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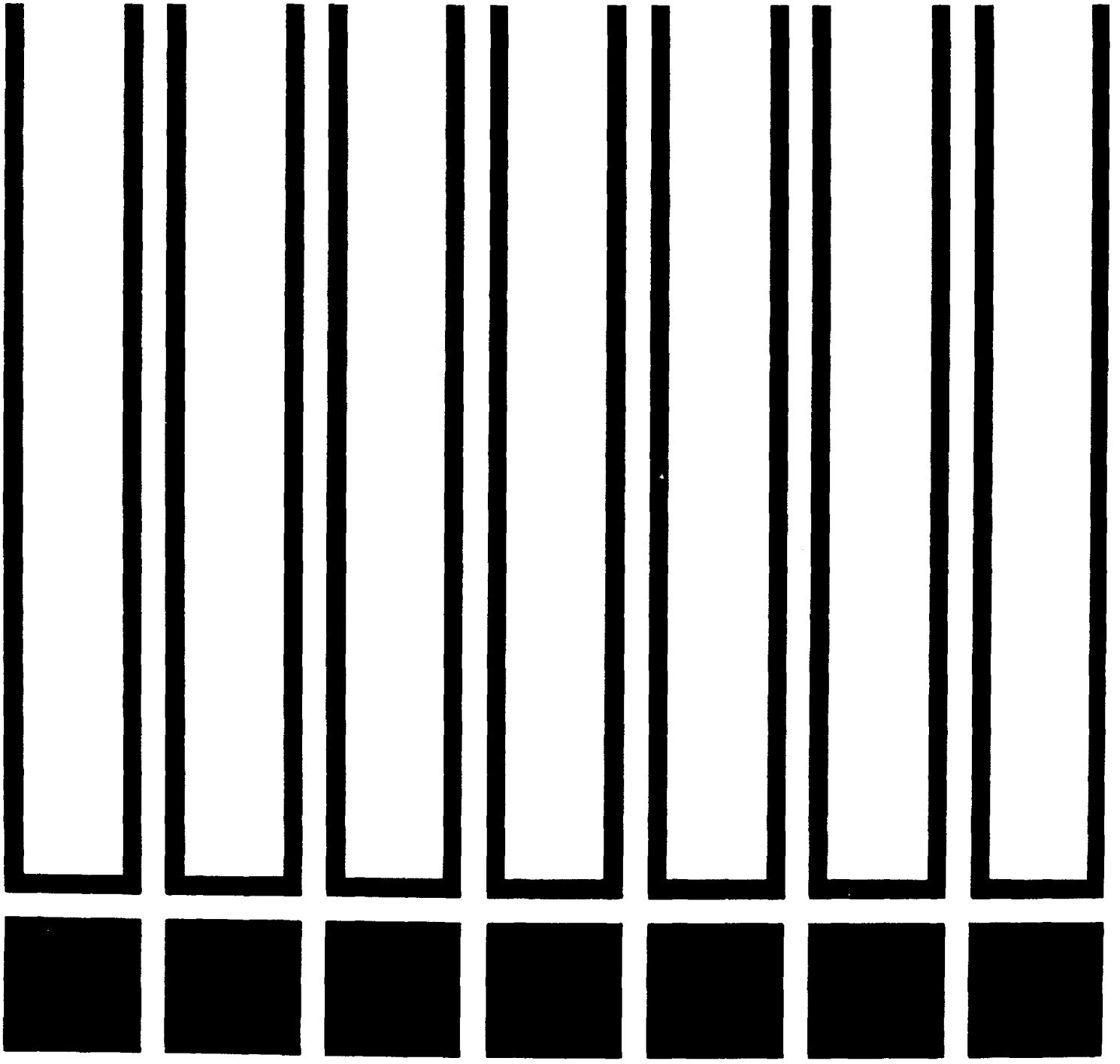

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service Center for Disease Control

National Institute for Occupational Safety and Health

criteria for a recommended standard....

OCCUPATIONAL EXPOSURE TO ISOPROPYL ALCOHOL

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
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 isopropyl alcohol by members of my staff, the valuable constructive comments by the Review Consultants on Isopropyl Alcohol, 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 isopropyl

alcohol. Lists of the NIOSH Review Committee members and of the Review Consultants appear on the following pages.

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The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for development of the criteria and the recommended standard for isopropyl alcohol. Stanford Research Institute developed the basic information and the final document for consideration by NIOSH staff and consultants under contract No. CDC-99-74-31. Donald M. Valerino, Ph.D., served as criteria manager for development of the document.

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CRITERIA DOCUMENT: RECOMMENDATION FOR AN OCCUPATIONAL EXPOSURE STANDARD FOR ISOPROPYL ALCOHOL

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I. RECOMMENDATIONS FOR AN ISOPROPYL ALCOHOL STANDARD

The National Institute for Occupational Safety and Health (NIOSH) recommends that employee exposure to isopropyl alcohol in the workplace be controlled by requiring compliance with the following sections. The standard is designed to protect the health and safety of employees for up to a 10-hour workday, 40-hour workweek over a working lifetime. Compliance with all sections of the standard should prevent adverse effects of isopropyl alcohol on the health and safety of employees. The standard is measurable by techniques that are valid, reproducible, and available to industry and governmental agencies. Sufficient technology exists to permit compliance with the recommended standard.

Because it appears that exposure to carcinogenic agent(s) may occur in the manufacture of isopropyl alcohol, it is recommended that employers engaged in the manufacture of isopropyl alcohol provide special medical surveillance procedures for employees and ensure that employees follow special work practices. Regulated areas shall be established and maintained where isopropyl alcohol is manufactured. Access to these regulated areas shall be limited to authorized persons. A daily roster shall be made of persons authorized to enter; these rosters shall be maintained for at least 30 years. Employers shall ensure that before employees leave a regulated area they remove and leave protective clothing at the point of exit. In addition, it is recommended that employers engaged in the manufacture of isopropyl alcohol install special engineering controls to prevent all exposures of employees to carcinogenic agents.

Although the workplace environmental limits are considered to be safe

levels based on information currently available to NIOSH, every effort should be made to maintain the exposure as low as technically feasible. The criteria and standard will be subject to review and will be revised as necessary.

These criteria and the recommended standard apply to workplace occupational exposures of employees to isopropyl alcohol. Synonyms for isopropyl alcohol include isopropanol, avantine, 2-propanol, sec-propyl alcohol, dimethyl-carbinol, lutosol, petrohol, and propan-2-ol.

"Manufacture of isopropyl alcohol" means a process involved in the production of isopropyl alcohol using sulfuric acid.

"Isopropyl alcohol-manufacturing area" is a controlled area consisting of all process equipment beginning with the reactor in which propylene feed enters and ending with the column where the refined isopropyl alcohol and other refined products emerge.

"Action level" means one-half of the time-weighted average limit (TWA) for isopropyl alcohol.

"Occupational exposure to isopropyl alcohol" means exposure at or above the action level. Exposure to isopropyl alcohol at concentrations less than one-half of the workplace environmental limit will not require adherence to the following sections, except for 4(a), 5(a,b), 6 (a-f), and 7. If "exposure" to other chemicals also occurs, provisions of any applicable standard for the other chemicals shall also be followed.

Section 1 - Environmental (Workplace Air)

(a) Workplace Environmental Limits

Employee exposure to airborne isopropyl alcohol shall not exceed 400

parts per million (400 ppm) parts of air by volume (approximately 984 mg/cu m of air) determined as a TWA exposure for up to a 10-hour workday, 40-hour workweek, with a ceiling of 800 ppm (approximately 1,968 mg/cu m) as determined by a sampling time of 15 minutes.

(b) Sampling, Collection, and Analysis

Procedures for collection of workplace environmental samples shall be as provided in Appendix I, or by a method shown to be equivalent in precision, accuracy, and sensitivity. Analysis of samples shall be as provided in Appendix II, or by any method shown to be equivalent in precision, sensitivity, and accuracy.

Section 2 - Medical

Medical surveillance shall be made available as designated below.

(a) Preplacement medical examinations shall include:

(1) Comprehensive or interim medical and work histories.

(2) Complete physical examination.

(b) For those workers employed in isopropyl alcohol-manufacturing areas, periodic examinations shall be made available on an annual basis. These examinations shall include, but shall not be limited to:

(1) Interim medical history and work history.

(2) Examinations giving particular attention to the skin, sinuses, and to the respiratory system. The examinations shall provide an evaluation of the workers' ability to use negative or positive pressure respirators.

(3) Such further tests as X-rays, laryngoscopy, and

bronchoscopy may be considered by the responsible physician.

(c) Periodic medical surveillance should be considered at an interval to be determined by the responsible physician for all employees occupationally exposed to isopropyl alcohol especially where there is concurrent exposure to chlorinated hydrocarbons in which case appropriate liver function tests may be needed.

(d) Examinations of current employees shall be performed within 6 months of the promulgation of a standard incorporating these recommendations.

(e) Appropriate health care shall be provided for employees with adverse effects reasonably assumed to have resulted from isopropyl alcohol exposure.

(f) Medical records shall be maintained for all persons with occupational exposure to isopropyl alcohol, for maintenance personnel with occasional occupational exposure, and for all employees engaged in the manufacture of isopropyl alcohol. Pertinent medical records, including information on required medical examinations, shall be retained for at least 5 years after the termination of the individual's employment, except for those workers employed in isopropyl alcohol-manufacturing areas in which case records shall be maintained for at least 30 years.

(g) Pertinent medical records shall be available to the medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employee or former employee, and of the employer.

Section 3 - Labeling (Posting)

(a) Containers of isopropyl alcohol shall bear the following label in addition to, or in combination with, labels required by other statutes, regulations, or ordinances:

ISOPROPYL ALCOHOL
(ISOPROPANOL)

WARNING! FLAMMABLE

Keep away from sparks and open flame.
Do not take internally.
Keep container closed.
Avoid contact with eyes.
Avoid prolonged or repeated breathing of vapor.
Use with adequate ventilation.

First Aid: In case of eye contact, flush with plenty of water; call a physician.

In case of
Fire: Use water, foam, dry chemical, or CO2.
Spill: Flush area with water spray.

(b) All containers used to collect residues and wastes in the isopropyl alcohol-manufacturing area shall carry a label stating:

CANCER-SUSPECT AGENT

(c) Areas where there is occupational exposure to isopropyl alcohol shall be posted with a sign reading:

ISOPROPYL ALCOHOL
(ISOPROPANOL)

WARNING! FLAMMABLE

Keep out sparks or open flames.
No smoking permitted.

(d) Isopropyl alcohol-manufacturing areas shall be posted with a sign reading:

CANCER-SUSPECT AGENT

AUTHORIZED PERSONNEL ONLY

These warning signs shall also be printed in the predominant language of non-English-reading employees. All employees shall be trained and informed of the hazardous areas, with special instructions given to illiterate employees.

Section 4 - Personal Protective Equipment and Clothing

(a) Protective Clothing

(1) A clean change of clothing shall be made available promptly to each employee whose clothes become wetted with isopropyl alcohol spills, and to each employee whose clothes become wetted with spills of any material in isopropyl alcohol-manufacturing areas.

(2) If it is necessary for employees to withdraw samples from the isopropyl alcohol-manufacturing process, employees shall be required to wear appropriate protective clothing including impervious suits, gloves, boots, and air-supplied hoods.

(3) Eye protective devices such as safety goggles or safety glasses shall be provided for any employee working in an operation that might result in isopropyl alcohol splashing into the eyes. Suitable eye protective devices shall conform to 29 CFR 1910.133.

(b) Respiratory Protection

(1) Engineering controls shall be used wherever feasible to maintain isopropyl alcohol concentrations below the prescribed limits. Such control equipment shall be sparkproof. Compliance with the permissible exposure limit may not be achieved by the use of respirators except:

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

(B) For nonroutine operations such as a brief exposure to isopropyl alcohol concentrations in excess of the workplace environmental limit as a result of maintenance or repair activities.

(C) During emergencies, when airborne concentrations of isopropyl alcohol may exceed the permissible limit.

