In plant IV, however, the flashpoint dropped from 105 to 101 F in one distillation. This may have been the result of an error in the testing method, but the Stoddard solvent was not retested because of insufficient sample size. The flashpoint changes presented in this article (AC Lloyd, written communication, January 1977) were not of the magnitude of those reported by Howanitz [134].

The discrepancy in the magnitude of flashpoint changes after the redistillation of used Stoddard solvent reported by Howanitz [134] and the data presented by the International Fabricare Institute (AC Lloyd, written communication, January 1977) could be because of the type of contaminant found in the used Stoddard solvent. The Stoddard solvent tested by Howanitz had been used to clean electric motors, whereas the other Stoddard solvent had been used to clean garments. The different contaminants could have an effect on the flashpoint of redistilled (used Stoddard solvent); however, the magnitude of this effect is not readily apparent. Consequently, whenever Stoddard solvent is redistilled, the flashpoint of the distillate should be checked.

Special precautions are necessary for entering tanks, extractors, or vessels which may contain refined petroleum solvents, for performing flame- or spark-generating operations such as welding and cutting, and for transferring refined petroleum solvents. Before any employee enters a vessel, all pipelines leading into or out of the vessel must be blanked to prevent the entry of refined petroleum solvent liquid or vapors [135]. The vessel interior should then be washed with water and then purged with air or with nitrogen followed by air. After the purging, the vessel atmosphere

should be tested with a combustible gas meter or other suitable instruments [135]. No one should enter a tank, vessel, or extractor without first being equipped with an appropriate respirator (if necessary) and a secured lifeline and harness. At least two other workers should watch at all times from outside the vessel. These workers should be equipped with respiratory protection (at least one being the positive pressure type) and secured lifelines and harnesses. One additional employee should be able to assist in the event of an emergency. The use of portable lights to illuminate the interior of tanks, vessels, or extractors when they are undergoing cleaning or repairs should be prohibited. Such interiors should be illuminated by reflected light [135]. Only nonferrous (sparkproof) tools should be used for scraping away clinging residues or accumulated deposits. Rags and other materials used to wipe up and absorb refined petroleum solvents should be placed in standard safety containers for subsequent disposal. Cutting or welding must be performed only when an authorized representative of the employer signs a permit indicating that all necessary safety precautions have been taken [135].

In 1945, Lawrence [33] reported an incident in which a worker was overcome by aviation spirit vapor while wearing an oxygen-breathing apparatus. The worker was not, however, wearing a harness and lifeline. Within 10 minutes after descending into a hole drilled near a large aviation fuel storage tank the worker was seen holding onto a crossbar and reeling drunkenly. At this point a second worker (totally unprotected) descended into the hole to assist the first worker. Both workers were subsequently overcome by the aviation spirit vapors. Both workers were eventually rescued and recovered following treatment. This particular

report is an example of an operation in which the proper safety equipment and proper emergency procedures were not used. The use of a harness and lifeline alone would probably have prevented the necessity of the second worker entering the hole and would have expedited the removal of the first worker.

The transfer of refined petroleum solvents by gravity flow or compressed air should be avoided. Where feasible, transfer from tank to process use should be through rigid pipe systems operated by remote control. When performed indoors, liquid transfers from portable containers should be through readily attached approved pumps and continuous armored hose lines [135]. If safety cans are used, they should be of the approved type, with a spring-closing lid and spout cover and designed to release internal pressure when they are subjected to heat [136]. When refined petroleum solvents are transferred from one container to another, the containers should be bonded or electrically grounded [118].

Containers of refined petroleum solvents should not be stored in direct sunlight, because of the possible generation of high pressure within the containers. Where tarpaulins or similar covering are used, they should be positioned to allow for air circulation [137]. Heating of an area should be by direct means. Open-flame devices must be prohibited in any area where refined petroleum solvents are used, stored, or handled [135].

Appropriate types of protective fire-resistant clothing, such as gloves, boots, aprons, and face shields (8-inch minimum), impervious to refined petroleum solvents should be provided and worn where needed to prevent repeated or prolonged skin contact [118]. In addition, whenever employees are required to handle solvent-saturated materials, such as when

removing clothes from a drycleaning operation, the materials should be kept as far from the breathing zone of the worker as possible [122]. Personal sampling should be performed during this operation to determine the need for respiratory protection. Additional information concerning work practices for drycleaning operations is given in Health and Safety Guide for Laundries and Dry Cleaners [122].

The employer should provide soap and water for washing skin contaminated with these solvents [118]. Handwashing with solvents such as Stoddard solvents, mineral spirits, and kerosene, or other refined petroleum solvents should be prohibited. If soap and water are not effective, the employer should provide an alternate cleanser. For additional skin protection, skin creams can be used during and after work. One such skin cream consists of 5% lanolin, 5% glycerol, 5% caster oil, 10% toilet soap, 23% kaolin, 1% carboxymethyl-cellulose, 0.5% antiseptic, and water to 100% [138]. For kerosene, a skin cream composed of 50% water, 25% glycerin, 10-15% cellulose-methasol gum, and 2-3% perservative, has been experimentally shown to protect human skin in contact with this solvent for up to 90 minutes [139].

Unless clothing is impervious to refined petroleum solvents, a change of clothing should be made available to any employee whose clothes become wetted with solvents. Contaminated clothing should be stored in closed containers until it is either removed by drying or laundering, or discarded. The employer should inform the persons laundering or otherwise handling the contaminated clothing of the hazardous properties of these solvents [118].

Chemical safety goggles (splashproof) and fullface shields (8-inch minimum) meeting the requirements of 29 CFR 1910.133 and ANSI Z87.1-1968 should be provided and worn in any operation where there is a reasonable probability that refined petroleum solvents could be splashed into the eyes. If these solvents are accidentally splashed into the eyes, copious amounts of water should be used to flush the eyes while the eyelids are lifted, and a physician should be contacted.

Whether employees should be allowed to wear contact lenses when working around eye irritants such as refined petroleum solvents is not readily answered. Under some circumstances, contact lenses may act as a barrier to eye contact from a splash, but under other circumstances they may act to retain the solvent in contact with the eye. The preferability of wearing contact lenses instead of conventional glasses with respirators is an obvious advantage, but at other times contact lenses may pose an overall disadvantage, since conventional glasses should also be somewhat effective as a barrier to splashes. As a minimum, supervisors should know of those employees wearing contact lenses so that appropriate decisions can be made in the event of splashes. Soft contact lenses should not be worn around irritant atmospheres because they can absorb the irritant materials.

When the concentrations of airborne refined petroleum solvents cannot be kept at or below prescribed limits by engineering controls, eg, during spills, equipment failure, maintenance, or vessel entry, special respiratory protection is required. The selection of proper respiratory devices is presented in Chapter I, Tables I-1, I-2, and I-3.

Protective clothing and equipment, including respirators, should be kept clean and maintained in good conditon. This equipment should be

cleaned and inspected by trained personnel after each use. Worn equipment should be replaced when necessary. The employer must ensure that all equipment is in working order and that it is stored properly when not in use.

During emergency operations, fire and explosion may be the primary hazards involved. A program for the rapid evacuation of the work area should be implemented. In addition, all potentially exposed employees should be aware of escape procedures, of the proper use and location of respirators designated for emergency situations, and of firefighting methods. Instructions should be given for transporting injured employees to areas where emergency medical care can be given.

Safety showers, eyewash fountains, and fire extinguishers should be located in or near areas where refined petroleum solvents splashes are likely to occur and must be properly maintained. Washing facilities, soap, and water, or an alternate cleanser should be available to employees. As a good hygienic practice, it is recommended that employees wash their hands before eating, smoking, or using toilet facilities.

The consumption or storage of food or beverages in exposure areas should be prohibited in accordance with provisions of 29 CFR 1910.141 (g)(2) and (g)(4).

In summary, precautions must be taken to guard against exposure of personnel to toxic concentrations of refined petroleum solvents and to the fire and explosion hazards associated with them. It is also important that employees be informed prior to job placement of any hazards associated with one or more of the refined petroleum solvents that they may come in contact with. The employees should also be informed whenever process changes could

alter their exposure. The safe handling of refined petroleum solvents is dependent on the employees' knowledge and proficiency in handling these materials. Proper initial training and periodic retraining of the employees concerning the correct use of equipment and protective devices required for the safe handling of these solvents is the responsibility of the employer. During these training programs, emergency procedures should be stressed. Recommended labels and posters should be displayed. The US Department of Labor "Material Safety Data Sheet" shown in Appendix V or a similar approved form must be filled out and filed in a location readily accessible to all employees who may be exposed to refined petroleum solvents. If the recommended work practices are observed and good engineering controls are installed, employees working with refined petroleum solvents should be adequately protected from various hazards associated with refined petroleum solvents, including overexposure, fire, and explosion.

VI. DEVELOPMENT OF STANDARD

Basis for Previous Standards

(a) Petroleum Ether

No previous health environmental limits for petroleum ether have been recommended.

(b) Rubber Solvent and Varnish Makers' and Painters' Naptha

In 1946, the Subcommittee on Threshold Limits of the American Conference of Governmental Industrial Hygienists (ACGIH) [140] adopted a maximum allowable concentration (MAC) of 500 ppm (2,000 mg/cu m) for all petroleum-derived naphthas. Most of the data compiled in the 1946 ACGIH publication were taken from three sources: the 1942 National Conference of Governmental Industrial Hygienists Subcommittee on Maximum Allowable Concentrations (now known as the ACGIH), Cook's compilation [141] of MAC's in 1945, which listed MAC values for the industrial atmospheric contaminants proposed or accepted by six states and two governmental agencies; and the recommendations of the American Standards Association Committee Z-37, now known as the American National Standards Institute (ANSI). In 1948, the ACGIH still regarded 500 ppm (2,000 mg/cu m) as the recommended environmental limit for petroleum-derived naphthas but changed the designation from MAC to a threshold limit value (TLV). Both the 1962 and 1966 ACGIH Documentation of Threshold Limit Values [142,143] recommended an 8-hour TWA concentration of 500 ppm (2,000 mg/cu m). These recommendations were based on the ACGIH recommendations for gasoline. From a review by Elkins [144], the ACGIH concluded that the aromatic hydrocarbon content of the petroleum naphthas in question should be used in determining

an appropriate TLV. The current federal occupational health standard (29 CFR 1910.1000) for petroleum distillates (naphtha) is 500 ppm (2,000 mg/cu m) as an 8-hour TWA concentration. In 1976, the ACGIH [117] recommended that the TLV for rubber solvent and varnish makers' and painters' naphtha be set at 400 ppm (1,600 and 1,800 mg/cu m, respectively). This was the first TLV assigned specifically for these two solvents.

(c) Mineral Spirits

No previous health or environmental limits for mineral spirits have been recommended.

(d) Stoddard Solvent

In his 1945 compilation of MAC's for the states of California, Connecticut, Massachusetts, New York, Oregon, and Utah, the US Public Health Service, and the American Standards Association, Cook [141] reported a limit for Stoddard solvents set only by New York at 750 ppm. This limit was used as a guide by the New York State Division of Industrial Hygiene for assessing occupational exposure. Reporting no specific basis on which the above standard was set, Cook recommended an MAC for Stoddard solvents of 500 ppm (approximately 2,950 mg/cu m calculated with an assumed molecular weight of 144) basing his proposal on work done with gasoline in 1927 by Sayers et al [145] and in 1943 by Drinker et al [146], and believing the higher boiling constituents of Stoddard solvents to be more toxic than those included in gasoline. Drinker et al [146] noted that gasoline vapor at concentrations of 1,000 ppm caused slight dizziness, nausea, and headache in several volunteers exposed for 1 hour. Sayers et al [145] observed similar symptoms in humans exposed at comparable

concentrations of ethyl gasoline (700-2,800 ppm) for 14.5-50 minutes. Nelson et al [55], also cited by Cook [141], reported that, based on the subjective responses of persons exposed to Stoddard solvent at concentrations of 400 ppm for brief, 3- to 5-minute periods, such a concentration could not be tolerated for an 8-hour exposure.

In 1946, the Subcommittee on Threshold Limits of the ACGIH [140] adopted an MAC for Stoddard solvents of 500 ppm (2,950 mg/cu m) based on recommendations by Cook [141]. In 1948, the ACGIH changed the name of Maximum Allowable Concentration to Threshold Limit Value. The ACGIH TLV tables for both 1948 [147] and 1949 [148] listed Stoddard solvents at 500 ppm as a TWA concentration. This recommended airborne concentration was set to prevent subjective symptoms. The recommended TLV was based on work done with gasoline by Sayers et al [145], Drinker et al [146], and Elkins [144]. In 1970, however, the ACGIH [149] lowered its TLV recommendation for Stoddard solvents to 200 ppm (1,180 mg/cu m) as an 8-hour TWA concentration. The 1971 Documentation of the Threshold Limit Values for Substances in Workroom Air [150] proposed a TLV of "150 or 200 ppm (approximately 800 or 1,100 mg/cu m)" for Stoddard solvents. To estimate the toxicity of Stoddard solvents, the ACGIH defined this solvent as a mixture of 85% nonane, isodecane, and their isomers, and 15% aromatic hydrocarbons, predominately isomers of trimethyl benzene, including the 1,3,5-isomer or mesitylene. For nonane and isodecane, a combined air concentration of 250 ppm was recommended based on a comparison of the increasing toxicity of pentane through octane series, and 50 ppm was recommended for mesitylene. These two recommended limits were incorporated into a composite formula for the determination of TLV's of mixtures,

yielding the estimated TLV of 150-200 ppm as a TWA concentration for Stoddard solvents [84]. In 1974, the ACGIH [84] published a notice of an intended reduction of the recommended limit for Stoddard solvents from 150-200 ppm to 100 ppm (575 mg/cu m). In 1976, this change was adopted by the ACGIH [117]. The following approach was used for the documentation of the current TLV: the estimated TLV for nonane and isodecane was reduced from 250 to 200 ppm, and the TLV for trimethyl benzene was reduced from 50 to 25 ppm. An additional statement was made that Stoddard solvents having flashpoints above 45 C should have a limit below 100 ppm. The short-term exposure limit (the maximal concentration, it was believed, to which workers can be safely exposed for a period up to 15 minutes) for Stoddard solvents was suggested to be 150 ppm (approximately 720 mg/cu m). In 1976, the ACGIH suggested for 140 flash aliphatic solvent, a type of Stoddard solvent, a limit of 25 ppm (150 mg/cu m) [117].

The current federal occupational standard (29 CFR 1910.1000) for Stoddard solvents is 500 ppm (2,950 mg/cu m) as an 8-hour TWA concentration.

The International Labour Office [151] published a report in 1970 on the "Permissible Levels of Toxic Substances in the Working Environment" for numerous countries. Finland was reported to have a standard for Stoddard solvents of 500 ppm (2,950 mg/cu m). In a 1975 survey [152] of "An International Comparison of Hygienic Standards for Chemicals in the Work Environment," the 1975 permissible level of Stoddard solvents for Sweden was listed as 600 mg/cu m, and the 1972 level of these solvents for the USSR as 300 mg/cu m. Aside from the references to the original publications, the report [152] did not cite specific data.

(e) Kerosene

At present, the ACGIH has no recommended TLV for kerosene, and no federal occupational exposure standard has been set for this substance. In 1967, the American Petroleum Institute [27] suggested that the 500-ppm TLV (2,000 mg/cu m) recommended by the ACGIH for petroleum naphthas as a TWA concentration might be used in assessing an occupational exposure limit for kerosene. In 1968, the USSR had a maximum air concentration of 300 mg/cu m for kerosene with a "C" or ceiling designation [151].

Basis for the Recommended Standard

(a) Permissible Exposure Limits

(1) Petroleum Ether

Toxicologic data suitable for recommending an environmental standard for petroleum ether are limited. Thus, to approximate the toxicity of petroleum ether, its components were evaluated.

Petroleum ether is a petroleum hydrocarbon mixture of alkanes, usually composed primarily of n-pentane (80%) and hexane (20%, mostly isohexane). Data that have been reported indicate that petroleum ether inhalation can cause CNS damage [37] and dermal toxicity [38]. Polyneuropathy has been associated with hexane exposure [40-43]. Yamamura [42] reported that sandal workers exposed to hexane at a concentration of 500-2,500 ppm (1,759-8,793 mg/cu m) for over 8 hours/day, 6-7 days/week, developed polyneuropathy. Inoue et al [44], reporting on the same study, indicated that some workers exposed at concentrations of n-hexane below 500 ppm (1,759 mg/cu m) developed polyneuropathy. Yamada [41] described the conditions under which 17 workers who were exposed to hexane vapor

developed polyneuropathy. Six workers were employed in a small laminating plant for about 10 hours/day, 6 days/week. During the laminating process, air levels of hexane ranged from 1,000 to 2,500 ppm (3,517 to 8,793 mg/cu m). The solvent used by these workers was composed of 16% methyl pentane, 20% methyl cyclopentane, and 64% n-hexane. The other 11 cases of polyneuropathy reported by Yamada occurred in a pharmaceutical plant where a 95% n-hexane solution was used. These workers lived as well as worked in the factory, where the concentration of airborne hexane was 500-1,000 ppm (1,759-3,517 mg/cu m).

Herskowitz et al [40] noted that three employees exposed to n-hexane for 6-10 months at concentrations which averaged 650 ppm (2,286 mg/cu m) developed sensorimotor polyneuropathy. Takeuchi et al [43] found that four persons exposed to petroleum benzine for 5 months to several years developed signs and symptoms of polyneuropathy. The petroleum benzine was composed of 13% n-pentane, 12.5% n-hexane, 10% n-heptane, 7.5% n-octane, 3% benzene, 3% toluene, and 57% unspecified components. Analysis of the workroom air indicated that the n-hexane and n-pentane concentrations probably did not exceed 240 and 210 ppm (844 and 618 mg/cu m), respectively.

Animal data also indicate the neurotoxic potential of n-hexane. In mice, the neurotoxic threshold concentration for n-hexane was reported by Miyagaki [79] to be 250 ppm (879 mg/cu m), and, at a concentration of 100 ppm (352 mg/cu m), no toxic signs were found. In these experiments, the animals were exposed to n-hexane for 24 hours/day, 6 days/week, for 1 year.

Because exposure to n-hexane at concentrations as low as 844-1,759 mg/cu m has been associated with polyneuropathy [41,43], and because

Miyagaki [79] reported that 879 mg/cu m was a neurotoxic threshold concentration in mice, whereas a concentration of 352 mg/cu m produced no neurotoxic signs in mice, NIOSH has recommended that the current federal environmental limit (29 CFR 1910.100) for hexane of 1,760 mg/cu m (500 ppm) be reduced to 350 mg/cu m (100 ppm) in a criteria document entitled Criteria for a Recommended Standard....Occupational Exposure to Alkanes [78].

Very little toxicologic data have been found on pentane, the major constituent of petroleum ether, in either animals or humans.

Although polyneuropathy in humans has not been attributed to exposure to hexane-free pentane alone, evidence indicates that it may be similar in toxicity to hexane. Five workers in a belt-manufacturing plant developed polyneuropahty as a result of exposure to a solvent that contained 80% pentane, 14% heptane, and only 5% hexane [45], although neither the concentration of the solvent nor the duration of exposure was mentioned. The authors concluded that pentane and heptane might also cause polyneuropathy. Pentane concentrations as low as 210 ppm may have caused, in part, the polyneuropathy in the brocade sash workers reported on by Takeuchi [43]. Truhaut et al [80] observed that components other than straight chain alkanes may cause neurologic disorders.

Since there is a possibility that n-pentane may cause polyneuropathy [43,45], NIOSH recommended a limit, as a TWA concentration, of 350 mg/cu m (120 ppm) for a 10-hour work shift for n-pentane [78]. This concentration offers a sufficient margin of safety to protect the worker from possible chronic neurologic disorders.