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

(A) For the purpose of determining the type of respirator to be used, the employer shall measure, when possible, the airborne concentration of isopropyl alcohol in the workplace initially and thereafter whenever process, worksite, or control changes occur which are likely to increase the isopropyl alcohol concentrations; this requirement does not apply when only atmosphere-supplying positive pressure respirators are used. The employer shall ensure that no worker is being exposed to isopropyl alcohol at concentrations in excess of the workplace environmental limits because of improper respirator selection, fit, use, or maintenance.

(B) A respiratory protection program meeting the requirements of 29 CFR 1910.134 shall be established and enforced by the employer.

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

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

(E) Respirators specified for use in higher concentrations of isopropyl alcohol may be used in atmospheres of lower concentrations.

(F) The employer shall ensure that respirators are adequately cleaned, and that employees are instructed on the use of respirators assigned to them, and on how to test for leakage.

(G) Where an emergency may develop which could result in employee injury from inhalation of isopropyl alcohol, the employer shall provide respiratory protection as listed in Table I-1.

TABLE I-1

RESPIRATOR SELECTION GUIDE

Concentration of Isopropyl Alcohol	Respirator Type
Less than or equal to 1,000 ppm	Chemical cartridge respirator with organic vapor cartridge(s)
Less than or equal to 5,000 ppm	Gas mask, full facepiece with chin-style canister for organic vapors
Less than or equal to 20,000 ppm	(1) Gas mask, full facepiece with front- or back-mounted chest-type canister for organic vapors; or (2) Type C supplied-air respirator with full facepiece, demand or continuous-flow type
Unknown concentration CAUTION! The lower explosive limit is approximately 20,000 ppm	(1) Self-contained breathing apparatus in pressure-demand mode with full facepiece; or (2) Combination supplied-air respirator pressure-demand type, with auxiliary self-contained air supply and full facepiece
Escape CAUTION! The lower explosive limit is approximately 20,000 ppm	(1) Positive pressure self-contained breathing apparatus; or (2) Combination supplied-air respirator pressure-demand type, with auxiliary self-contained air supply and full facepiece

Section 5 - Informing Employees of Hazards from Isopropyl Alcohol

(a) At the beginning of employment, employees who will work in areas required to be posted in accordance with Section 3 shall be informed of the hazards, signs and symptoms of overexposure, emergency procedures, and precautions to ensure safe use and to minimize exposure. First aid procedures shall be included. This information shall be posted in the workplace and kept on file, readily accessible to the worker.

(b) Employers shall ensure that all such workers have current knowledge of job hazards, maintenance procedures, and cleanup methods, and that they know how to use respiratory protective equipment and protective clothing.

(c) In addition, employees and members of emergency teams who work adjacent to isopropyl alcohol systems or containers, where a potential for emergencies exists, shall participate in periodic drills, simulating emergencies appropriate to the work situation. Drills shall be held at intervals not greater than 6 months. Drills should cover, but should not be limited to:

Evacuation procedures.
Handling of spills and leaks, including decontamination.
Location and use of emergency firefighting equipment, and handling of isopropyl alcohol systems and/or containers in case of fire.
First aid and rescue procedures, including prearranged procedures for obtaining emergency medical care.
Location, use, and care of protective clothing and respiratory protective equipment.
Location of shut-off valves or switches.
Location, purpose, and use of safety showers and eye-wash fountains.
Operating procedures including communication procedures.
Entry procedures for confined spaces.

Deficiencies noted during drills shall be included in the continuing educational program, together with the required remedial actions. Records of drills and training conducted shall be kept for one year and made available for inspection by authorized personnel as required.

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

(e) Employees in the isopropyl alcohol-manufacturing areas shall be informed of the possible cancer hazard.

Section 6 - Work Practices

Isopropyl alcohol presents a significant fire hazard. Therefore, appropriate regulations for Class I B flammable liquids as provided in 29 CFR 1910.106 shall be followed.

(a) Engineering Controls

(1) Engineering controls shall be established to reduce exposure of employees to isopropyl alcohol vapors through implementation of adequate ventilation systems. If a local exhaust ventilation system is used, it shall be designed and maintained to prevent the accumulation or recirculation of isopropyl alcohol vapor into the workplace environment. Quarterly checks shall be made to ensure that the ventilation system is functioning properly. Such control equipment shall be sparkproof.

(2) An isopropyl alcohol-manufacturing process shall be a closed process in order to minimize exposures to possible carcinogenic agents. Weekly checks shall be made to ensure that the process is completely contained and the results of such checks shall be recorded. If

a leak exists, it shall be corrected promptly regardless of the concentration of isopropyl alcohol in the air.

(b) Sources of Ignition

(1) Precautions shall be taken to prevent the ignition of isopropyl alcohol vapor.

(2) Workplaces in which explosive concentrations of isopropyl alcohol vapor may develop shall meet regulations for Class I, Division 2, as specified by the National Electrical Code.

(3) Spark- and flame-generating operations, such as cutting or welding, and use of internal combustion engines shall be started only after an authorized representative of the employer signs a permit declaring the operation to be safe. This should be done only after a calibrated combustible gas meter or other suitable meter indicates that the concentration of isopropyl alcohol vapor is less than 0.2% by volume (10% of the lower explosive limit, or 2,000 ppm).

(4) Isopropyl alcohol in bulk quantity shall not be dispensed into containers unless the nozzle and the container are bonded. The container and the nozzle shall be grounded properly as required by 29 CFR 1910.106.

(5) Smoking shall be prohibited in isopropyl alcohol work areas.

(c) Loading and Unloading

(1) Safety showers, eyewash fountains, and fire extinguishers, such as dry chemicals approved for Class B fires, shall be installed in bulk loading and unloading areas. Safety showers, eyewash fountains, and fire extinguishers shall be checked to ensure they are in

working order before loading or unloading isopropyl alcohol.

(2) If there is a leak, the operation shall be stopped and resumed only after necessary repair or replacement has been completed.

(3) Bonding facilities for protection against sparks from discharge of static charge during the loading of tank vehicles shall be provided as required by 29 CFR 1910.106.

(d) Storage

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

(2) Storage of isopropyl alcohol in aluminum containers shall be prohibited.

(e) Disposal

(1) Spills shall be washed with water. Where it is not possible to wash a spill with water, the area should be cordoned off until it is cleaned by other means, such as a vacuum system.

(2) Wastes and residues produced in isopropyl alcohol-manufacturing areas shall be collected in impervious containers and incinerated in such a manner that no possible carcinogenic products are released.

(f) Vessel Entry

(1) Entry into confined spaces, such as tanks, pits, tank cars, and process vessels which have contained isopropyl alcohol 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 prescribed procedures will be followed.

(2) Confined spaces which have contained isopropyl alcohol shall be inspected and tested for oxygen deficiency, the airborne concentration of isopropyl alcohol and other contaminants, and the space shall be thoroughly ventilated, cleaned, neutralized, and washed, as necessary, prior to entry.

(3) Inadvertent entry of isopropyl alcohol into the confined space while work is in progress shall be prevented. Isopropyl alcohol supply lines shall be disconnected and blocked off.

(4) Confined spaces shall be ventilated while work is in progress to keep any airborne isopropyl alcohol concentration below the limit and to prevent oxygen deficiency.

(5) Individuals entering confined spaces where they may be exposed to isopropyl alcohol shall be equipped with the necessary personal protective equipment and a lifeline tended by another worker outside the space, who shall also be equipped with the necessary protective equipment.

(g) Emergency Procedures

For all work areas in which there is a reasonable potential for emergencies, procedures as specified below, as well as any other procedures appropriate for a specific operation or process, shall be formulated in advance and employees shall be instructed in their implementation:

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

(2) Firefighting procedures shall be established. These shall include procedures for emergencies involving release of isopropyl alcohol vapor. In case of fire, isopropyl alcohol sources shall be shut

off or removed. Isopropyl alcohol containers shall be removed or cooled with water spray. Chemical foam, carbon dioxide, or dry chemicals shall be used for fighting isopropyl alcohol fires, and proper respiratory protective devices and protective clothing shall be worn.

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

(4) Nonessential employees shall be evacuated from exposure areas during emergencies. The perimeters of hazardous exposure areas shall be delineated, posted, and secured.

(5) Only personnel properly trained in the relevant procedures and adequately protected against the attendant hazards shall shut off sources of isopropyl alcohol, clean up spills, and repair leaks.

Section 7 - Sanitation Practices

(a) Handwashing facilities, soap, and water shall be made available. Any isopropyl alcohol spill on the body shall be promptly washed.

(b) Eating and smoking shall be prohibited in the work area.

(c) Maintenance practices shall attempt to control leakage and prevent the accidental escape of isopropyl alcohol. Prompt repair of equipment and cleanup of spills and leaks shall be accomplished.

Section 8 - Monitoring and Recordkeeping Requirements

Workroom areas where it has been determined on the basis of an industrial hygiene survey that environmental levels do not exceed half the time-weighted average environmental limits are not considered to have occupational exposure to isopropyl alcohol. Records of these surveys, including the basis for concluding that environmental levels do not exceed the action level, shall be maintained until a new survey is completed. Surveys shall be repeated when a process change indicates to a qualified person in authority the need for reevaluation.

Requirements set forth below apply to work areas in which there is occupational exposure to isopropyl alcohol.

(a) An adequate number of breathing zone samples shall be collected and analyzed to characterize the TWA and ceiling concentrations of each operation and work location in which there is occupational exposure to isopropyl alcohol.

This sampling and analysis shall be repeated every 6 months except as otherwise indicated by a professional industrial hygienist. The first sampling period shall be completed within 6 months of the effective date of the promulgation of a standard based on these recommendations. Additional sampling and analysis shall be performed whenever changes in process, worksite, climate, or engineering controls are likely to cause an increase in airborne concentrations. If initial, periodic, or special evaluations indicate TWA or ceiling concentration limits are exceeded, corrective engineering or other control measures shall be promptly instituted to ensure the safety of employees, until concentrations below these environmental limits are achieved. In such cases, sampling of each

operation and work location shall be conducted at least monthly until two consecutive 30-day sampling periods have shown that concentrations of isopropyl alcohol are at or below the workplace environmental limits.

(b) Records shall be maintained and shall include sampling and analytic methods, types of respiratory protective devices used, and TWA and ceiling concentrations found. Each employee shall have access to data on his own environmental exposures. Pertinent records of required medical examinations, including records of occupational accidents and environmental exposures within the workplace, shall be maintained for at least 30 years after the worker's employment in isopropyl alcohol-manufacturing areas has ended. For all other areas of isopropyl alcohol exposure, pertinent records shall be maintained for at least 5 years after the worker's employment has ended. These records shall be available to the designated medical representatives of the Secretary of Labor, of the Secretary of Health, Education,and Welfare, of the employer, and of the employee or former employee.

II. INTRODUCTION

This report presents the criteria and the recommended standard based thereon which were prepared to meet the need for preventing occupational diseases arising from exposure to isopropyl alcohol or its manufacture. 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 of employees from exposure to hazardous chemical and physical agents. It should be pointed out that any criteria and recommended standard should enable management and labor to develop more healthful work environments. Simply complying with the recommended standard should not be the final goal.

These criteria for a standard for isopropyl alcohol are part of a continuing series of criteria developed by NIOSH. The proposed standard applies only to the processing, manufacture, and use of isopropyl alcohol in products as applicable under the Occupational Safety and Health Act of 1970. This standard was not developed for the population-at-large and any extrapolation beyond general occupational exposures is not warranted. It

is intended to (1) protect against the fire hazard posed by isopropyl alcohol, (2) protect against the development of harmful effects of isopropyl alcohol exposure, (3) protect against the development of cancer in the isopropyl alcohol-manufacturing areas, (4) be measurable by techniques that are valid, reproducible, and available to industry and governmental agencies, and (5) be attainable with existing technology.

The development of the recommended standard for occupational exposure to isopropyl alcohol has revealed deficiencies in the data base in the following areas:

(1) epidemiologic studies of employees exposed to chemicals used or produced during isopropyl alcohol manufacture by the current sulfuric acid and propylene process;

(2) animal studies designed to determine long-term and short-term effects of isopropyl alcohol at concentrations up to 400 ppm.