Because the TWA concentration limits for all C5-C8 alkanes recommended by NIOSH are 350 mg/cu m [80], NIOSH also recommends that a TWA concentration for petroleum ether, a mixture of 80% n-pentane and 20% isohexane, be set at 350 mg/cu m. This recommended standard assumes additive toxic effects between hexane and pentane which is a premise consistent with data and analysis presented in the criteria document on alkanes [78].

(2) Rubber Solvent

Carpenter et al [9] found that a concentration of 1,700 mg/cu m (430 ppm) of rubber solvent produced transient eye or nose irritation in one of seven volunteers; all seven subjects noted olfactory fatigue. At higher concentrations, progressively more subjects showed signs of sensory irritation. Carpenter et al [9] reported that concentrations of 1,900-7,900 mg/cu m (480-2,000 ppm) produced no mortality or other signs of adverse effects except for an increase in serum alkaline phosphatase in rats repeatedly exposed to rubber solvent. The increase in serum alkaline phosphatase occurred in rats exposed at 1,900 mg/cu m (480 ppm) of rubber solvent. This was the lowest concentration tested. Although no solvent-induced microscopic lesions were found in any tissue during necropsy, and this enzyme activity change was not observed in dogs similarly exposed, the possibility exists that the increase in alkaline phosphatase was indicative of a functional change that presaged a morphologic change. Considering the possibility of potential tissue damage as a result of exposure to rubber solvent at 1,900 mg/cu m, and since no toxicologic data are available to indicate a specific concentration between 0 and 1,900 mg/cu m that would prevent long-term toxic effects, NIOSH

recommends that 350 mg/cu m be established as a TWA concentration limit for rubber solvent. In arriving at this recommended limit, NIOSH recognizes that rubber solvent is composed primarily of C5-C8 hydrocarbons (41.5% paraffins and 53.6% naphthenes) [9], and, since all C5-C8 alkanes have a TWA concentration limit of 350 mg/cu m [78], it is appropriate that a limit similar to those for alkanes be adopted for rubber solvent. This recommended standard assumes additive toxic effects between the C5-C8 alkanes, and this premise is consistent with data and analysis presented in Criteria and Recommendations for a Standard....Occupational Exposure to Alkanes [78].

Although no specific data on the dermal effects of rubber solvent have been found, alkanes and solvents that boil below 232 C (450 F) are known to be primary irritants [59,78], and thus, rubber solvent should be considered to be a dermal irritant. Dermal exposure to this solvent should, therefore, be minimized. The benzene content of rubber solvent should be evaluated to assure that the federal exposure limit for benzene is not exceeded.

(3) Varnish Makers' and Painters' Naphtha

Carpenter et al [17] observed that olfactory fatigue occurred in volunteers exposed to VM and P naphtha at concentrations of 660-4,100 mg/cu m (140-880 ppm). Solvent concentrations from 660 to 2,100 mg/cu m (140 to 450 ppm) caused slight or transitory eye and throat irritation in two of seven subjects. Carpenter et al also found that rats and dogs subjected to repeated daily inhalation of VM and P naphtha at 0-5,800 mg/cu m (0-1,200 ppm) for 6 hours/day, 5-days/week, for 65 days developed no outward signs of distress. Slight changes in the percentage of

reticulocytes and immature neutrophils were noted in dogs at concentrations of 1,300 mg/cu m, the lowest concentration tested, or greater. Exposure of dogs at 5,800 mg/cu m of VM and P naphtha caused an increase in serum alkaline phosphatase activities after 13 weeks of exposure. Rats exposed to VM and P naphtha showed no major changes in hematologic or clinical chemistry values as a result of solvent exposure.

Since sensory irritation was observed in humans exposed for only 15 minutes at a concentration of VM and P naphtha at 660 mg/cu m, and because there were alterations in the reticuloyte and immature neutrophil counts in dogs exposed at 1,300 mg/cu m for 6 hours/day for 13 weeks, NIOSH recommends that a TWA concentration limit of 350 mg/cu m be adopted for VM and P naphtha. It is felt that this limit is sufficiently low to prevent sensory irritation and long-term toxicity. In recommending this limit, NIOSH recognizes that VM and P naphtha is composed of about 26.0% C5-C8 paraffins and 21.2% C5-C8 naphthenes [17], for which all C5-C8 alkanes have a limit of 350 mg/cu m and that there is a similarity in the toxicity between VM and P naphtha and rubber solvent [9,17].

No studies have been found on the effect of dermal exposure to VM and P naphtha, but it is evident that, since C5-C8 alkanes, Stoddard solvents, and mineral spirits are primary irritants [51,75,78], VM and P naphtha, whose boiling range overlaps the ranges of these solvents, has solvent properties similar to these other solvents. VM and P nahptha is, accordingly, also considered to be a dermal irritant. Thus, contact of the skin as well as the eyes should be avoided.

The benzene content of VM and P naphtha should be evaluated to ensure that federal exposure limits are not exceeded.

(4) Mineral Spirits

While mineral spirits and Stoddard solvents are not always considered the same petroleum products and are used differently for different purposes in industry, their boiling ranges (Stoddard solvents, 160-210 C; mineral spirits, 150-200 C) [1] are almost identical, and, therefore, their chemical compositions are similar. In fact, many investigators use the terms mineral spirits and Stoddard solvents interchangeably [3,4,18,19,21].

White spirits (mineral spirits) at concentrations of 2,500 mg/cu m or greater have been shown to cause nausea and vertigo in humans [48]. Concentrations of 625-2,500 mg/cu m (about 98-392 ppm) of white spirits for periods up to 2 hours had no effect on performance tests, such as perceptual speed, reaction time, short-term memory, numerical ability, and manual dexterity [50]. Exposure to white spirits at 4,000 mg/cu m (627 ppm) for 50 minutes caused a prolongation of the reaction time and a possible impairment of short-term memory [50]. The concentration of white spirits in the alveolar air during exposure to 4,000 mg/cu m, at rest, was similar to the alveolar air concentration of this solvent when the white spirits concentration was 2,500 mg/cu m and the subject was doing light manual work [48,50]. Thus, as should be expected, physical activity can increase the solvent concentration in the lungs and magnify its toxic potential.

Rector et al [82] observed that five species of animals exposed continuously for 60-90 days or exposed intermittently for 8 hours/day, 5 days/week, for 6 weeks to mineral spirits at 1,271 mg/cu m (200 ppm) showed no consistent pattern of dose-related hematologic relationships or any

remarkable gross changes except for lung irritation. Deaths were not seen at any concentration in rats, rabbits, dogs, or monkeys; however, some guinea pigs exposed at concentrations of 363 mg/cu m (57 ppm) or greater died. No guinea pigs died as a result of exposure at 288 mg/cu m (37 ppm). Animals intermittently exposed at 593-1,353 mg/cu m (93-212 ppm) displayed no adverse toxic signs except for slight lung irritation. The lung irritation was seen mainly in the animals exposed at 1,353 mg/cu m for 8 hours/day, 5 days/week, for 6 weeks.

Unless workers are several times more sensitive to intoxication by these hydrocarbons than the animals tested by Rector and coworkers [82], these animal data do not argue for a limit as low as those for the previously discussed solvents, 350 mg/cu m, inasmuch as the exposures were continuous rather than the intermittent type of exposure encountered in occupational exposure. Other tests with humans [48,50], limited mainly to acute sensory or performance responses, also suggest that a higher limit might be acceptable. However, none of these data give assurance that chronic intoxication, such as the polyneuropathy associated with one or more of the lower molecular weight hydrocarbons, might not occur. Exposures to jet fuels, ie, to mixtures of kerosene and gasoline, have caused polyneuropathy [77]. While the C5-C8 alkanes present in the jet fuel might have caused the neurologic effects, a contribution by higher boiling fractions seems possible. Since the workers described did not have eye irritation, it seemed to the authors that kerosene, which, unlike gasoline, is not a significant eye irritant, was the major component in the exposure mixture. In view of the uncertainties, it is proposed that a more conservative approach be followed until more definitive data are available,

specifically, that the same limit proposed for lower boiling fractions be recommended, viz, 350 mg/cu m as a TWA concentration.

Mineral spirits have been shown to cause dermatitis [72], and Stoddard solvents have been recognized as being capable of causing skin irritation [51,75] and possibly aplastic anemia [52,53] after dermal exposure. Of these several cases of aplastic anemia, one may have been from myelodepressant drugs. While benzene may not be expected to be an important contaminant of mineral spirits or Stoddard solvents, because of the boiling range, there is no other evident cause of anemia. From present knowledge, there seems to be no reason in addition to a small number of case histories to suggest that aliphatic hydrocarbons can cause aplastic anemia, but further research on the point seems warranted. Since there is a similar composition between mineral spirits and Stoddard solvents, it is recommended that dermal exposure to mineral spirits be avoided. The benzene content of mineral spirits should be evaluated to ensure that the federal exposure limit for benzene is not exceeded.

(5) Stoddard Solvents

There are four classes of Stoddard solvents that are used in the drycleaning industry: regular Stoddard solvent, 140 flash solvent, odorless solvent, and low end point solvent [24]. Inhalation toxicologic data exist for only two of the four classes: regular Stoddard solvent [21] and 140 flash solvent [56]. The studies [51-53,55] that did not specify the specific class of this solvent were considered to be regular Stoddard, since it is the solvent primarily used by the drycleaning industry and is commercially known as "Stoddard solvent" [25]. Henceforth in this

discussion, regular Stoddard solvent will be referred to as simply as Stoddard solvent.

The effects of Stoddard solvent exposure on humans have been reported by several investigators [21,51-53,55,75], but few were quantitative inhalation studies. Carpenter et al [21] noted that Stoddard solvent at a concentration of 144 mg/cu m (24 ppm) was not irritating to humans. At a concentration of 850 mg/cu m (150 ppm), slight and transitory eye irritation occurred during a 5-minute exposure in one of six subjects, but at 2,700 mg/cu m (470 ppm), definite eye, nose, and throat irritation was observed. Nelson et al [55] found that Stoddard solvent in excess of 400 ppm (2,290 mg/cu m) was irritating to the eyes, nose, and throat of most volunteers, and suggested that a concentration of less than 400 ppm would be an acceptable concentration for an 8-hour day, in terms of comfort.

Carpenter et al [56] examined the human sensory toxic effects of 140 flash aliphatic solvent, a type of Stoddard solvent. Minor eye irritation was the only discomfort expressed by one of six subjects exposed to 140 flash aliphatic solvent at either 110 or 310 mg/cu m (17 or 49 ppm) for 15 minutes. All subjects experienced olfactory fatigue at both concentrations. No other signs of irritation were reported.

Animal experiments also have examined toxic effects of Stoddard solvent. In 1975, Carpenter et al [21] saw that rats and dogs subjected to repeated daily inhalation of Stoddard solvent at 1,900 mg/cu m (330 ppm) for 6 hours/day, 5 days/week, for 13 weeks survived the exposures. The authors reported that the only toxic effects at the 1,900 mg/cu m exposure were a change in the blood urea nitrogen levels in rats, marked tubular regeneration in the kidneys, and an insignificant but distinct dilation of

the loops of Henle at either 8 or 13 weeks. Similar renal changes were seen after 8 and 13 weeks' exposure at 1,100 mg/cu m (190 ppm) of Stoddard solvent. Solvent exposure did not cause blood or tissue changes in dogs.

Carpenter et al [56] demonstrated that rats and dogs repeatedly exposed at concentrations of 230 mg/cu m (37 ppm) of 140 flash aliphatic solvent had no treatment-related effects at any of the levels tested.

Following the same argument (qv) previously presented on mineral spirits, an environmental limit of 350 mg/cu m as a TWA concentration is recommended for Stoddard solvents until more definitive data are available. Compliance with this limit should prevent sensory irritation and long-term toxicity.

Braunstein [51] and Larsen and Shmunes [75] showed that contact with liquid Stoddard solvent caused dermatitis in industrial workers. Scott et al [52] found four cases and Prager and Peters [53] reported one case of aplastic anemia after dermal exposure to Stoddard solvent. Stoddard solvents are capable of causing skin irritation from dermal exposure [51-53,75], so dermal exposure to Stoddard solvents must be avoided. As mentioned in the discussion of mineral spirits, dermal exposure to Stoddard solvent has been associated with several cases of aplastic anemia [52,53], but this seems unlikely to occur from present knowledge with benzene-free solvents. But the benzene content of Stoddard solvents should be evaluated to ensure that the federal exposure limit for benzene is not exceeded.

(6) Kerosene

Carpenter et al [67] reported that acute human exposure at 140 mg/cu m (20 ppm) of deodorized kerosene was innocuous. None of the subjects expressed discomfort or irritation during or after a 15-minute

inhalation period. Fifty percent of the subjects, however, developed olfactory fatigue. Rats and dogs exposed at 100 mg/cu m (14 ppm) of deodorized kerosene for 6 hours/day, 5 days/week, for 67 days showed no toxic effects. In the Carpenter study, deodorized kerosene was used and, as such, may not truly reflect the toxicity of regular kerosene since deodorized kerosene contains less aromatics (3.9% versus 5-20%) than regular kerosene [27,67]. Volkova et al [90] showed that aerosol exposure to unpurified kerosene was more toxic than purified kerosene, but there is no indication that any grade of kerosene causes toxicity at concentrations of 100 mg/cu m or below. Although short-term exposures to aerosols for 8 hours/day for 1 day or 6 hours/day for 4 days did not produce signs of systemic toxicity (dermal irritation did occur), aerosol exposure to unpurified kerosene at 500-12,000 mg/cu m for 2 hours/day for 2-4 weeks caused leukocytosis, tracheitis, bronchitis, and pneumonia [90]. Similar aerosol exposure to purified kerosene, however, did not produce any significant signs of toxicity [90]. Thus, exposure to kerosene in the aerosol form should be minimized, unless proper respiratory equipment is used, to prevent the possible accumulation of kerosene in the lungs which could result in pneumonitis. Because kerosene is less volatile than the other solvents discussed in this criteria document, hydrocarbon mists are more likely at a specific concentration with kerosene than with the other solvents. Thus, an environmental limit lower than than those recommended for the other solvents is proposed in the absence of definitive data delineating safe from unsafe concentrations of kerosene. Therefore, 100 mg/cu m, as a TWA concentration, is recommended for kerosene. While particulates may exist at even lower concentrations, it is believed that

kerosene vapor, rather than particulate, will more often be formed at this concentration [67], while at higher concentrations more particulate formation is likely.

Kerosene has been shown to cause skin irritation [60-62,67,85] and possibly bone marrow depression [57-59], probably from benzene absorption [57,58], after dermal exposure. Therefore, when this substance is used, care must be taken to prevent dermal exposure. Thirty minutes of dermal kerosene exposure has caused changes in skin structure [62]. The skin has developed a burning sensation during the 1st hour of kerosene exposure, erythema by the 2nd hour, and blister formation by the 12th hour [139]. A solution of 40% kerosene has been shown to be innocuous to the human skin, but 55, 70, and 85% kerosene solutions caused dermatitis in 24, 85, and 100% of volunteers, respectively [61]. Naphthenic-type kerosene has a greater skin-irritating potential than paraffinic-type kerosene [60]. Kerosene has also been shown to augment the toxicity of a skin-sensitizing agent [86]. Thus, it is possible that other sensitizing agents which may come in contact with the worker's skin may heighten the response to dermal kerosene exposure. Kerosene should never be ingested since, in addition to its oral toxicity [88], aspiration can occur and result in pneumonitis and possibly in death [70,89,92,93,153,154]. The benzene content of the kerosene should also be evaluated to ensure that federal exposure limits are not exceeded.

In summary, it is recommended that 350 mg/cu m be adopted as a TWA concentration limit for up to a 10-hour work shift in a 40-hour workweek for petroleum ether, rubber solvent, varnish makers' and painters' naptha, mineral spirits, and Stoddard solvents. On a volume/volume basis, these

concentrations are equal to about 114 ppm for petroleum ether, 88 ppm for rubber solvent, 75 ppm for varnish makers' and painters' naphtha, 55 ppm for mineral spirits, and 59 ppm for Stoddard solvents. The recommended TWA concentration limit for kerosenes is 100 mg/cu m (about 14 ppm). In addition, a ceiling concentration limit of 1,800 mg/cu m (about 590 ppm of petroleum ether, 454 ppm of rubber solvent, 386 ppm of varnish makers' and painters' naphtha, 282 ppm of mineral spirits, and 306 ppm of Stoddard solvents), based on a sample collection period of 15 minutes, is recommended to protect workers from short-term exposures that might cause effects, such as vertigo or other adverse reactions, which could result in accidents. No ceiling limit is believed needed for kerosene.

It is recognized that many workers handle small amounts of petroleum ether, rubber solvent, varnish makers' and painters' naphtha, Stoddard solvents, mineral spirits, and kerosene or work in situations where, regardless of the amount used, there is only negligible contact with these substances. Under these conditions, it should not be necessary to comply with many of the provisions of these recommended standards, which have been prepared primarily to protect workers' health under more hazardous circumstances. Concern for the workers' health requires that protective measures be instituted below the enforceable limit to ensure that exposures stay below that limit. For these reasons, action levels for petroleum ether, rubber solvent, and varnish makers' and painters' naphtha have been defined as 200 mg/cu m (about 66 ppm for petroleum ether, 50 ppm for rubber solvent, and 43 ppm for varnish makers' and painters naphtha, thereby delineating those work situations which do not require the expenditure of health resources for environmental and medical monitoring and associated

recordkeeping. The action levels for Stoddard solvents, mineral spirits and kerosene are identical to the TWA concentration for these solvents because of the lower volatility of these solvents and the lower likelihood of developing toxicity. The action levels have been chosen on the basis of professional judgment rather than on quantitative data that delineate nonhazardous areas from areas in which a hazard may exist. Because of nonrespiratory hazards such as those resulting from skin or eye contact or from ingestion of petroleum ether, rubber solvent, VM and P naphtha, mineral spirits, Stoddard solvents, and kerosene, it is recommended that appropriate work practices and protective measures be required regardless of the air concentration.

(b) Sampling and Analysis

Sampling and analytical methods are reviewed in Chapter IV and Appendices II, III, and IV. According to the recommended sampling method, solvent vapors (except petroleum ether) are collected in charcoal-filled tubes and then desorbed from the charcoal with carbon disulfide or toluene. An aliquot of the solution of desorbed solvents and carbon disulfide is analyzed with a gas chromatograph. The areas of the resulting peaks are determined and compared with those of injected standards. The sampling method was chosen because it is the best available at the present time and is expected to provide adequate collection efficiency for airborne solvents. The gas-chromatographic method of analysis was selected because it is reliable, sensitive, and relatively simple to perform. Moreover, the method is capable of analyzing for the constituent compounds in these solvents (eg, benzene and toluene), many of which have federal standards. The method is not entirely specific for solvents. Other compounds having

retention times similar to the solvents being analyzed will interfere with the analysis; however, mass spectrometry can be used to identify most of the eluted interfering compound. Petroleum ether can also be sampled and analyzed by a combustible gas meter.

(c) Medical Surveillance and Recordkeeping

Physical examinations should include medical and work histories, complete blood counts, urinalysis, and appropriate liver function tests. The selection of tests to be included in the physical examination are based on studies which indicated that refined petroleum solvents may cause liver or kidney effects. While aplastic anemia occasionally encountered in solvent exposures may be the result of exposure to benzene, a complete blood count is a desirable additional test and should be performed even if the solvent is known to be benzene-free.

Medical records should be kept by the employer for all employees exposed to refined petroleum solvents in the workplace. These records should be kept for at least 30 years after employment has ended, in keeping with the requirements of the Toxic Substances Control Act.