To fill these information gaps, a concerted effort is required by those people involved with the health and safety of employees exposed to isopropyl alcohol.

III. BIOLOGIC EFFECTS OF EXPOSURE

Isopropyl alcohol, CH3CHOHCH3 (formula weight 60.09), is a colorless, volatile liquid at room temperature. Its physical and chemical properties are presented in Table XII-1. [1,2] It is synthesized primarily from propylene, either by indirect hydration (strong-acid process) or by direct catalytic hydration (weak-acid process). [3] At present, the direct catalytic hydration technique has replaced the older indirect hydration technique in the US. Isopropyl alcohol can be synthesized from acetone. [4]

In the strong-acid process, propylene gas and 88-93% sulfuric acid in an approximate ratio of 1.5:1.0 were fed to a reactor maintained at 25-60 C and containing a mixture of isopropyl sulfates (CS Weil, written communication, September 1975). The reaction time was noted to be "long (hours)." Di-isopropyl sulfate, so formed, was hydrolyzed with hot water to isopropyl alcohol, isopropyl ether, and dilute (approximately 40%) sulfuric acid. The resulting overhead vapors consisted of approximately 90% isopropyl alcohol, 10% isopropyl ether, and 1% steam-distillable polymer oils. The overhead product was condensed, stored in tanks, and diluted to a constant isopropyl alcohol content. On standing, isopropyl ether and the polymer oils separated into a top layer which was removed by decantation. The bottom layer of aqueous isopropyl alcohol was refined in 2 columns and hydrocarbon oils were removed as side streams from both columns. The residue in the initial reactor contained heavier oils (tars) and carbon. Tars were removed from the dilute acid by skimming. The acid was then concentrated and recycled. Isopropyl oil was found to contain

largely polypropylenes composed of 3 and 4 propylene molecules. Less than 1% each of benzene, toluene, alkyl benzenes, polyaromatic rings, hexane, heptane, acetone, ethanol, isopropyl alcohol, and isopropyl ether were present.

In the new weak-acid process, propylene gas is absorbed in, and reacted with, 60% sulfuric acid maintained at 85 C. [4] The reaction time is reported to be "short (seconds)." Isopropyl hydrogen sulfate, so formed, is hydrolyzed to isopropyl alcohol, which is then vaporized in the stripping column. The vapor is neutralized with dilute sodium hydroxide solution and cooled. The condensate consists of isopropyl ether, isopropyl alcohol, acetone, oils, inerts, and water. The condensate is refined in distillation columns. Heavy oils and water are removed as a residue from the column.

From these two descriptions, the following differences are evident: in the old process, the acid used was concentrated (88-93%) and the reaction took place in a mixture of isopropyl sulfates at 25-60 C. The reaction time was long and the polymer oils produced were of high molecular weight. The role of the acid was defined as a reactant. In the current process where weak (60%) sulfuric acid is employed, the reaction takes place in the acid itself and the reaction time is short. The polymer oils produced are of low molecular weight. The role of the acid in the new process is defined as a catalyst. The composition of the oil produced in the weak-acid process has not been reported.

"Rubbing alcohol" is defined as 70% isopropyl alcohol and 30% water in this document. This term is included in the text of the document whenever it was stated by the authors of the papers discussed. It is not

interchangeable with isopropyl alcohol.

Extent of Exposure

In 1964, almost 1,504 million pounds of isopropyl alcohol were produced in the US. [3] Production was estimated to have increased to about 1,919 million pounds in 1970. [3] More than half of the isopropyl alcohol produced is used in the manufacture of acetone. [3] Other principal uses are in extraction processes and as a solvent, chiefly for oils, perfumes, gums, and synthetic resins. It is also used in liniments, skin lotions, cosmetics, and pharmaceuticals. [5]

NIOSH estimates that approximately 141,000 employees are potentially exposed to isopropyl alcohol in the US.

Historical Reports

In the 1920's, as the pharmaceutical and cosmetic uses of isopropyl alcohol began to expand, interest in its toxicity and human effects increased. In 1922, Pohl [6] stated that before a final decision could be made regarding the possibility of internal use of isopropyl alcohol, the fate of isopropyl alcohol in the animal should be determined. His experiments involved several species of animals. In one experiment, a dog was administered 5 cc of isopropyl alcohol by esophageal catheter. The exhaled air over the next 12 hours was collected and examined for acetone and isopropyl alcohol. Both acetone and isopropyl alcohol were present in the exhaled air. Following the administration of isopropyl alcohol in rabbits, both acetone and isopropyl alcohol were detected in the exhaled

air. The ratio of acetone to isopropyl alcohol was about 88:12. Daily ingestion of 3-5 cc of isopropyl alcohol up to a total of 224 cc by a dog caused no changes in weight gain. Simultaneous administrations in dogs and rabbits of isopropyl alcohol with adrenaline, pituglandol, oxyphenylethylamine, or histamine produced no significant changes. Changes in protein metabolism were measured by the alterations in the total nitrogen content of the urine following isopropyl alcohol administration. Based on these results, Pohl concluded that isopropyl alcohol could be consumed in reasonable amounts.

In 1927, Fuller and Hunter [7] reported the effects of oral doses of 20-30 cc of 50% isopropyl alcohol on 7 healthy subjects. Two subjects received an initial dose of 20 cc, followed about 3 weeks later by 3 consecutive daily doses of 30 cc. Another subject received an initial dose of 10 cc followed about 6 weeks later by 3 consecutive daily doses of 30 cc. A fourth subject was given 30 cc for 3 consecutive days. The final 3 subjects received single doses of 30 cc each. The immediate effect was a lowering of blood pressure, both systolic and diastolic. In 1 subject, the blood pressure was reduced from 132/80 to 124/78 within the first 30 minutes after ingestion of the isopropyl alcohol. The pulse rate varied in all subjects, sometimes rising and sometimes falling, the effect being different on the same subject on different days. The subjective symptoms included a sensation of warmth, dizziness, and headache. These symptoms were severe throughout the first day of the test. On the subsequent days, the effects subsided within 1-3 hours. In 2 cases, drowsiness also occurred on the first day of the test but not thereafter. The authors concluded that tolerance was established. Prior to the ingestion of

isopropyl alcohol, urine examination for acetone was negative in all subjects. During the experiment, acetone was detected in the urine, but neither its amount nor the method of analysis used was specified.

In 1928, Weese [8] compared the anesthetic and lethal concentrations in air of various alcohols including isopropyl alcohol. The lethal concentration was found to be 20 mg/liter while the narcotic concentration was 16-27 mg/liter. The animals were exposed to the narcotic concentrations daily for 3-4.5 hours. Histologic examination of the liver revealed fatty degeneration while the lungs, heart, and kidneys did not show any significant damage.

Other investigators studied the comparative toxicities of various alcohols in animals. [8-12] In 1932, Hufferd [9] demonstrated the narcotic effects in guinea pigs of various alcohols, including isopropyl alcohol, at various oral doses. Narcosis was judged by sluggishness, loss of control of hind and fore limbs, and inability of the animals to be aroused when held by the hind legs and shaken violently. In 1938, Starrek [13] compared the toxicities of various alcohols, including isopropyl alcohol. Isopropyl alcohol ranging from 5 to 10 mg/g was subcutaneously injected into 5 mice. Staggering gait and dyspneic respiration, followed by deep anesthesia at higher doses, were observed. At a dose of 6 mg/g (6 g/kg), the mouse died within 20 hours. The effects of inhalation of isopropyl alcohol vapor were investigated in 14 mice. Isopropyl alcohol on filter paper was placed in bottles and evaporated. Two mice were then placed in each bottle for 100-480 minutes. The animals were observed for 14 days. Walking difficulties, lying on the side, and loss of reflexes were the main signs used for evaluating the effects. The author concluded that isopropyl alcohol was

narcotic, but less so than n-propyl alcohol.

In 1942, Mestre [12] reported that subcutaneous administration of 20% isopropyl alcohol induced narcosis in rabbits. Distribution of isopropyl alcohol in various organs following the ingestion of an aqueous solution of isopropyl alcohol was studied in dogs. It was observed that there was more alcohol in the kidneys and muscles than in the lungs, liver, or brain. Acetone was identified as a possible metabolite and detected in the expired air and in the urine. The author attempted to identify the metabolic pathway of isopropyl alcohol and determined that an alcohol dehydrase enzyme was involved.

In view of the increased use of isopropyl alcohol, Keeser [14] reviewed its toxicity in 1951. He commented that "preparation and processing of isopropyl alcohol in the chemical industry, its use in histological technology, for the production of cosmetics and disinfection of the hands, are not fraught with danger." This comment was based on "experience" but no data or details were given to substantiate it.

Effects on Humans

In 1948, McCord et al [15] reported 3 cases of alcoholics ingesting unspecified amounts of isopropyl alcohol. A profound coma occurred in each case. Acetone was present in the urine of 2 subjects. The treatment included gastric lavage upon admission, fluids, and symptomatic therapy. Recovery was complete within 1-3 days.

In 1962, Adelson [16] reported 5 cases of fatal intoxication following ingestion of various unknown amounts of rubbing alcohol. These involved suicide victims and chronic alcoholics. The ages of the patients

ranged from 31 to 83 years. In 4 cases, death occurred within 3 hours to 14 days after hospital admission and resulted from profound CNS depression and ultimate respiratory failure. One patient was pronounced dead on arrival at the hospital. Autopsy indicated that pulmonary congestion and edema were present in 4 cases. One patient had nephrosclerosis, bronchiectasis, and myocardial fibrosis that were not attributed to isopropyl alcohol. Another patient had "hemoglobinuric nephrosis," characterized by the presence of hemoglobin in the urine, thought to be secondary to shock. Hemorrhagic gastritis probably due to intense vomiting and uremia was also present. Adelson also found that the isopropyl alcohol levels in the blood and the urine were not related to each other. The author surveyed the literature on isopropyl alcohol intoxication and noted that in general there was a narrow range of isopropyl alcohol levels in the blood of comatose patients, ie, 128-200 mg/100 ml. However, he did not explain the fact that 2 of his 5 patients had blood isopropyl alcohol levels of 0 and 20 mg/100 ml, and both were comatose. Moreover, in the case of the patient with no isopropyl alcohol detected in the blood, the only evidence of isopropyl alcohol poisoning was an empty isopropyl alcohol bottle found with him. It is possible that the bottle could have contained something else. King et al [17] reported a patient in coma who had ingested about 1 liter of rubbing alcohol. The patient was an alcoholic with a history of isopropyl alcohol ingestion. The blood isopropyl alcohol level was 440 mg/100 ml, a much higher level than that observed by Adelson. [16] Since the amounts of isopropyl alcohol ingested were not known, blood levels could not be related to the doses. The analytical methods used for determining isopropyl alcohol were not discussed by either Adelson [16] or

King et al. [17]

Chapin [18] reported that following the ingestion of approximately 1 pint (0.47 liter) of rubbing alcohol a known alcoholic developed edema, oliguria, and nitrogen retention resulting from acute renal insufficiency. Renal insufficiency may have been due to the presence of shock, gastrointestinal bleeding, or even to a preexisting disease from chronic alcoholism. In a similar case reported by Juncos and Taguchi, [19] a chronic alcoholic consumed about 1 pint (0.47 liter) of rubbing alcohol. Kidney damage and acute renal insufficiency followed by hemolysis and myopathy complicated the case. Again, it was not possible to distinguish the direct effects of isopropyl alcohol from preexisting conditions. In both cases, [18,19] the patients survived.

Extracorporeal hemodialysis has been reported to be a successful treatment for the removal of isopropyl alcohol from the blood. [17,20] In 1967, Freireich et al [20] reported that a 59-year-old man who had ingested 1 liter of rubbing alcohol was in deep coma and shock. The blood isopropyl alcohol level was 346 mg/100 ml and was reduced to 212 mg/100 ml before any treatment and to 60 mg/100 ml after 3 hours of hemodialysis. It was further reduced to 3 mg/100 ml, 38.5 hours after the dialysis was discontinued. The recovery was prompt and complete. This is believed to be the first reported case of the use of hemodialysis in isopropyl alcohol poisoning. In 1970, King et al [17] reported using the same treatment on a 28-year-old man who had ingested 1 liter of rubbing alcohol. In this instance, deep coma and shock were also present and the blood isopropyl alcohol was 440 mg/100 ml, 4.5 hours after admission to the hospital. After 5 hours of dialysis, the isopropyl alcohol level in the blood

decreased to 100 mg/100 ml. Again, the patient appeared to recover completely and promptly.