(d) Personal Protective Equipment and Clothing

The use of safety goggles and face shields (8-inch minimum) is recommended to prevent eye irritation when contact of solvents with the eyes is likely. Other personal protective equipment should include respirators, appropriate gloves, and protective clothing. It must be remembered that the solvents discussed in this document are all dermal irritants. The types of respiratory protective devices described in Tables I-1, I-2, and I-3 are those approved under the provisions of 30 CFR 11 for the concentrations specified.

(e) Informing Employees of Hazards

The employer should develop a continuing education program to ensure that all employees occupationally exposed to refined petroleum solvents have current knowledge of job hazards, signs and symptoms of overexposure, proper maintenance and emergency procedures, proper use of protective clothing and equipment, and precautions to ensure safe use of, and minimal exposure to, these solvents. Where a potential for emergencies exists, periodic drills should be held to provide employees with an opportunity to develop skill in dealing with emergency situations.

(f) Work Practices

Work practices and environmental controls are discussed in Chapters V and IV, respectively. They are directed to the prevention of undue skin contact and to the prevention of fire and explosion. Precautions against fire and explosion hazards are emphasized to ensure that flammable or combustible substances are handled properly and that their vapors do not build up to explosive levels in the work environment. In the event of eye or skin contact, contaminated clothing should be removed immediately and the eyes and skin should be flushed with water since all the refined petroleum solvents examined in this document are primary irritants.

(g) Monitoring and Recordkeeping Requirements

To ensure that sampling and analysis information is available for later reference and possible correlation to disease states, the employer should keep records of environmental monitoring for at least 30 years.

VII. RESEARCH NEEDS

Although there have been numerous studies on "solvent" toxicity, many investigators failed to adequately specify the type of solvent used in their studies. In future experiments, it is imperative that the physical and chemical characteristics of a solvent, such as boiling range, flashpoint, evaporation rate, and aromatic as well as benzene content, be given so that the solvent can be adequately defined. This information is necessary since manufacturers may give identical names to chemically dissimilar products. Universally accepted definitions are needed for all solvents.

All the solvents examined in this document need further toxicologic evaluation. There are few animal or human inhalation studies concerning petroleum ether, rubber solvent, VM and P naphtha, Stoddard solvent, mineral spirits, and kerosene; there have been no quantitative inhalation studies on petroleum ether or nondeodorized kerosene. Additional studies on these solvents should be undertaken, using various species of animals. More human studies should also be undertaken.

The exact mechanism of the CNS depressant action of these solvents has not been fully elucidated, and future studies should explore this area. The role of benzene in solvent toxicity should be evaluated. The possibility of a synergistic or additive toxic effects of multiple solvent usage should be examined. Research is needed on the effects of solvents on behavior and reflexes. The possibility that workers become lethargic or lose mental acuity during exposure to small amounts of solvents should be

studied. These questions should be answered by using both epidemiologic studies and animal experimentation.

More studies on the dermal effects of solvents on both animals and humans are needed to determine the onset of skin irritation. The teratogenic, mutagenic, and carcinogenic potentials of these solvents should also be assessed. Additionally, long-term epidemiologic studies should be undertaken to evaluate solvent toxicity and to correlate observed effects with exposure concentrations of the solvents to which workers are exposed during normal working conditions.

More specific and efficient sampling devices should be designed and improved analytical procedures developed for personal, automatic, and continuous monitoring systems.

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IX. APPENDIX I

BENZENE HAZARD

Benzene, an aromatic hydrocarbon derived primarily through the refinement and fractionation of crude petroleum, has a boiling point of 80.1 C (176 F) at 760 mmHg, and it may be a contaminant of some samples of refined petroleum solvents, especially if the solvent has a boiling range near or encompassing the boiling point of benzene. The extent of this contamination will also vary depending on the inherent chemical composition of the crude oil and the method of distillation in the refinery [155].

It has been shown by Elkins et al [156] that the vapor pressure of benzene in mixtures deviates from Raoult's Law and, therefore, the benzene vapor concentration resulting from handling such mixtures will frequently be higher than would be expected from the composition of the solvent.

Elkins and Pagnotto [157] felt that, if the benzene content of a solvent ranged from 1-4% in volume, ordinary use of the solvent would not produce benzene vapor hazards, but, if the concentration of benzene was greater than 5%, the possibility of "substantial" exposure to benzene vapors resulting from the "free" use of the solvent must be considered.

Benzene has been recognized as causing serious deleterious effects such a blood dyscrasias in humans and experimental animals, and, in 1974, NIOSH issued criteria and recommendations for occupational exposure to this compound [158]. Acute poisoning by benzene results primarily from its narcotic action. The inhalation of a high concentration of benzene (ie, 3,000 ppm for 0.1-1 hour) may cause a state of excitation and euphoria

(benzol jag) followed by drowsiness, fatigue, vertigo, nausea, and vomiting. With higher concentrations (ie, 7,500 ppm for 0.5-1 hour) or longer exposure times, convulsions followed by paralysis, loss of consciousness, and death from respiratory failure may result. The inhalation of small amounts of benzene over long periods have caused blood dyscrasias including aplastic anemia, leukopenia, and thrombocytopenia. Additional signs and symptoms of chronic toxicity may include headache, dizziness, fatigue, loss of appetite, irritability, nervousness, and nosebleed and other hemorrhagic manifestations. When Criteria for a Recommended Standard....Occupational Exposure to Benzene [158] was published, NIOSH recognized that there were data which suggested a relationship between the exposure to benzene and the occurrence of leukemia. However, at that time, there were insufficient epidemiologic investigations of the long-term relations of mortality and morbidity due to leukemia in the population at large and in those who work with benzene to classify it as a carcinogen.

In 1976, NIOSH issued an Update Criteria and Recommendations for a Revised Benzene Standard [159] and recognized that there was now sufficient evidence to conclude that benzene is leukemogenic. Since benzene causes progressive, malignant diseases of the hematopoietic system, NIOSH recommended that, for regulatory purposes, benzene should be considered carcinogenic in man. It was also recommended that the use of benzene as a solvent or diluent in open operations should be prohibited. NIOSH recommended that occupational exposure be controlled so that no worker will be exposed to benzene in excess of 3.2 mg/cu m (1 ppm) in air as determined by an air sample collected at 1 liter/minute for 2 hours.

As a consequence of the toxicity and carcinogenic potential of benzene, the benzene content of a solvent should be determined, and, if it is found to be present, air monitoring should be instituted to ensure compliance to the federal standard. When occupational exposure to benzene occurs, work practices like those described in Criteria for a Recommended Standard....Occupational Exposure to Benzene [158] should be instituted.

X. APPENDIX II

METHOD FOR THE SAMPLING AND ANALYSIS OF PETROLEUM ETHER

Atmospheric Sampling

A combustible gas meter should be used to determine petroleum ether concentrations in areas where exposure is suspected. Instruments used for this purpose must be approved as intrinsically safe by the Mining Enforcement and Safety Administration. When a combustible gas meter is used to evaluate conformance with the recommended environmental limits, a sufficient number of samples must be taken so that representative TWA and ceiling concentrations may be determined.

Sampling Procedure

Follow the instructions which are given in the manual for each combustible gas meter type. Typically, the sampling procedure will require the following steps:

(a) Sweep the combustion chamber free of combustible gases and fill it with fresh air.

(b) Turn on the batteries and apply the proper voltage to the bridge.

(c) Balance the bridge to zero deflection on the meter while the fresh air is in the open chamber.

(d) Draw the air sample into the meter and record the meter reading. Repeat this at least three times; calculate and record the average of the readings.

(e) Determine the concentration of petroleum ether samples from a calibration curve.

(f) Record a description of sampling location and conditions such as temperature, pressure, equipment used, time, rate of sampling, and any other pertinent information.

XI. APPENDIX III

METHOD FOR SAMPLING REFINED PETROLEUM SOLVENTS IN AIR

In order to evaluate conformance with the recommended environmental limits, air concentrations of rubber solvent, varnish makers' and painters' naphtha, mineral spirits, Stoddard solvents, and kerosene must be measured within the individual worker's breathing zone. Sampling procedures must conform with the following criteria.

Atmospheric Sampling

Collect breathing zone or personal samples representative of the individual employee's exposure. At the time of sample collection, record a description of sampling location and conditions, equipment used, time and rate of sampling, and any other pertinent information. Collect enough samples to permit calculation of a TWA exposure for every operation or location in which there is exposure to any refined petroleum solvents.

(a) Equipment

The sampling train consists of a charcoal tube and a vacuum pump.

(1) Charcoal tubes: Glass tubes, with both ends flame-sealed, 7-cm long with a 6-mm OD and a 4-mm ID, containing two sections of 20/40 mesh activated charcoal separated by a 2-mm portion of urethane foam. The primary section contains 100 mg of charcoal, the backup section, 50 mg. A 3-mm portion of urethane foam is placed between the outlet end of the tube and the backup section. A plug of glass wool is placed in front of the primary section. Tubes with the above specifications are commercially

available. It should be noted that when conditions of very high humidity exist, evident by the visible condensation within the tube, the collection efficiency of the sampling tube will be seriously reduced.

(2) Pump: A battery-operated pump, complete with clip for attachment to the employee's belt, capable of operating at 200 ml/minute or less.

(b) Calibration

The accurate calibration of a sampling pump is essential for the correct interpretation of the volume sampled. The frequency of calibration is dependent on the use, care, and handling to which the pump is subjected. Pumps should also be recalibrated if they have been misused or if they have just been repaired or received from a manufacturer. If the pump receives hard usage, more frequent calibration may be necessary. Maintenance and calibration should be performed on a regular schedule and records of these should be kept.

Ordinarily, pumps should be calibrated in the laboratory both before they are used in the field and after they have been used to collect a large number of field samples. The accuracy of calibration is dependent on the type of instrument used as a reference. The choice of calibration instrument will depend largely on where the calibration is to be performed. For laboratory testing, a soapbubble meter is recommended, although other standard calibrating instruments can be used. The actual setups will be similar for all instruments.