Reports have not been found on intoxication resulting from only inhalation of isopropyl alcohol. However, the effects of combined inhalation and skin absorption have been reported in 4 patients. [21-24] All 4 were sponged with isopropyl alcohol to reduce fever. These were not healthy subjects, and any effects following the sponging might not be attributable to isopropyl alcohol alone. Three of these patients were children who became comatose after the sponging. Garrison [21] reported one child's blood alcohol level to be 128 mg/100 ml, as measured 4.5 hours after admission to the hospital. McFadden and Haddow [22] found another child's serum isopropyl alcohol level to be 40 mg/100 ml, 12 hours after admission. Senz and Goldfarb [24] found that in a third child, blood contained 130 mg of isopropyl alcohol/100 ml, 95 minutes after admission. In this case, [24] inhalation was probably the principal route of entry. In all cases, [21,22,24] recovery occurred within 34 hours. In 1969, Wise [23] reported that immediately following an isopropyl alcohol sponge bath, an elderly man had a blood level of 10 mg isopropyl alcohol/100 ml but the amount of isopropyl alcohol used was not noted. The author did not state in his article that there were any signs of intoxication. Based on these studies, [21,22,24] it appears that high levels of isopropyl alcohol in the blood following the use of isopropyl alcohol for sponge baths may result in coma.

In general, isopropyl alcohol is not a strong dermal irritant, as is evidenced by the small number of cases of irritation reported after application to the skin of this widely used compound. Nixon et al [25]

tested skin irritation by isopropyl alcohol in at least 6 volunteers. Isopropyl alcohol was applied on their backs in about 4-sq cm areas. The sites were evaluated for erythema and edema 4, 24, and 48 hours after the application. There was no tissue destruction observed and the irritancy of isopropyl alcohol was judged to be negligible. Contact dermatitis due to isopropyl alcohol has been reported. [26-28] One of the first of these cases was reported by Wasilewski. [26] A patient developed a pruritic dermatitis around an injection site which had been previously cleaned with 70% isopropyl alcohol. Multiple small blisters appeared on the fingertips which held the alcohol swab against the skin. Closed patch tests for 70% isopropyl alcohol and commercially prepared 70% isopropyl alcohol yielded a pruritic vesicular reaction to each after 48 hours. All dilutions of isopropyl alcohol down to, and including, 5% elicited a vesicular skin response. An almost identical case was reported by McInnes, [27] when a patient developed eczema on the hand at the site of a venipuncture and on the fingers that held a swab saturated with 70% isopropyl alcohol. However, no patch test was used to verify if pure isopropyl alcohol was the cause of the dermatitis.

Richardson et al [28] reported that 5 patients who had developed contact dermatitis from a swab saturated with isopropyl alcohol were given patch tests for various components of a swab. These included the metallic packaging material, the plastic inner lining, the dried fabric of the swab, a dried swab resaturated with 70% isopropyl alcohol, and a moist fresh swab. The authors did not state with what the swabs were moistened. Twenty control subjects were also patch-tested with fresh moist swabs. The results indicated that all 5 patients developed contact dermatitis from the

fresh moist swab but not from the swab saturated with 70% isopropyl alcohol. The patches had to be removed by the end of 24 hours because of intense discomfort. All the control subjects had negative reactions to the swabs after 48 hours. The authors suggested that the skin irritant was some substance in the swab other than 70% isopropyl alcohol.

Fregert et al [29] observed that 2 out of 4 people who were allergic to ethyl alcohol responded positively to a patch test for commercially available isopropyl alcohol. However, the concentrations of the alcohol used for patch tests were not given, and controls were not used. Therefore, in a follow-up study, the same authors [30] tested these 2 patients and 20 control subjects for hypersensitivity to "gas chromatographically pure" isopropyl alcohol and 2-butanol. Both patients but no controls developed strong eczematous reactions to isopropyl alcohol and to 2-butanol.

Therefore, it is possible that some individuals may develop contact dermatitis from isopropyl alcohol. Although the study by Richardson et al [28] demonstrated that some people apparently allergic to isopropyl alcohol were allergic to another substance, Fregert et al [30] clearly showed that some individuals are in fact allergic to isopropyl alcohol.

In 1969, Wills et al [31] investigated the biochemical effects of daily ingestion of diluted isopropyl alcohol on 3 groups consisting of 8 healthy men each. The men in one group drank a daily dose of 2.6 mg/kg (0.003 ml/kg), while those in the second group drank a daily dose of 6.4 mg/kg (0.008 ml/kg). The third group was a control group who drank a placebo. The experiment was conducted for 6 weeks. During this time, various measurements were made on blood, serum, and urine on the first,

third, and seventh day of each week. Serum cholesterol, acid and alkaline phosphatase, and glutamic-oxaloacetic transaminase activities were all normal. Retention of sulfobromophthalein in serum at the end of the experiment did not increase significantly in any group, suggesting that there had been no subacute liver damage. Ophthalmoscopic examinations at the end of the experiment showed no changes from examinations made before initiation of the experiment. Conclusions on chronic effects cannot be deduced from a 6-week study in this instance. The authors noted that there were in general no deleterious effects. Acetone was present in 2% of the urine samples of the subjects receiving 6.4 mg/kg. The analytical method used to detect acetone was not described. In summary, Wills et al [31] did not find any adverse effects of isopropyl alcohol ingestion in doses of 2.6 mg/kg and 6.4 mg/kg.

In 1927, Kemal [32] gave isopropyl alcohol orally, in doses ranging from 0.1-20.0 g, to 4 healthy men. The subjects consumed isopropyl alcohol in single quantities of 0.1-20 g or in 3 repeated quantities of 5 g each at 2-hour intervals (in 1 case at 3-hour intervals). Acute effects, if any, were not reported. Isopropyl alcohol was found to be partially excreted as acetone in the urine and in exhaled air. Following qualitative detection of acetone in the urine by various techniques including iodoform reactions, quantitative determination was made using iodometry. However, Kemal did not report sufficient data to allow the calculation of the percentage of isopropyl alcohol recovered as acetone. Acetone was initially detected in the urine within the first hour and in exhaled air within the first 15 minutes. As much as 100 mg of acetone/hour was detected in the urine. In addition, acetone was detected in the urine after the ingestion of only

0.25 g of isopropyl alcohol, if administered in an abundant quantity of fluid. Hahn [33] reported that a total of 8 mg of acetone was detected in the exhaled air of a man during the first hour following the ingestion of 720 mg of isopropyl alcohol. Complete methodological details of the experiment were not given.

In 1943, Nelson et al [34] attempted to determine the sensory threshold of various compounds, including isopropyl alcohol. This experiment was done as a part of a laboratory course in industrial hygiene. Ten healthy volunteers were exposed for 3-5 minutes to isopropyl alcohol at various estimated concentrations. After every exposure, each person was asked to classify the effect of the vapor on the eyes, nose, and throat, and to give a subjective opinion of whether he could work in such an atmosphere for an 8-hour day. The subjects reported "mild irritation of the eyes, nose and throat" at 400 ppm. At 800 ppm, these effects were "not severe" but this atmosphere was declared "unsuitable" to work in for an 8-hour day by a "majority" of the volunteers. Two hundred ppm was the highest concentration estimated "satisfactory for 8-hour exposure." This study has many drawbacks. The exposure concentrations were estimated and not analytically determined. The validity of an extrapolation from a 3- to 5-minute exposure to an 8-hour workday is questionable.

Two separate reports [35,36] of human experiments indicated the odor threshold for isopropyl alcohol to be 40, 50, and 200 ppm. It appears that isopropyl alcohol vapor can be detected by odor before any irritation occurs, because irritation of the eyes, nose, and throat has been reported to occur at 400 ppm. [34]

In 1958, Scherberger et al [35] reported the design of an air blender in which air-vapor mixtures of known concentrations were formulated. This was a dynamic system and therefore suitable for establishing odor thresholds. The minimum identifiable odor level for isopropyl alcohol was found to be 200 ppm by 3 subjects. Vapor concentrations were determined using a mass spectrometer. Details concerning the experimental design were not given and therefore valid conclusions cannot be drawn from the data presented.

In 1966, May [36] reported that an experiment to measure the odor threshold for various substances, including isopropyl alcohol was devised. A panel of 8 men and 8 women sniffed various concentrations of isopropyl alcohol prepared in 5- to 10-liter bottles. All of the concentrations were determined using gas chromatography. The author reported that the "smallest perceptible" concentration of isopropyl alcohol was 40 ppm. At 50 ppm, the odor was "definitely perceptible." This is a much lower odor threshold than had been previously reported.

In summarizing the effects of isopropyl alcohol on humans, no recorded cases of industrial poisoning by pure isopropyl alcohol by any route of entry were found in the literature. However, there are many case reports of isopropyl alcohol poisoning in chronic alcoholics. [16-19] Such reports are of limited value in assessing the clinical picture of isopropyl alcohol poisoning because of the preexistence of numerous degenerative disorders common in the chronic alcoholic.

Isopropyl alcohol intoxication from ingestion manifests itself in nausea, vomiting, headache, giddiness, and depression. [16] These symptoms are soon followed by coma with or without shock. [16,17] In the absence of

shock, patients usually respond quickly to treatment and make a complete and uncomplicated recovery. [21,22] When shock is present, death may occur within the first 24 hours. [16]

There are a few case reports of combined effects of inhalation and skin absorption. [21-23] These cases suggest that combined skin absorption and inhalation of large amounts of isopropyl alcohol may result in coma. One set of human experiments [34] has shown that isopropyl alcohol vapor is a mild irritant to eyes, nose, and throat. A few cases [26,27,29,30] indicating that some people may develop contact dermatitis from isopropyl alcohol have been reported, but in general isopropyl alcohol produces minimal, if any, adverse skin effects. Although the complete metabolic pathway for isopropyl alcohol is unknown, acetone has been identified in the urine and in exhaled air as a metabolite. [15,32] Ashkar and Miller [37] and Vermeulen [38] cautioned that isopropyl alcohol intoxication may be misdiagnosed as diabetic acidosis due to the presence of acetone in the urine. They suggested that the absence of both acidosis and hyperglycemia should distinguish between the 2 conditions. Except for the presence of isopropyl alcohol in the blood, and sometimes of acetone in the urine, there appear to be no reported characteristic biochemical abnormalities.

Epidemiologic Studies

Weil et al [39] reported that in the early 1940's the presence of a carcinogen in the isopropyl alcohol-manufacturing area was suspected. In 1950, an epidemiologic investigation was undertaken by Weil et al. [39] The information on cause of death was obtained from insurance records of death claims spanning the 23-year period of 1928-1950. These records

included all deaths which had occurred among the employees at the plant during that period. However, the records did not include either individuals who might have died but were not employed at the time of their deaths or who had retired and were therefore lost from observation. The only information on the employee population included in the report was for December 31, 1938 and December 31, 1948, at which times 2,261 and 6,165 employees, respectively, were on the payroll.

During the 23-year period, a total of 182 men had worked in the isopropyl alcohol-manufacturing unit. Of these, 71 men had worked in this process for more than 5 years, and in these, 7 neoplasms of the respiratory tract were discovered. Four were malignant tumors of the paranasal sinuses. One was a malignant tumor of the lung, 1 a malignant tumor of the vocal cords, and 1 a nonmalignant tumor (papilloma) of the vocal cords. The nonmalignant papilloma of the vocal cords was removed successfully without recurrence. Four years later, this patient died of accidental causes. At the time of publication (1952), 3 of these 7 individuals had died from the carcinoma. The diagnoses included 1 primary carcinoma of the lung and 2 cancers of the paranasal sinuses. The periods of exposure for the 7 reported cases ranged from 6 to 16 years. In the 3 fatal carcinoma cases, the mean age was 36 years, with a range of 31-41 years.