Instructions for calibration with the soapbubble meter follow. If another calibration device is selected, equivalent procedures should be used. The calibration setup for personal sampling pumps with a charcoal

tube is shown in Figure XIV-1. Since the flowrate given by a pump is dependent on the pressure drop across the sampling device, in this case a charcoal tube, the pump must be calibrated while operating with a representative charcoal tube in line.

(1) Check the voltage of the pump battery with a voltmeter to ensure adequate voltage for calibration. Charge the battery if necessary.

(2) Break the tips of a charcoal tube to produce openings of at least 2 mm in diameter.

(3) Assemble the sampling train as shown in Figure XIV-1.

(4) Turn on the pump and moisten the inside of the soapbubble meter by immersing the buret in the soap solution. Draw bubbles up the inside until they are able to travel the entire buret length without bursting.

(5) Adjust the pump flowmeter to provide the desired flowrate.

(6) Check the mercury manometer to ensure that the pressure drop across the sampling train does not exceed 1 inch of mercury at 1 liter/minute or less.

(7) Start a soapbubble up the buret and measure with a stopwatch the time it takes the bubble to move from one calibration mark to another.

(8) Repeat the procedure in (7) above at least three times, average the results, and calculate the flowrate by dividing the volume between the preselected marks by the time required for the soapbubble to traverse the distance. If, for the pump being calibrated, the volume of

air sampled is calculated as the product of the number of strokes times a stroke factor (given in units of volume/stroke), the stroke factor is the quotient of the volume between the two preselected marks divided by the number of strokes.

(9) Data for the calibration include the volume measured, elapsed time or number of strokes of the pump, pressure drop, air temperature, atmospheric pressure, serial number of the pump, date, and name of the person performing the calibration.

(c) Sampling Procedure

(1) Break both ends of the charcoal tube to provide openings of at least 2 mm, which is half the ID of the tube. A smaller opening causes a limiting orifice effect which reduces the flow through the tube. The smaller section of charcoal in the tube is used as a backup section and therefore is placed nearest the sampling pump. Use tubing to connect the back of the tube to the pump, but tubing must never be put in front of the charcoal tube. The tube is supported in a vertical position within the employee's breathing zone.

(2) Sample a maximum of 10 liters of air at a flowrate not in excess of 200 ml/minute. A sampling rate of 20 ml/minute would collect a volume of 9.6 liters in an 8-hour period. For the determination of ceiling concentrations the sampling time is 15 minutes at a sampling rate of 200 ml/minute. In addition to the personal and ceiling samples, a bulk air sample may also be collected. This air sample should be taken by drawing air through a charcoal tube at 200 ml/minute for 4-6 hours.

(3) Measure and record the temperature and pressure of the atmosphere being sampled.

(4) Treat at least one charcoal tube in the same manner as the sample tubes (break, seal, and ship), except do not draw air through it. This tube serves as a blank.

(5) Immediately after samples are collected, cap the charcoal tubes with plastic caps. Do not use rubber caps. To minimize breakage during transport, pack capped tubes tightly in a shipping container.

Shipping Samples

Prior to shipping, the charcoal tubes should be packed tightly and padded to minimize breakage during shipping. A sample of the bulk material (approximately 20 ml), of the same batch of material which was being used in the plant at the time of the sampling, should be submitted to the laboratory in a glass container with a polymer-lined cap. This sample should not be transported in the same container as the charcoal tubes.

XII. APPENDIX IV

ANALYTICAL METHOD FOR REFINED PETROLEUM SOLVENTS

The following analytical method is adapted from those described by White et al [160] and from Method Nos. s382 and s380 of the Physical and Chemical Analysis Branch of NIOSH [103,104]. This analytical method will yield adequate results for refined petroleum solvents with boiling ranges from 120-200 C, eg, varnish makers' and painters' naphtha, mineral spirits, and Stoddard solvents. By collecting two samples of rubber solvent and desorbing one with carbon disulfide and the other with toluene, this method should provide adequate results for rubber solvent. To obtain the best results for kerosene, the gas-chromatographic conditions should be changed from isothermal to a temperature programmed mode of operation. The gas-chromatographic conditions and columns stated in this Appendix have not been tested for all refined petroleum solvents and some modifications may be required for adequate results.

Principle of the Method

Refined petroleum solvent vapor trapped on an activated charcoal from a known volume of air is desorbed with carbon disulfide, except petroleum ether or other solvents with boiling points below 60 C, which should be desorbed with toluene. An aliquot of the desorbed sample is injected into a gas chromatograph. The area of the resulting peak is determined and compared with those obtained from injection of standards.

Range and Sensitivity

This method was developed to analyze Stoddard solvents over the range of 1,417-5,940 mg/cu m at an atmospheric temperature and pressure of 24 C and 749 mmHg [103]. For a 3-liter sample, the useful range of this method was 295-8,850 mg/cu m at a detector sensitivity that gives nearly full deflection on the strip chart recorder for a 26.6-mg sample. By increasing the air sample size, it should be possible to detect airborne solvent concentrations below 195 mg/cu m provided the desorption efficiency is adequate. Desorption efficiency must be determined over the range used.

The upper limit of the range of the method is dependent on the absorptive capacity of the charcoal tube. This capacity varies with the concentrations of the Stoddard or other refined petroleum solvents and other substances in the air. The first section of the charcoal tube held 26.3 mg of Stoddard solvent when a test atmosphere containing 6,026 mg/cu m of Stoddard solvent in air was sampled at 0.19 liter/minute for 23 minutes; at that time, the concentration of Stoddard solvent in the effluent was less than 5% of that in the influent.

Interferences

Any compound which has about the same retention time as Stoddard, or other refined petroleum solvents, under the gas-chromatographic conditions for this method, given below, will interfere with the analysis. This type of interference can be overcome by changing the operating conditions of the instrument, usually the column, the column temperature, or both. When the humidity is so great that condensation occurs in the sampling tube, organic vapors will not be trapped efficiently.

Precision and Accuracy

The coefficient of variation for the total analytical and sampling method for Stoddard solvents in the range of 1,417-5,940 mg/cu m was 0.052, which represents a standard deviation of 153.4 mg/cu m at the OSHA standard level. The average values obtained using the overall sampling and analytical methods were 4.7% lower than the "true" value at the OSHA standard level. The coefficient of variation for the total analytical and sampling method for petroleum distillates (varnish makers' and painters' naphtha) in the range of 937-3,930 mg/cu m was 0.052, which represents a standard deviation of 104 mg/cu m at the OSHA standard level. The data were based on validation experiments using the internal standard method. Precision and accuracy data are not available for rubber solvent and kerosene. The data for mineral spirits are assumed to be similar as that for Stoddard solvents.

Advantages and Disadvantages

(a) The sampling device is small, portable, and does not contain liquids. Interferences are minimal and most of those that do occur can be eliminated by altering chromatographic conditions. The tubes are analyzed by an instrumental method, which by changing the gas-chromatographic conditions or columns, is capable of qualitating and quantitating complex mixtures such as refined petroleum solvents.

(b) The amount of sample that can be taken is limited by the number of milligrams that the tube will hold before loading. The possibility of sample loss exists when the sample value obtained for the backup section of the charcoal tube exceeds 25% of that found on the front

section. Furthermore, the precision of the method is limited by reproducibility of the pressure drop across the tubes. This drop will affect the flowrate and cause the volume to be imprecise because the pump is usually calibrated for only one tube.

Apparatus

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

(b) The following is a list of gas-chromatographic columns that can be used in the analysis of all refined petroleum solvents with the exception of petroleum ether. Columns (3) and (4) may be used where it is desirable to separate aromatics from aliphatics.

(1) Stainless steel column (6 feet x 1/8 inch) packed with 1.5% OV-101 on 100/120 mesh Chromosorb W (recommended for mineral spirits, Stoddard solvents, and kerosene).

(2) Stainless steel column packed with 10% OV-101 on 100/120 mesh Supelcoport (recommended for rubber solvent and varnish makers' and painters' naphtha).

(3) Stainless steel column (8 feet x 1/8 inch) packed with 10% TCEP on 100/120 mesh Chromosorb PAW.

(4) Stainless steel column (8 feet x 1/8 inch) packed with 7% tetracyanoethylated pentacrythrilol (Penta) on 100/120 mesh Chromosorb PAW.

(5) Stainless steel column (20 feet x 1/8 inch) packed with 10% FFAP on 80/100 Chromosorb W AW DMCS.

(6) Stainless steel column (10 feet x 1/8 inch) packed with 10% SP-2100 on 100/120 Supelcoport.

(c) A mechanical or electronic integrator or a recorder for determining peak area.

(d) Small (2-ml) glass test tubes or equivalent with glass- or polymer-lined stoppers.

(e) A 10-μl syringe and other conveniently sized syringes for preparation of the standards.

(f) Delivery pipets, 1.0-ml type graduated in 0.1-ml increments.

(g) Volumetric flasks, about 10-ml.

Reagents

(a) Carbon disulfide or toluene chromatographic quality.

(b) The refined petroleum solvent bulk sample.

(c) Undecane, or other suitable internal standard.

(d) Hydrogen, purified.

(e) Helium, purified.

(f) Compressed air, filtered.

Analysis of Samples

All glassware used for the laboratory analysis should be washed in detergent and rinsed with tap and distilled water.

(a) Preparation: Score each charcoal tube, including the blank from field samples, with a file and break open in front of the first section of charcoal. Remove and discard the glass wool. Transfer the charcoal in the first (larger) section to a small stoppered test tube. Remove and discard the foam separating sections and transfer the second

section of charcoal to another test tube. Analyze the two charcoal sections separately.

(b) Desorption: Prior to analysis, pipet 1.0 ml of carbon disulfide into each test tube to desorb the Stoddard or other refined petroleum solvents from the charcoal. Desorption is complete in 30 minutes if the sample is stirred occasionally. For some solvent solutions with a boiling range below 160 C, it may be necessary to take two samples. One should be desorbed with carbon disulfide to analyze for the high-boiling components and the other sample desorbed with toluene to analyze for the low-boiling components.

If an automatic sample injector is used, the sample vials should be capped as soon as the carbon disulfide is added to minimize volatilization. For the internal standard method, desorb using 1.0 ml of carbon disulfide containing a known amount of the chosen internal standard.

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

(c) Typical gas-chromatographic operating conditions are:

(1) 30 ml/minute (60 psig) helium flowrate.

(2) 35 ml/minute (25 psig) hydrogen flowrate.

(3) 400 ml/minute (60 psig) air flowrate.

(4) 225 C injector temperature.

(5) 250 C manifold temperature (detector).

(6) 75 C column temperature (recommended for mineral spirits, Stoddard solvents and kerosene).

(7) 85 C column temperature (recommended for rubber solvent and varnish makers' and painters' naphtha).

The gas-chromatographic conditions have been chosen such that the solvent-related peaks elute as a cluster of unresolved peaks. Observe distinctive patterns in searching for interferences and adjust the gas-chromatographic conditions accordingly. These conditions were specifically chosen for Stoddard or other refined petroleum solvents. Some alteration in these conditions may be necessary for other refined petroleum solvents.

One method that would reduce the number of peaks needed to quantitate a refined petroleum solvent air sample is the use of head-space samples. Using the supplied liquid bulk sample, head-space volatiles are prepared and sampled with a charcoal tube. This tube is then desorbed with carbon disulfide and analyzed using a gas chromatograph. A portion of the bulk sample is then diluted with carbon disulfide and analyzed in the same manner as the head-space sample. Comparing the two chromatograms should show three or four peaks that have the same relative area for both samples. These three or four peaks can then be used to quantitate the solvent. This method is particularly useful for multiple exposure samples. The bulk air sample referred to in Appendix III could be used instead of the head-space sample of this purpose.

(d) Injection: The first step in the analysis is the injection of the sample into the gas chromatograph. Employ the solvent flush injection technique. This eliminates difficulties arising from blowback or distillation within the syringe needle, thus increasing the accuracy and

reproducibility of the injected sample volume. First, flush the 10.0-μl syringe with carbon disulfide several times to wet the barrel and plunger, then draw 3.0-μl of carbon disulfide into the syringe. Next, remove the needle from the carbon disulfide and pull the plunger back about 0.2-μl to separate the solvent flush from the sample with an air pocket to be used as a marker. Immerse the needle in the sample and withdraw a 1- to 2-μl portion, taking into consideration the volume of the needle since the sample in the needle will be completely injected. After the needle is removed from the sample and prior to injection in the gas chromatograph, pull the plunger back a short distance to minimize sample evaporation from the tip. Make duplicate injections of each sample and of the standard. No more than a 3% difference between the peak areas of the similar samples should be accepted as a valid result.

(e) Measurement of area: The areas of the sample peaks are measured by electronic integration or some other suitable method of area measurement. Preliminary sample results are read from a standard curve prepared as outlined below.

Determination of Desorption Efficiency

The desorption efficiency of a particular compound can vary from one laboratory to another and also from one batch of charcoal to another. Thus, it is necessary to determine at least once the percentage of Stoddard or other refined petroleum solvents that is removed in the desorption process. Repeat this procedure for each new batch of charcoal in use.

Place the same amount of activated charcoal as in the first section of the sampling tube (100 mg) into a 2.5-inch, 4-mm ID glass tube, flame-

sealed at one end. This charcoal must be from the same batch as that used in sampling and can be obtained from unused charcoal tubes. Cap the open end with Parafilm or equivalent. Inject a known amount of solvent directly into the activated charcoal with a microliter syringe and cap the tube with more Parafilm or equivalent.

Prepare six tubes at each of three concentrations (0.5x, 1x, and 2x of the standard) by adding an amount of analyte equivalent to that present in a 10-liter sample at the selected level. Allow the tubes to stand overnight to assure complete adsorption of the solvent onto the charcoal. These six tubes are referred to as the samples. Treat a parallel blank tube in the same manner, except add no solvent to it. Desorb and analyze the sample and blank tubes in exactly the same manner as the sampling tube described for unknown air samples.

Prepare two or three standards by injecting the same volume of the solvent or into 1.0 ml of carbon disulfide with the same syringe used in the preparation of the sample. These are analyzed with the samples.

If the internal standard method is used, prepare a calibration standard by using 1.0 ml of carbon disulfide containing a known amount of the internal standard.

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

$$\text{desorption efficiency} = \frac{\text{average weight recovered (mg)}}{\text{weight added (mg)}}$$

Calibration and Standards

The bulk samples of the analyte should be used for the calibration. It is convenient to express the concentration of standards in terms of mg/ml of carbon disulfide because samples are desorbed in 1 ml of carbon disulfide. Use the density of the solvent tested to convert milligrams into microliters for easy measurement with a microliter syringe. Prepare a series of standards varying in concentration over the range of interest and then analyze under the same gas-chromatographic conditions and during the same time period as the unknown samples. Prepare standard curves by plotting concentration in mg/ml versus peak area.

For the internal standard method, use carbon disulfide containing a predetermined amount of internal standard. The analyte concentration in mg/ml is plotted versus the area ratio of the solvent peaks to that of the internal standard.

Calculations

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

Make corrections for the blank from the field sampling for each sample by subtracting the amounts of Stoddard or other refined petroleum solvents found on the front and back sections of the blank from the amounts found in the respective sections of the sample:

corrected amount = amount on sample - amount on blank

Add the corrected amounts present in the front and in the backup sections of the same sample tube to determine the total amount of Stoddard or other refined petroleum solvents in the sample. Divide this total amount by the desorption efficiency to obtain the adjusted total amount of Stoddard or other refined petroleum solvents in the sample:

$$\text{adjusted total amount} = \frac{\text{total amount}}{\text{desorption efficiency}}$$

The concentration of Stoddard or other refined petroleum solvents in the air sampled, expressed in mg/cu m, is given by the quotient of the adjusted amount, in mg, divided by the volume of air sampled, in cu m:

$$\text{concentration (mg/cu m)} = \frac{\text{adjusted amount (mg)}}{\text{volume of air sampled (cu m)}}$$

Another method of expressing concentration is ppm:

$$\text{concentration (ppm)} = \text{concentration (mg/cu m)} \times \frac{24.45}{MW} \times \frac{760}{P} \times \frac{(T + 273)}{298}$$

where:

24.45 = molar volume (liter/mole) at 25 C (78 F) and 760 mmHg

760 = standard pressure

P = pressure (mmHg) of air sampled

T = temperature (degrees C) of air sampled

MW = molecular weight of Stoddard solvent (or other refined petroleum solvents (g/mole)

298 = standard temperature (degrees K)

XIII. APPENDIX V

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.

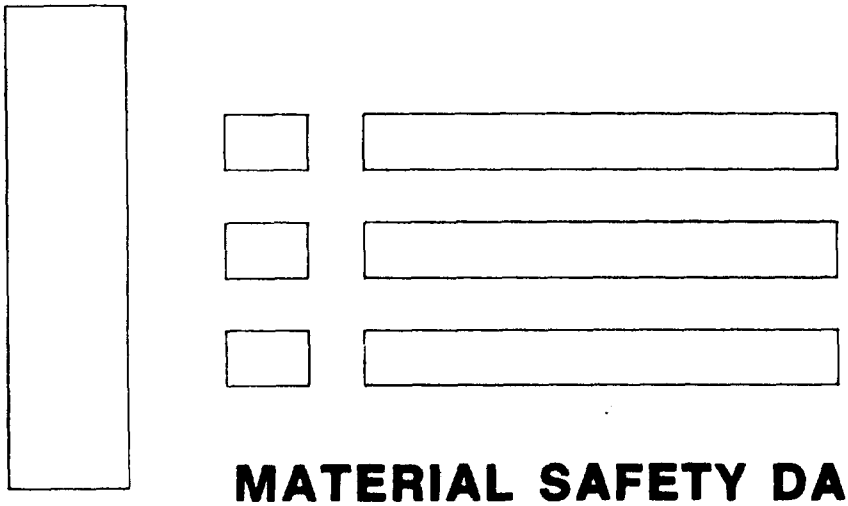
(i) Section IX. Special Precautions

"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 _____

XIV. TABLES AND FIGURE

TABLE XIV-1

CHEMICAL AND PHYSICAL PROPERTIES OF SOME REFINED PETROLEUM SOLVENTS

Petroleum Ether (a)	
Boiling range	30-60 C (86-140 F)
Predominant molecular species	C5-C6
Molecular weight	Average 74.96
Appearance and odor	Clear water-white liquid; sweet ethereal odor
Specific gravity (60 F)	0.630-0.660
Vapor pressure (mmHg) at 12.6 C	100
Vapor density (air=1)	2.5
Solubility	Insoluble in water; readily soluble in most organic solvents
Evaporation rate (ethyl ether=1)	1.1
Autoignition point	246 C (475 F)
Flashpoint range (closed)	-57 to -46 C (-70 to -50 F)
Flammable limits (in air)	1.1-8.0 %
Flammability category (OSHA)	Class IB
Extinguishing media	Foam, carbon dioxide, dry chemical
Conversion factors (at 760 mmHg and 25 C, assuming a molecular weight of 75)	1 ppm = 3.07 mg/cu m 1 mg/cu m = 0.326 ppm
Rubber Solvent (b)	
Boiling range	45-125 C (113-257 F)
Predominant molecular species	C5-C8
Molecular weight	Approximately 97
Appearance and odor	Clear water-white liquid; pleasant aromatic odor
Specific gravity (60 F)	0.674-0.850
Vapor pressure (mmHg)	Unknown
Vapor density (air=1)	Approximately 3.4
Solubility	Insoluble in water; readily soluble in most organic solvents
Evaporation rate (butyl acetate=1)	Approximately 4
Autoignition point	Minimum 260 C (500 F)
Flashpoint range (closed)	-46 to -13 C (-50 to 9 F)
Flammable limits (in air)	1.1-6.5 %
Flammability category (OSHA)	Class IB