The results [39] indicated that there were a total of 258 deaths among all plant employees from all causes during the 23-year period. Of this number, 34 (13.2%) employees were reported to have died of some form of cancer. Of the 34 who died of cancer, 5 (14.7%) were reported to have died of cancer of the respiratory tract. In interpreting these results, the authors reported that, according to the United States' vital statistics

for 1948, cancer caused 13.5% of the deaths from all causes and cancer of the respiratory tract was responsible for 9.6% of all cancer deaths. Weil et al [39] reported further that the upper respiratory and alimentary tracts were found to be the sites of 5.8% of all cancers in a study conducted in Connecticut during the years 1935-1946. Cancers of the paranasal sinuses occurred relatively infrequently, constituting about 0.2% of all human cancers and about 3% of the cancers of the upper respiratory and alimentary tracts. Also, the paranasal sinus cancers were encountered more often in males than in females in the age group 60-70 years. The median age was 54 years.

From 1928-1950, a period of 23 years, 25 men were generally employed in the suspect isopropyl alcohol-production operation at one time. This would be equivalent to 575 (23 x 25) man-years of exposure. Although the age distribution of the population is not known, the expected death rate from all causes in the general poluation is 0.9%. [40] Therefore, 0.9% of 575, or about 5 deaths, would be expected. An expected proportional cancer mortality of 13.5% as stated by Weil [39] for 1948 was 0.68 (0.135 x 5) cancer deaths. Thus if "respiratory" cancer deaths accounted for 9.6% of all cancer deaths, the expected number of respiratory cancer deaths would have been 0.065 (0.096 x 0.68).

Of more importance, if paranasal sinus cancer is responsible for 0.2% of all human cancers, 0.0014 (0.002 x 0.68) paranasal sinus cancers would be expected. Instead, Weil et al [39] reported 4 paranasal sinus cancers, 2 of which were fatal.

The authors [39] concluded that "a high incidence of respiratory cancer was evident when it was considered that the three patients whose

cancers were fatal plus the two surviving patients with cancers of the sinuses and one with cancer of the vocal cords for a total of six, were encountered among only 71 individuals working for more than 5 years in this unit. In other words, cancer of the respiratory tract developed in 8.4% of employees exposed for more than five years."

There are several drawbacks to this study. [39] The number of deaths reported does not represent in any known way the actual causes of death which occurred in individuals exposed to the process for 5 or more years during the period 1928-1950, because an unknown number of individuals so exposed were lost to observation. From the data, there is no way of determining how many such individuals had died or the causes involved. A further problem is that the study is not age-adjusted and, therefore, comparisons to state or national statistics are not necessarily valid. For example, Weil et al [39] emphasized that among the fatal cases reported in the paper, 1 died at age 31, 1 at 36, 1 at 41, and the others died while in their "early 40's." This may suggest an unusually low age at death in the population, or simply that no one older than the mid-40's worked in the particular unit of interest for perhaps reasons unrelated to exposure.

Because of the lack of a control population, the authors cited [39] certain vital statistic data to support the contention that "a high incidence of respiratory cancer is evident" in a group of 71 employees who were employed for 5 or more years in the manufacture of isopropyl alcohol. However, the accuracy of these comparisons cannot be confirmed because classification according to the International Classification of Diseases Adapted for Use in the United States (ICDA) were not given. Also, other possible causative factors, such as smoking, were not considered.

Nevertheless, it can be concluded that there was a very clear excess of paranasal sinus cancers in the population studied [39] and that the apparent mean latency period was 12 years. Thus, an epidemiologic association appears to exist between the manufacture of isopropyl alcohol and paranasal sinus cancer. The significance of 1 lung cancer and 1 vocal cord cancer cannot be established from studies of such a small group, since age distribution and other important factors are unknown.

In 1966, Hueper [41] referred to the work of Nale and Hueper during 1937-1946, in which they found 6 cancers of the respiratory system (4 nasal sinuses, 1 lung, and 1 larynx) in about 75 employees in an isopropyl alcohol plant. This plant had been in operation since 1928. Although the original paper by Nale and Hueper has not been found, according to Weil (written communication, September 1975), these cases of cancers were the same as those reported by Weil earlier. [39] In a written communication, Hueper confirmed that these cancers occurred in the same plant as the one referred to by Weil. [39] Hueper further added that the majority of the afflicted workers were foremen who sustained severe respiratory contact with isopropyl oil fumes during frequent accidents, such as pipe breakage. In addition, minor exposures also occurred during sample withdrawal for quality control tests. Hueper [41] referred further to unpublished observations by Eckardt that the incidence of nasal sinus and laryngeal cancers in men working in an identical isopropyl alcohol-manufacturing plant was 21 times the expected incidence in the general population aged 45-54. Two sinus cancers and 2 larynx cancers occurred in a total of 11 cancers among 779 employees. All the cancer victims had worked in this plant for more than 9 years. Both the above studies [39,41] indicated that

the latency period of such cancers was 10-12 years.

In yet another report, Hueper [42] stated that 5 additional cases of cancers developed since the 7 reported by Weil. [39] The incidence of cancer of the nasal sinuses and of the larynx for the second group was 134.5/100,000. Based on a normal rate of 6.3, the incidence of these cancers was 21.3 times the expected rate. These appear to include the 4 cases observed by Eckardt. [43] A written communication from CU Dernehl on September 9, 1975, confirmed that 5 additional cancers had developed. This report also added that the last cancer occurred in 1959. All cancers occurred in individuals who had worked in the strong-acid isopropyl alcohol-manufacturing process prior to 1945. Eckardt [43] reported that the differences between the strong-acid process and the weak-acid process, accompanied by better engineering controls in the weak-acid process, have been sufficient to eliminate the cancer hazard. He stated that the production of isopropyl alcohol was transferred to a modern, completely enclosed operation in a different refinery and that no cancers had developed at the new plant in the last 20 years. He also stated that instead of using concentrated sulfuric acid, the new production process used dilute sulfuric acid. However, no studies have been found that furnish information about the incidence of cancers in recent years.

Based on these reports [39,41,43] and written communications, isopropyl alcohol production by the process investigated, ie, the strong-acid process, must be considered to present a cancer hazard. However, there is no evidence that isopropyl alcohol itself is the carcinogen.

In 1974, Bittersohl [44] examined the cancer rate in a factory where propyl and butyl alcohols were manufactured. The author apparently did not

distinguish between propyl alcohol and isopropyl alcohol. The cancer rate was 8 times higher in a group of workers exposed to propyl alcohol, butyl alcohol, and asbestos, than in a control group exposed to none of these substances. The cancer rate was twice as high in the group exposed to all 3 substances as in a group exposed exclusively to asbestos. Bittersohl concluded that there was no convincing proof of any carcinogenic effect of isopropyl alcohol.

Animal Toxicity

In 1948, Smyth and Carpenter [45] reported that 4 out of 6 rats died within 14 days after a single 8-hour exposure to isopropyl alcohol by inhalation at 16,000 ppm. The concentration of isopropyl alcohol was estimated rather than analytically determined. Carpenter et al [46] reported that inhalation of isopropyl alcohol at an estimated single concentration of 16,000 ppm for a 4-hour period resulted in "2-4" deaths out of 6 rats. Based on these results, the authors placed isopropyl alcohol in a "slight" hazard category. These experiments were range-finding tests. The concentrations used were extremely high and therefore of little value in assessing the effects of inhaling isopropyl alcohol vapor at levels found in the occupational environment.

In 1974, Baikov et al [47] investigated the effects of chronic inhalation of isopropyl alcohol by rats. The animals were exposed to isopropyl alcohol continuously for 24 hours/day for 86 days at concentrations of 20, 2.5, and 0.6 mg/cu m (approximately 8.14, 1.02, and 0.24 ppm). The animals inhaling isopropyl alcohol at 20 mg/cu m (8.14 ppm) showed changes in the latent period of unconditional reaction, increases in

the retention of BSP, the total leukocyte count, and the number of abnormal fluorescent leukocytes. They also showed a decrease in the blood nucleic acid content, the blood oxidase and catalase activities, and the amount of coproporphyrin in blood. All of these changes were statistically significant. Animals inhaling isopropyl alcohol at 2.5 mg/cu m (1.02 ppm) demonstrated some of the same effects, but none were statistically significant. In animals inhaling isopropyl alcohol at 20 mg/cu m (8.14 ppm), post mortem findings included hyperplasia of the spleen with the development of hemorrhages of the sinuses and erosion of follicular cells, some evidence of liver parenchymal cell dystrophy, hyperplastic ependymal cells, and degenerative changes in the cerebral motor cortex. None of these effects were observed in animals inhaling isopropyl alcohol at 0.6 mg/cu m (0.24 ppm). Based on this continuous exposure study, the authors suggested that 0.6 mg/cu m (0.24 ppm) be adopted as the maximum daily average concentration.

The physiological responses observed in this study, [47] such as the increase in abnormal fluorescent leukocytes, are obscure, and it is therefore difficult to interpret their significance. Additional inadequacies of this study include insufficient experimental details, lack of control animals, lack of data on individual animals, and the lack of details of the statistical analyses. Also, there is no indication of variability. In view of all these deficiencies, conclusions regarding the short-term or long-term effects of the inhalation of isopropyl alcohol cannot be drawn.

In 1927, Fuller and Hunter [7] reported on the oral toxicities of isopropyl and ethyl alcohols for up to 2 weeks in 9 rabbits, 3 dogs, 2

cats, 2 chickens, and 1 monkey. The results of administration of isopropyl alcohol to guinea pigs were unsatisfactory and were not reported by the authors. The alcohols were mixed with an equal volume of water and administered by a catheter. Doses ranged from 5 to 20 cc of the 50% solution. Ethyl alcohol and isopropyl alcohol were given alternately to some animals, but details as to which and how many animals received the alternate doses were not given. The immediate effect of isopropyl alcohol intoxication included inertia and a state of collapse in rabbits and chickens. Cats immediately passed into a stupor from which they recovered several hours later. The effect on the dogs and on the monkey was never as severe as that observed in cats. The dose received by one cat is calculated to be 7.3-9.8 ml/kg and 2.75-5.5 ml/kg for a monkey. Drowsiness, signs of nausea, and vomiting lasting about 24 hours occurred in the monkey. The authors reported that the monkey, rabbits, and chickens acquired tolerance to isopropyl alcohol. This conclusion was based on the observation that the signs following the first dose of isopropyl alcohol diminished in intensity following the ingestion of subsequent doses of isopropyl alcohol. Possible effects resulting from the interaction between isopropyl alcohol and ethyl alcohol were not reported by the authors. This study lacked proper controls; the only control animal used was one rabbit. The effects observed, however, are similar to those observed by others. [48,49]

Morris and Lightbody [50] administered isopropyl alcohol at a dose of 6 cc/kg to 6 young adult rabbits. Acetone was found in all first and second 24-hour urine samples. Five animals continued to excrete acetone in the urine during the third 24-hour period. No acetone was found in the

fourth 24-hour collection period. In another experiment, they gave isopropyl alcohol in a single dose of 6.5-8.0 cc/kg to 36 rabbits by stomach tube. The alcohol was administered in 25 cc of 0.85% sodium chloride solution. Thirty-four of the 36 rabbits were dead within 80 hours of administration.

In another experiment, the authors [50] gave isopropyl alcohol in a daily dose of 2.5 cc/kg by stomach tube to 10 rabbits for 11 days. Each daily dose produced the same degree of incoordination of movement in every animal. Also, the time required for the animal to recover from narcosis remained the same for the 11-day period of isopropyl alcohol administration. Hence, the authors concluded that tolerance was not established in the rabbits.

Tolerance as defined by these authors [7,50] was very subjective and therefore difficult to evaluate. The reports on tolerance were made during the period 1927-1938. No recent reports were found in the literature, except for the investigation in 1945 by Lehman et al. [49] They reported that 3 dogs acquired a tolerance within 7 months to 4% isopropyl alcohol given in drinking water. Tolerance was manifested by a greater coordination at a given isopropyl alcohol level in blood and an increased rate of removal of the alcohol from the blood. The definitions of tolerance used by all these authors [7,49,50] differed considerably.