TABLE XIV-1 (CONTINUED)

CHEMICAL AND PHYSICAL PROPERTIES OF SOME REFINED PETROLEUM SOLVENTS

Rubber Solvent (continued)	
Extinguishing media	Foam, carbon dioxide, dry chemical
Conversion factors (at 760 mmHg and 25 C, assuming a molecular weight of 97)	1 ppm = 3.97 mg/cu m 1 mg/cu m = 0.252 ppm
Varnish Makers' and Painters' Naphtha (c)	
Boiling range	95-160 C (203-320 F)
Predominant molecular species	C7-C11
Molecular weight	Approximately 87-114
Appearance and odor	Clear water-white to yellow liquid; pleasant aromatic odor
Specific gravity (60/60 F)	0.7275-0.7603
Vapor pressure (mmHg) at 20 C	2-20
Vapor density (air=1)	Approximately 3.0
Solubility	Insoluble in water; readily soluble in most organic solvents
Evaporation rate (butyl acetate=1)	0.3-1.7
Autoignition point	232 C (450 F)
Flashpoint range (closed)	-6.7 to 12.8 C (20 to 55 F)
Flammable limits (in air)	0.90-6.0 %
Flammability category (OSHA)	Class IB
Extinguishing media	Foam, carbon dioxide, dry chemical
Conversion factors (at 760 mmHg and 25 C, assuming a molecular weight of 114)	1 ppm = 4.66 mg/cu m 1 mg/cu m = 0.215 ppm
Mineral Spirits (d)	
Boiling range	150-200 C (302-392 F)
Predominant molecular species	C9-C12
Molecular weight	Approximately 144-169
Appearance and odor	Clear, water-white; pleasant sweet odor
Specific gravity	0.77-0.81
Vapor pressure (mmHg) at 20 C	0.8
Vapor density (air = 1)	Approximately 5
Solubility	Insoluble in water
Evaporation rate (butyl acetate=1)	Approximately 0.1
Autoignition point	Unknown
Flashpoint range (closed)	30.2-40.5 C (86-105 F)

TABLE XIV-1 (CONTINUED)

CHEMICAL AND PHYSICAL PROPERTIES OF SOME REFINED PETROLEUM SOLVENTS

Mineral Spirits (continued)	
Flammable limits (in air)	1.0-6.0 %
Flammability category (OSHA)	Class II
Extinguishing media	Foam, carbon dioxide dry chemical
Conversion factors (at 760 mmHg and 25 C, asssuming a molecular weight of 156)	1 ppm = 6.38 mg/cu m 1 mg/cu m = 0.157 ppm
Stoddard Solvents (e)	
Boiling range	160-210 C (320-410 F)
Predominant molecular species	C9-C11
Molecular weight	Average 135-145
Appearance and odor	Colorless liquid with kerosene-like odor
Specific gravity	0.75-0.80
Vapor pressure (mmHg) at 25 C	4-4.5
Vapor density (air=1)	5
Solubility	Insoluble in water; readily soluble in most organic solvents
Evaporation rate (butyl acetate=1)	Less than 1
Autoignition point range	232-260 C (450-500 F)
Flashpoint (closed, minimum)	37.8 C (100 F) for 3 types 60 C (140 F) for 1 type
Flammable limits (in air)	0.9-6.0 %
Flammability category (OSHA)	Class II
Extinguishing media	Foam, carbon dioxide, dry chemical
Conversion factors (at 760 mmHg and 25 C, assuming a molecular weight of 141)	1 ppm = 5.77 mg/cu m 1 mg/cu m = 0.173 ppm
Kerosene (f)	
Boiling range	175-325 C (347-617 F)
Predominant molecular species	C9-C16
Molecular weight	Approximately 170
Appearance and odor	Water-white to straw colored; odorless-aromatic
Specific gravity (20/4 C)	0.8
Vapor pressure (mmHg)	Unknown
Vapor density (air=1)	4.5
Solubility	Insoluble in water
Evaporation rate	Unknown

TABLE XIV-1 (CONTINUED)

CHEMICAL AND PHYSICAL PROPERTIES OF SOME REFINED PETROLEUM SOLVENTS

	Kerosene (continued)
Autoignition point	229 C (444 F)
Flashpoint range (closed)	37.8-73.9 C (100-165 F)
Flammable limits (in air)	0.7-5.0 %
Flammability category (OSHA)	Class IB
Extinguishing media	Foam, carbon dioxide, dry chemical
Conversion factors (at 760 mmHg and 25 C, assuming a molecular weight of 170)	1 ppm = 6.95 mg/cu m 1 mg/cu m = 0.144 ppm

(a) Adapted from references 1,3-8,11
(b) Adapted from references 1,9,11,14,124,129
(c) Adapted from references 1,10,11,17,18,124,127
(d) Adapted from references 1,3,5,12-14,18,82,124
(e) Adapted from references 1,11,18,19,21,56,124,126
(f) Adapted from references 4,5,18,27,67,125,128

TABLE XIV-2

OCCUPATIONS WITH POTENTIAL EXPOSURES TO SOLVENTS

Adhesive makers	Leather japanners
Ammonia synthesis workers	Metal cleaners
Asphalt coating workers	Naphtha workers
Ceramic production workers	Oil processors
Degreasers, metal	Painters
Detergent makers	Paintmakers
Drycleaners	Perfume extraction workers
Enamel makers, synthetic	Petrochemical workers
Farmers	Petroleum refinery workers
Fat and oil processors	Photographic chemical makers
Fungicide handlers	Printers
Garage workers	Resin makers
Heating fuel handlers	Rocket fuel handlers and makers
Herbicide handlers	Rubber coaters and makers
Hydrogen manufacturing workers	Stainers
Ink production workers	Stain makers
Insecticide handlers	Typesetters
Jet fuel handlers and makers	Varnish makers
Kerosene handlers	Waxmakers
Laboratory workers, chemical	Wood preservation makers
Lacquers	Wool process workers

Adapted from references 1,2,5,10,19,27,29-31

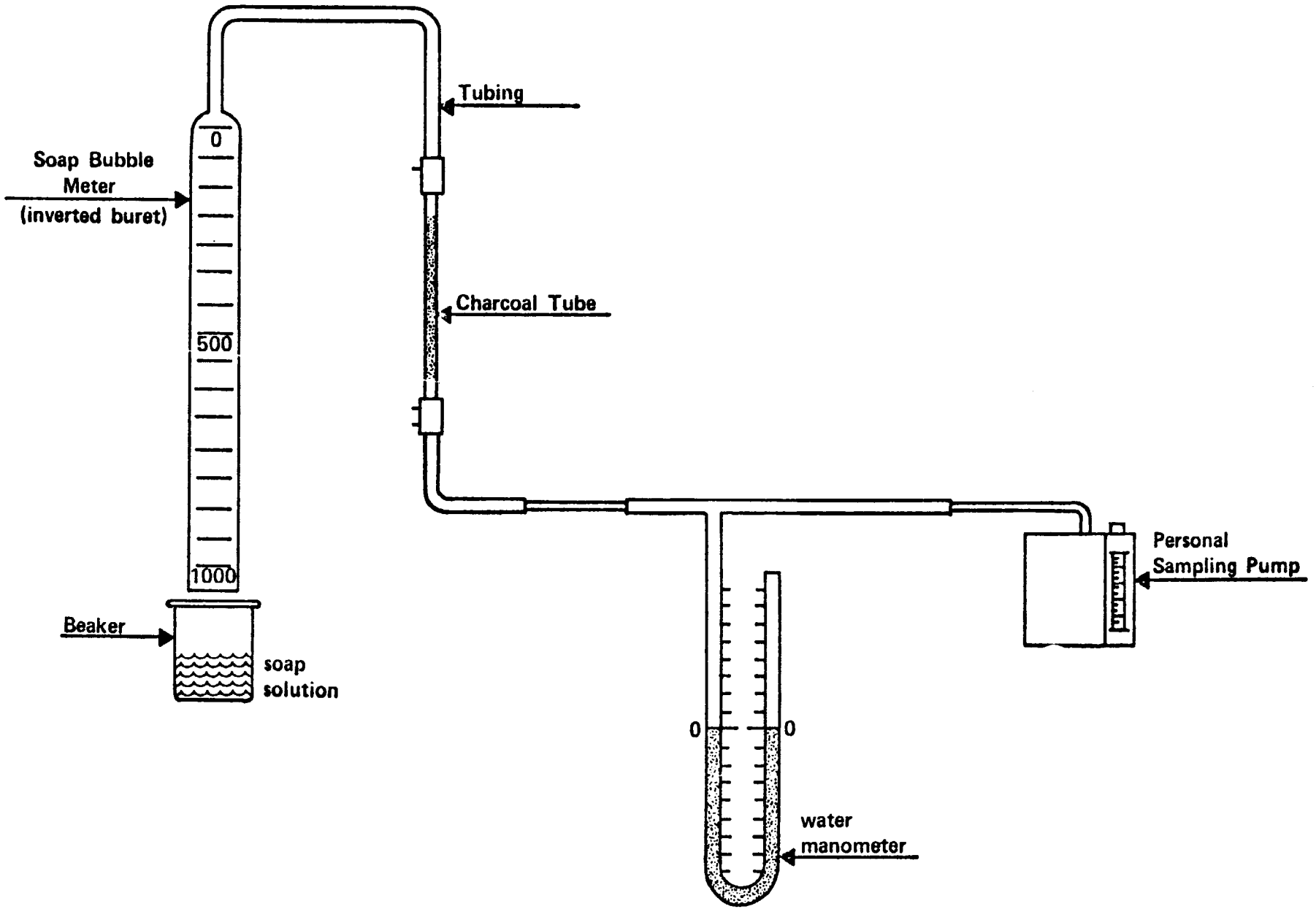


FIGURE XIV–1

CALIBRATION SETUP FOR PERSONAL SAMPLING PUMP WITH CHARCOAL TUBE

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