In 1944, Lehman and Chase [48] gave 0.5-10.0% isopropyl alcohol solutions to 5 groups of 5 white rats each weighing about 50 g. Consumption was entirely voluntary. Two other groups were given water and served as controls. This experiment was carried out over a period of 27 weeks. The daily dose was estimated to range from 0.75 to 5.28 ml/kg.

Retardation of growth and body weight loss were the general effects observed. Examination of the brain, pituitary and adrenal glands, lungs, heart, liver, spleen, and kidneys showed no evidence of gross or microscopic changes.

In 1960, Wallgren [51] investigated the intoxication produced in rats by several alcohols, including isopropyl alcohol. A group of 15 animals were orally administered 0.043 moles/kg (2.58 g/kg or 3.28 ml/kg) isopropyl alcohol in tap water. As a control, all animals were orally administered 3 mg/g of ethyl alcohol. Six consecutive tests at 20-minute intervals were given. Each animal was placed on a tilted plate with rough surface. The angle of the plate at which the animals slid was the measure of intoxication. The performance before alcohol administration was used as a reference. The lowest performance of animals treated with isopropyl alcohol was 60.4 ± 6.9 percentage of the initial performance without alcohol, and occurred about 80 minutes after the dose administration. Isopropyl alcohol was rated to be about 2-3 times as intoxicating, on a molar basis, as n-propyl alcohol.

In 1971, Kimura et al [52] determined the oral LD50 for isopropyl alcohol to be 5.6, 6.0, and 6.8 ml/kg in 14-day-old, young adult, and older adult white rats, respectively. Munch [53] reported a value of 133 millimoles/kg (10.2 ml/kg) as the oral LD50 for rabbits. The LD50 was determined as that quantity causing death in 1/2 of the rabbits within 24 hours after administration. Hodge and Downs [54] observed that the approximate lethal range of 70% isopropyl alcohol by oral administration was 5-10 ml/kg in rats. The lethal range was defined as the range between the highest dose tolerated by all treated rats and the lowest dose that

killed all treated rats. The animals were observed for a period of at least 2 weeks.

In an experiment with rabbits, Marzulli and Ruggles [55] used 70% isopropyl alcohol as a reference standard in a collaborative study of the Draize eye irritation test. Temporary effects, such as conjunctival redness, corneal opacity, and iritis, were caused by 0.1 ml of 70% isopropyl alcohol.

The acute dermal LD50 in rabbits was determined to be 16.4 ml/kg by Smyth and Carpenter. [45] Isopropyl alcohol was applied to an area on the clipped belly of albino rabbits. Further details of the experiment were not given. Steele and Wilhelm [56] and Macht [10] observed that isopropyl alcohol failed to produce any adverse effects when applied dermally to guinea pigs, dogs, and white rats. Nixon et al [25] reported that isopropyl alcohol did not cause any tissue destruction when applied to intact and abraded skins of rabbits and guinea pigs.

In 1945, Lehman et al [49] studied the isopropyl alcohol blood levels of dogs, cats, rabbits, and pigeons after iv administration. All species, except rats, were divided into 2 groups of 3 animals each, one group receiving 0.987 g/kg and the other 1.974 g/kg of isopropyl alcohol. Rats were divided into 2 groups of 18. They received the same doses. Blood alcohol concentrations were measured at hourly intervals up to 6 hours. It was observed that the rate of disappearance of the alcohol from the blood stream after iv administration of a single dose was dependent on the amount of the dose. The method used to detect isopropyl alcohol in blood was identical to that designed for ethyl alcohol. Metabolite measurements were not made. Furthermore, it was not evident whether the disappearance of

isopropyl alcohol from the blood was due to excretion, metabolism, or diffusion into tissues.

Wax et al [57] studied the absorption and distribution of isopropyl alcohol in groups of 3 dogs each. Thirty minutes after injection of 1.25 cc/ kg of isopropyl alcohol in 10% solution into the stomach and intestinal loop, it was found in all tissues examined, including the brain and liver. The absorption of the alcohol occurred from all portions of the digestive tract, most rapidly from the intestine as a whole, and least rapidly from the stomach. It was observed that ethyl alcohol administered iv might exert some inhibition on the intestinal absorption of isopropyl alcohol. No statistical tests substantiating the significance of the results were reported by the authors. [57] Average absorption from intestinal loops ranged from 67.4 to 91.1%. Average absorption from stomach was only 41.1%. Average milligram percent distribution in various tissues ranged from 25.3 in muscle to 155.7 in spinal fluid. However, there were large variations in isopropyl alcohol levels. For example, the distribution of isopropyl alcohol in the brain ranged from 20 to 100 mg% but was averaged to read 48.3 mg%. Considering the large range of the tissue alcohol levels and the small number of animals used, it is difficult to draw quantitative conclusions from this study.

Ellis [58] studied the metabolic fate of isopropyl alcohol in blood perfused through a rabbit liver in situ. Isopropyl alcohol in quantities of 100 mg or 300 mg/100 ml of perfusing blood produced a progressive rise in acetone concentration in blood. The author noted that the amount of acetone produced was insufficient to account for all the isopropyl alcohol metabolized and suggested that the metabolic transformation of isopropyl

alcohol involved some pathway or pathways other than oxidation to acetone. It was further suggested that conjugation with glucuronic acid might be an alternative mechanism. Kamil et al [59] observed that in rabbits this mechanism appeared to be the alternate metabolic process to oxidation. However, it accounted for only about 10% of the isopropyl alcohol administered.

Nordmann et al [60] examined the enzymes involved in the metabolism of isopropyl alcohol. Groups of 4-10 rats were administered ip pyrazole, an inhibitor of alcohol dehydrogenase and catalase, or 3 amino-1,2,4-triazole, an inhibitor of catalase alone. Isopropyl alcohol was then administered either ip at a dose of 1 g/kg (1.27 ml/kg) or by stomach tube at a dose of 6 g/kg (7.63 ml/kg). The control animals received an equal volume of saline or water. Isopropyl alcohol and acetone levels in the blood were monitored at 0.5, 1.5, 3, 4, 6, 8, and 20 hours after isopropyl alcohol administration. Animals receiving 3-amino-1,2,4-triazole did not show any significant difference in the blood isopropyl alcohol or acetone levels from those found in the animals receiving just isopropyl alcohol. In contrast, pretreatment with pyrazole markedly reduced the blood isopropyl alcohol clearance and delayed the rate of acetone production. The authors concluded that catalase did not play an important role in the oxidation of isopropyl alcohol.

A quantitative relationship between the dose of isopropyl alcohol and the amount of acetone or any other metabolite has not been established. The exact metabolism therefore is not clearly understood. Part of isopropyl alcohol is oxidized to acetone [58] and some probably conjugates with glucuronic acid, [59] but these processes have not accounted for all

of the isopropyl alcohol administered. Since no quantitative relationships were established, a biologic index of exposure cannot be formulated.

Beauge et al [61] administered 6 g/kg (7.63 ml/kg) of isopropyl alcohol to 6 rats by gastric intubation. Six control rats were administered an identical volume of water. Four hours later, the animals were administered labeled palmitate ip. The rats were then decapitated 30 minutes later. Fragments of liver were removed and the lipids were extracted to determine the concentrations of triglycerides and phospholipids. The results indicated that there was an accumulation of triglycerides in the livers of experimental animals. Nordmann et al [62] confirmed these observations. They administered isopropyl alcohol 6 g/kg by stomach tube to 8 rats and decapitated them 8 hours later. The results indicated that liver triglycerides were significantly higher in the experimental animals than in the controls. The dose of the alcohol used was extremely high. Beauge et al [63] administered orally 300 mg/kg of pyrazole, an inhibitor of alcohol dehydrogenase and catalase, to groups of 8 rats each. Isopropyl alcohol at a dose of 3 g/kg (3.82 ml/kg) was administered 23 hours later by stomach tube. The animals were killed 8 hours later and examined for hepatic triglycerides and for the isopropyl alcohol and acetone concentrations in the blood. Compared to the animals receiving isopropyl alcohol alone, the animals receiving both isopropyl alcohol and pyrazole showed an increased blood isopropyl alcohol level accompanied by a decreased blood acetone level. The hepatic triglyceride content of the animals treated with pyrazole and isopropyl alcohol did not differ significantly from that of the controls, but it was elevated in the animals receiving isopropyl alcohol without pyrazole. The authors

concluded that isopropyl alcohol-induced fatty liver was related to the metabolism of isopropyl alcohol, and that acetone may play a significant role. However, it should be noted that no attempt was made to find any histopathological evidence to support the conclusion that isopropyl alcohol induced fatty liver.

Divincenzo and Krasavage [64] injected guinea pigs ip with 500 mg/kg and 1,000 mg/kg of undiluted isopropyl alcohol. Twenty-four hours later, no increase in serum ornithine carbamyl transferase activity was observed. The authors concluded that liver damage was absent. Microscopic examination revealed that the liver was normal. However, the serum ornithine carbamyl transferase activity is not a frequently used index of early liver damage.

From these reports, [61,64] it can be concluded that isopropyl alcohol increases the concentration of triglycerides in the livers of rats. However, lack of any histological evidence prevents any conclusions regarding induction of fatty liver by isopropyl alcohol.

In 1967, Cornish and Adefuin [65] studied the capacity of various alcohols, including isopropyl alcohol, to potentiate the toxicity of carbon tetrachloride. Isopropyl alcohol at a dose of 2.34 g/kg (2.98 ml/kg) was administered by intubation to 6 rats, 16-18 hours prior to inhalation of carbon tetrachloride. Six control animals and 6 animals receiving only isopropyl alcohol were included in the study. The exposure period to carbon tetrachloride at 1,000 ppm was 2 hours. The serum glutamic-oxaloacetic transaminase (SGOT) activity increased significantly compared to the control animals, indicating that isopropyl alcohol potentiated carbon tetrachloride toxicity at the dosage used. However, as noted by the

authors, the combined industrial exposures to isopropyl alcohol and carbon tetrachloride would rarely be as high as those used in this experiment.

In 2 separate studies, Traiger and Plaa [66,67] reported that isopropyl alcohol at a dose of 2.5 ml/kg (1.96 g/kg) combined with 0.0075 ml/kg [66] or 0.1 ml/kg [67] of carbon tetrachloride increased serum glutamic-pyruvic transaminase (SGPT) activity. Traiger and Plaa [68] and Plaa et al [69] conducted further experiments to determine whether isopropyl alcohol potentiated the toxicity of other chlorinated hydrocarbons as measured by SGPT activity. Isopropyl alcohol at a dose of 2.5 ml/kg was administered by forced feeding to 106 mice divided into 4 groups. Eighteen hours after isopropyl alcohol administration, each group was injected ip with 1 of the 4 chlorinated hydrocarbons in doses ranging from 0.05 to 2.5 ml/kg. The authors observed that in mice the toxicities of chloroform, 1,1,2-trichloroethane, and trichloroethylene were enhanced by both isopropyl alcohol and acetone. The hepatotoxicity of 1,1,1-trichloroethane was not augmented. Acetone produced greater enhancement of the SGPT-elevating power of 1,1,2-trichloroethane than isopropyl alcohol; isopropyl alcohol had a greater effect on the hepatotoxic actions of chloroform and trichloroethylene than acetone. The authors also undertook preliminary studies, [68] which indicated that administration of isopropyl alcohol or acetone by inhalation-augmented liver injury induced by ip administration of carbon tetrachloride. Moreover, the degree of augmentation observed was related to the hepatotoxicity of the chlorinated hydrocarbon. Therefore, the authors concluded that the likely combination in the occupational environment that might result in a hazardous situation should be predictable on the basis of the hepatotoxicity of the chlorinated

hydrocarbon involved. In 2 separate studies, Traiger and Plaa [70,71] found that acetone was capable of potentiating carbon tetrachloride toxicity. Plaa and Traiger [72] carried out a dose-response study using isopropyl alcohol alone and acetone alone, followed 18 hours later by carbon tetrachloride. SGPT activity was used as a measure of hepatotoxicity. Elevated SGPT activity was evident when isopropyl alcohol was administered in the range of 0.41-4.70 ml/kg or when acetone was administered in the range of 0.35-4.00 ml/kg. The authors noted that the marked potentiation of carbon tetrachloride hepatotoxicty by isopropyl alcohol could have been due to a combined effect of unaltered isopropyl alcohol and acetone which were slowly eliminated. This observation was further supported by the results of a study by Sipes et al, [73] who examined the effect on rat liver microsomes of 2.5 ml/kg of acetone and isopropyl alcohol each. The authors assumed that isopropyl alcohol increases the toxicity of carbon tetrachloride by inducing liver microsomal enzymes. The binding capacity of liver microsomes with some chlorinated hydrocarbons and various other compounds was enhanced by both isopropyl alcohol and acetone.

Cote et al [74] investigated the effect of isopropyl alcohol pretreatment on carbon tetrachloride-induced alteration of hepatic morphology at the ultrastructural level. Isopropyl alcohol at 2.5 ml/kg was administered by mouth 18 hours prior to a threshold dose of carbon tetrachloride at 0.1 ml/kg ip. Alterations of the liver structure comparable to those occurring after the administration of 1.0 ml/kg of carbon tetrachloride alone were observed. The organelle most affected was the endoplasmic reticulum. Also, lysosomal alterations, as measured by an

increase in the ratio of free to total acid phosphatase activity, were present in the animals treated with both substances. The authors concluded that hepatocytes from isopropyl alcohol-treated rats may be more sensitive to the toxic effects of carbon tetrachloride or its metabolite. They also suggested that isopropyl alcohol could stimulate drug-metabolizing enzymes or could act on the endoplasmic reticulum in such a way as to facilitate the attack of carbon tetrachloride on this organelle.

In summarizing the effects of isopropyl alcohol in animals, effects of inhalation, germane to occupational exposure, remain inadequately studied. Most animal experiments involve routes of administration other than inhalation. The few inhalation studies found used isopropyl alcohol either at very high concentrations, such as 16,000 ppm, [45,46] or at very low concentrations, such as less than 10 ppm. [47] Reports on acute or chronic effects of inhalation of isopropyl alcohol at levels usually encountered in the industrial environment, such as up to 400 ppm, have not been found in the literature. Oral intoxication effects include narcosis, [8,9,48] salivation, [48] and vomiting. [48] Conclusive evidence of liver damage has not been reported. However, accumulation of liver triglycerides following isopropyl alcohol administration has been observed. [61,62] Although acetone has been identified as a metabolite, [58] the precise metabolic routes for isopropyl alcohol are unknown. [58] Other animal studies [65-71] showed that when isopropyl alcohol was administered prior to carbon tetrachloride it increased the hepatotoxicty of the latter.

Thus, existing animal studies are not adequate for understanding all the acute and chronic effects of isopropyl alcohol inhalation in humans. Table XII-2 presents a summary of the results of animal experiments.

Carcinogenicity, Teratogenicity, and Mutagenicity

Subsequent to the discovery of an abnormal incidence of paranasal and sinus cancers in employees involved in isopropyl alcohol manufacture, Weil et al [39] undertook animal studies to identify the carcinogen. The following substances were tested: isopropyl alcohol, isopropyl oil from 2 manufacturing processes, unidentified distillates, and chromatographic fractions of the oils. Inhalation and subcutaneous injection studies were performed on mice. In the inhalation studies, mice were exposed 5 days/week, 3-7 hours/day, for 5-8 months. The undiluted samples were administered subcutaneously in 0.025-ml amounts for 20 - 40 weeks. In some studies, 4-8 mg of the sample dissolved in 1 ml lard were administered in 2-6 biweekly doses. The results of these studies are summarized in Table III-1 and III-2.

As indicated in Table III-1, [39] inhalation of isopropyl alcohol produced no significant numbers of tumors in the species studied. The suspected carcinogen, isopropyl oil from only 1 of the 2 plants was tumorigenic. Tumors were induced in only 3 of 21 groups of mice in the inhalation study and in 1 of 13 groups of mice in the injection study. Lung tumors found in these groups included adenomas and adenocarcinomas. No mammary or sinus tumors were found. The carcinogenic potential of the oil was generally less than that of a well-recognized and studied carcinogen, methylcholanthrene. Although this study is fairly well-designed, it suffers from one major drawback. After examining 74 mice from the first inhalation study for sinus tumors and finding none, Weil et al [39] discontinued the search in subsequent experiments. Since the

TABLE III-1

SUMMARY OF THE RESULTS* OF INHALATION STUDIES IN 6 STRAINS OF MICE

Substance	Concentration	Strain					
		C3H	ABC	CFW	C57	CF1	ABCT
Isopropyl oil, first plant	0.004 ml/liter	12/41**	32/56	-	0/34	-	-
"	0.008 ml/liter	14/41**	37/46	-	0/7	-	-
"	0.002 ml/liter	-	-	13/47	-	62/21	13/46
"	0.004 ml/liter	-	-	14/49	-	72/25	8/38
"	"	-	19/36	22/32	-	35/52	-
Isopropyl oil, second plant	0.002 ml/liter	-	-	13/46	-	63/35	10/39
"	0.004 ml/liter	-	-	16/51	-	44/36	18/34**
Isopropyl alcohol	0.0075*** mg/cu m	6/36	24/41	-	10/47	-	-
Isopropyl sulfate + isopropyl oil	0.00025 mg/cu m	-	17/23	40/20	-	36/52	-
"	0.00425 mg/cu m	-	21/34	39/28	-	38/48	-
Room air (control)		3/69	32/78	-	4/52	-	-
"		-	-	9/56	-	67/21	0/21
"		-	14/42	16/51	-	26/51	-

* % of mice with tumors/number of mice killed
** Significantly greater than control values (P values not given)
*** In a communication of Sept 11, 1975, Weil noted there was an error and the actual metered concentration was 7,700 mg/cu m (3,130 ppm)

From reference 39

TABLE III-2

SUMMARY OF THE RESULTS* OF SUBCUTANEOUS INJECTION STUDIES IN 6 STRAINS OF MICE

Substance	Strain					
	C3H	ABC	CFW	C57	CF1	ABCT
Undiluted isopropyl oil, first plant	26/46	35/52	-	-	-	-
"	7/43	57/47**	-	4/46	-	-
"	-	32/38	-	-	-	-
"	0/29	11/28	-	-	-	-
"	-	21/38	-	-	-	-
Undiluted isopropyl oil, second plant	6/36	56/36	-	3/38	-	-
"	-	37/38	-	-	-	-
Isopropyl oil in lard distillation residue	3/36	52/40	-	3/37	-	-
"	0/27	38/34	-	3/30	-	-
"	0/21	38/40	-	0/34	-	-
Isopropyl oil in lard chromatographic sample	0/36	41/39	-	0/38	-	-
"	0/28	40/40	-	6/36	-	-
"	3/32	36/39	-	3/34	-	-
"	-	-	0/25	-	29/21	0/21
"	-	-	6/31	-	24/21	4/28
Methyl cholanthrene in lard (control)	-	-	47/19	-	67/3	57/14**
"	-	-	50/12	-	41/56	-
"	-	58/24**	-	-	-	-

TABLE III-2 (CONTINUED)

SUMMARY OF THE RESULTS* OF SUBCUTANEOUS INJECTION STUDIES IN 6 STRAINS OF MICE

Substance	Strain					
	C3H	ABC	CFW	C57	CF1	ABCT
No treatment	28/25	32/37	50/12	3/34	41/46	57/14**
"	8/40	37/59	-	11/45	-	-
"	-	26/35	-	-	-	-
"	16/25	68/39	-	0/23	-	-
"	0/29	23/30	-	-	-	-
"	-	-	22/27	-	19/16	17/30
"	-	-	37/30	-	42/31	-
Lard control	36/53	35/51	-	-	-	-
"	24/25	26/50	-	4/44	-	-
"	0/29	38/40	-	4/27	-	-
"	-	-	22/32	-	40/20	7/29
"	-	-	34/35	-	52/29	-
"	-	30/37	-	-	-	-

* % of mice with tumors/number of mice killed (see text for dosage)
** Significantly greater than control values (P values not given)

From reference 39

remaining mice were not examined, sinus tumors may have been present but overlooked.

Weil conducted a second series of experiments to determine the tumorigenic potential of isopropyl oil produced in the present weak-acid process, and to compare it with that of the isopropyl oil from the strong-acid process. Experiments were done with mice and dogs and the results were made available in a communication written on September 11, 1975.

Groups of mice consisting of approximately 40 of each strain received subcutaneous injections of isopropyl oils from each process, a mixture of oils from both processes, or isopropyl alcohol. The strains used were C3H, CFW, CF-1, dba, and A/He. The animals received 20 weekly injections of 0.025 ml each in the inguinal region. Five months after the first injection, when the animals were about 8 months old, they were killed and examined for the presence of pulmonary tumors, especially adenomas. Mice from the untreated control groups of each strain were also examined. The results are presented in Table III-3.

As indicated in Table III-3, the only significant result observed was the 48.1% lung tumor incidence produced when a mixture of isopropyl oils from both the old and the new processes was injected into mice. These results provide little information regarding the difference in the carcinogenic potentials of the isopropyl oils from the 2 processes. It is noteworthy that the incidence of tumors in the animals receiving isopropyl oil obtained from the strong-acid process was not significantly higher than that in the controls. The incidence of tumors in the control animals was extremely high, ranging from 0% in the C3H strain to 41.7% in the A/He strain.

In the skin-painting assay (CS Weil, written communication, September 1975), groups of 30 Rockland all-purpose mice were painted on their clipped backs 3 times/week for 1 year with isopropyl alcohol, isopropyl oil from the strong-acid process, isopropyl oil from the weak-acid process, or distilled water. The positive controls used were catalytically cracked petroleum oil, 0.02% dimethyl benzanthracene (DMBA), and 0.2% methyl cholanthrene (MC). The results are summarized in Table III-4.

TABLE III-3

RESULTS OF SUBCUTANEOUS INJECTIONS
IN MICE

Strain	Process	Substance	No. of Mice Killed	% Tumorous Lungs
C3H (Salk-Mars,Pa)	Strong-acid	Isopropyl oil	23	0.0
"	"	"	22	0.0
"	Weak-acid	"	30	0.0
"	"	"	31	3.2
"	Both	Isopropyl oils	29	3.4
"	"	"	32	3.1
"	-	Isopropyl alcohol	22	4.5
"	-	None	33	0.0
C3H (Rockland)	Weak-acid	Isopropyl oil	20	20.0
"	"	"	35	14.3
"	Both	Isopropyl oils	22	13.6
"	-	None	25	16.0
C3H (Jax)	Weak-acid	Isopropyl oil	37	5.4
"	"	"	42	0.0
"	Both	Isopropyl oils	41	7.3
"	-	None	33	0.0
"	Weak-acid	Isopropyl oil	37	13.5
"	"	"	36	16.7
"	-	None	39	18.0
"	Weak-acid	Isopropyl oil	25	16.0
"	"	"	28	7.1
"	"	"	26	3.8
"	-	None	24	12.5

TABLE III-3 (CONTINUED)

RESULTS OF SUBCUTANEOUS INJECTIONS
IN MICE

Strain	Process	Substance	No. of Mice Killed	% Tumorous Lungs
C3H (Jax + Texas inbred)	Weak-acid	Isopropyl oil	33	9.1
"	"	"	34	8.8
"	"	"	33	3.0
"	-	None	34	11.8
C3H (Cum)	Weak-acid	Isopropyl oil	32	9.4
"	"	"	34	17.6
"	-	None	32	6.2
CFW (Carworth)	"	Isopropyl oil	23	13.0
"	"	"	22	13.6
"	Strong-acid	"	29	24.1
"	Both	Isopropyl oils	25	28.0
"	-	None	25	12.0
CF-1 (Carworth)	Weak-acid	Isopropyl oil	24	37.5
"	"	"	22	22.7
"	Strong-acid	"	28	28.6
"	Both	Isopropyl oils	27	48.1*
"	-	None	30	20.0
"	Weak-acid	Isopropyl oil	34	11.8
"	"	"	30	13.3
"	"	"	34	14.7
"	-	None	28	21.4

TABLE III-3 (CONTINUED)

RESULTS OF SUBCUTANEOUS INJECTIONS
IN MICE

Strain	Process	Substance	No. of Mice Killed	% Tumorous Lungs
dba (Rockland)	Weak-acid	Isopropyl oil	25	16.0
"	"	"	21	19.0
"	Both	Isopropyl oils	14	21.4
"	-	None	21	23.8
dba (Jax)	Weak-acid	Isopropyl oil	36	2.8
"	"	"	40	2.5
"	Both	Isopropyl oils	37	2.7
"	-	None	38	5.3
A/He (Jax)	Weak-acid	Isopropyl oil	33	30.3
"	"	"	36	22.2
"	-	None	36	41.7
A/He (Jax)	Weak-acid	Isopropyl oil	28	28.6
"	"	"	26	38.5
"	"	"	28	35.7
"	-	None	27	25.9
A/He (Cum)	Weak-acid	Isopropyl oil	33	18.2
"	"	"	33	39.4
"	-	None	33	24.2

*P = 0.05, which was reported to be of borderline significance

From Weil (written communication, September 1975)

TABLE III-4

RESULTS OF SKIN APPLICATION
IN GROUPS OF 30 ROCKLAND ALL-PURPOSE MICE

Substance Applied	Process	Number of Mice with Tumors
Isopropyl alcohol	Strong-acid	0
Isopropyl oil	"	3 (all papillomas)
"	Weak-acid	0
Positive control (catalytically cracked petroleum oil)	-	25 (25 with papillomas, 16 with carcinomas)
Negative control (distilled water)	-	2 (all papillomas)
Isopropyl oil	Strong-acid	3 (all papillomas)
"	"	3 (all papillomas)
Positive control 0.02% DMBA	-	4 (4 with papillomas, 1 with carcinoma)
0.2% MC	-	15 (15 with papillomas, 13 with carcinomas)
Negative control (distilled water)	-	1 (1 with both carcinoma and papilloma)

From Weil (written communication, September 1975)

As indicated in Table III-4, isopropyl alcohol from the strong-acid process and isopropyl oil from the weak-acid process produced no tumors in mice. There was no significant difference between the number of mice with tumors in the groups painted with distilled water or with isopropyl oil obtained from the strong-acid process. In all cases, the positive control animals developed a high tumor incidence. These experiments also failed to bring out the difference between the carcinogenic potentials of the 2 oils in question. In these experiments, isopropyl oil from the strong-acid process failed to produce a significant number of tumors when compared to controls. In all cases, the incidence of tumors in the negative control animals was comparable to that observed in the experimental animals.

In order to determine whether sinus tumors can develop in dogs, 4 groups of 5 mongrel dogs were exposed to aerosols of isopropyl oil obtained from the strong-acid process (CS Weil, written communication, September 1975). The dogs received weekly inhalation exposures for 2 years and then were rested for 14 months. Subsequently, they were exposed every third week for the next 2 years. Another group of 4 dogs received direct sinus instillations of strong acid-produced isopropyl oil, once a month for 48 months. The approximate ages at death ranged from 9 to 12.25 years. X-rays were taken at frequent intervals and were negative. At autopsy, several dogs had tumors that were judged not to be uncommon. No sinus tumors were detected but the incidence of benign thyroid adenomas was found to be increased.

In summary, although the epidemiologic evidence [39] suggests that a carcinogen was present in the strong-acid process, animal experiments (CS

Weil, written communication, September 1975) present little evidence of carcinogenicity of the oils from either the new or the old processes. However, the results do raise a new problem. Isopropyl oil from the old, strong-acid process did not consistently produce a significant number of tumors in the subcutaneous injection assay, in the skin-painting assay, or in the sinus instillation experiment. Therefore, the animal studies are inadequate for determining the identity of the carcinogen in either of the processes. However, there is no evidence that isopropyl alcohol is a carcinogen. Inconclusive results from the animal studies might be associated with the nature of the chemicals being tested, the unusually high tumor incidence in the control animals, or the use of animals that might not be appropriate models for tumorigenic studies. Thus, whether the hazard is present or eliminated in the newer weak-acid process remains unknown.

No evidence of teratogenicity of isopropyl alcohol was found in the literature. McLaughlin et al [75] observed that isopropyl alcohol did not produce teratogenic effects when injected into chicken eggs. However, Walker [76] stated that different modes of administration for the test substance in chicken eggs altered the results and he did not consider chicken egg experiments reliable. In order to ascertain the effect of isopropyl alcohol on reproduction and growth, Lehman et al [49] gave 2.5% isopropyl alcohol in drinking water to 6 female and 3 male rats. The rats were 38-40 days old at the start of the experiment and were mated when they were 120 days old. This was repeated through 2 generations. Forty-four young in the first generation and 66 in the second were produced. Comparison of growth curves showed that 2.5% isopropyl alcohol in drinking

water retarded the very early growth in the first generation. Literature on the mutagenic effects of isopropyl alcohol has not been found.

Correlation of Exposure and Effect

Very few of the reports discussed are germane to the subject of occupational exposure to isopropyl alcohol. The reports in which exposure levels are well documented and established involve primarily routes of administration other than inhalation and skin absorption. [7, 48,50,57] There is only one reported study [39] on the effects on humans of long-term exposures to isopropyl alcohol alone.

A report [34] was found that related the effects of isopropyl alcohol inhalation in humans to the airborne levels. In 1943, Nelson et al [34] exposed 10 human subjects in a chamber to isopropyl alcohol at various concentrations for 3-5 minutes. Exposure to isopropyl alcohol at 400 ppm and 800 ppm caused irritation of eyes, throat, and nose. The subjects believed they would prefer to work for 8 hours in an atmosphere containing 200 ppm or less of isopropyl alcohol. In 1974, Baikov [47] studied the effects of inhalation of isopropyl alcohol in animals but the interpretation of the observed biologic changes is difficult, because experimental design and analysis of data were not described in sufficient detail to allow evaluation of the conclusions. No conclusive comments can be made from the results of the above inhalation studies [34,47] with respect to short-term and long-term effects of the inhalation of isopropyl alcohol.

Marzulli and Ruggles [55] reported that 0.1 ml of 70% isopropyl alcohol caused some conjunctival redness, corneal opacity, and iritis in

rabbits. These effects were temporary, but isopropyl alcohol can be classified as a moderate eye irritant. Acute effects of oral doses of isopropyl alcohol (0.32 ml/kg and 0.14-0.21 ml/kg) include drowsiness, headache, and lowering of blood pressure in man. [7] Several investigators have found that narcosis is a prominent effect of isopropyl alcohol intoxication. [7,8] In 1969, Wills et al [31] reported that low levels of isopropyl alcohol did not cause liver damage in humans.

Weil et al [39] conducted an epidemiologic study which indicated that a carcinogen was present in the isopropyl alcohol-manufacturing process using the strong-acid process. Animal experiments failed to establish or confirm the identity of a carcinogen.

IV. ENVIRONMENTAL DATA

Sampling and Analytical Methods

There are many general methods of sampling and analysis for alcohols. Many of these methods were found to be suitable for related alcohols or other organic vapors and can be adopted for isopropyl alcohol.

Sampling with plastic bags [77-80] or glass bottles [81] involves obtaining a definite volume of the environmental air at a known temperature and pressure. This type of "grab" sample is collected over a very short time, from a few seconds to a maximum of 2 minutes. Thus, sampling techniques involving the use of these collection devices are best suited for information on ceiling concentrations. However, the transportation of the collected samples is often inconvenient due to the bulkiness of the containers. [78] Reports on the use of plastic bags and glass bottles specifically for sampling isopropyl alcohol have not been found in the literature.

Another type of collection device involves the passage of a known volume of air through an absorbing or adsorbing medium to collect the isopropyl alcohol. [82-86] With such devices, samples can be collected over recorded periods of time and the resultant data analyzed to calculate the TWA concentration. Impingers and bubblers can be used to collect isopropyl alcohol vapors in water by sampling at a known rate for a specified period of time. U-shaped glass tubes containing water have been used to collect isopropyl alcohol vapors. [86] Efficiency data have not been found, but, in order to maintain a high efficiency, it is often necessary to use more than one impinger, bubbler, or U-tube in series. The

main disadvantage of such a sampling system is that it is not convenient for obtaining a breathing zone sample. Since the collection medium is liquid, some loss of the sample can occur due to spillage.

Of the various techniques, adsorption offers the greatest ease of collection. Activated charcoal [84,85] and silica gel [33,82,83] are common adsorbents. Hahn [33] collected 720 mg of isopropyl alcohol on approximately 23 g of purified, dry silica gel. Liquid isopropyl alcohol was pulled by a water jet pump into silica gel in a glass tube 26.5 cm long and 3.0 cm in diameter. A second tube of the same size was connected in series with the first one to determine the amount of isopropyl alcohol adsorbed. The alcohol was then desorbed by passing steam through the tubes and condensing it in a large coil cooler. The second tube yielded no isopropyl alcohol and so the author concluded that 23 g of silica gel was sufficient to adsorb 720 mg of isopropyl alcohol. Analysis revealed that the efficiency of yield was 97-99%. The amount of silica gel and the size of the glass tubes required are large. Hence, this technique may not be suitable for taking personal samples in breathing zones of employees. Details, such as specificity, sensitivity, and precision, were not recorded. Silica gel has a greater tendency to adsorb moisture than does charcoal and therefore functions best in dry environments. However, the necessity still exists for a sampling technique convenient for industrial environments, which are seldom dry.

Collection on charcoal is suitable for taking breathing zone samples and convenient because of the short sampling time required. Transporation of samples is also convenient because of the small size of the containers. The chief advantage of the charcoal tube is that it is a small, portable

sampling device that contains no liquid. The disadvantage is that the amount of sample which can be taken is limited by the weight of the sample that the tube will hold before overloading occurs. When the amount of sample obtained for the backup section of the charcoal trap exceeds 25% of that found in the front section, the possibility of sample loss exists. Also, during storage of the sample, the more volatile compounds will migrate throughout the charcoal tube until steady state is reached. [87]

The precision of the charcoal tube method is limited by the reproducibility of the pressure drop across the charcoal tubes. Because the pump is usually calibrated only for a single tube, this drop will affect the flowrate and cause the volume to be imprecise. The other disadvantage is that isopropyl alcohol tends to be displaced from charcoal by a large amount of less polar organic vapors. [87]

Despite the limitations of the charcoal tube, it is the method of choice. Details concerning its use are presented in Appendix I. Because the charcoal tube collects a large number of organic vapors, the use of a specific analytical method is mandatory.

The choice of an appropriate analytical method depends largely on the collection technique. If the sample is in a water solution, as in the case of impingers and bubblers, colorimetric analysis [86,88] and the Knipping-Ponndorf method [89] are suitable. These methods are also suitable for samples collected on silica gel. Isopropyl alcohol is desorbed by passing steam through the gel and condensing the steam. In one of the colorimetric analyses, [88] isopropyl alcohol is oxidized by a measured quantity of potassium dichromate in the presence of concentrated sulfuric acid. Excess dichromate is determined by further reaction with s-diphenylcarbazide to

form a colored complex. The concentration of the complex can then be measured with a spectrophotometer. The concentration of the isopropyl alcohol can be calculated from the amount of dichromate used up in the oxidation. The major drawback is that interference can be caused by a large number of oxidizable substances, including other alcohols and some metallic ions.

In another colorimetric technique, [86] 2 ml of 10% potassium persulfate is added to 2 ml of water containing isopropyl alcohol. The mixture is maintained at 50-54 C in a water bath for 30 minutes and then cooled. To this, 0.2 ml of 1% potassium persulfate is added and the mixture is again maintained at 50-54 C for 30 minutes. It is then cooled to room temperature. To this mixture, 0.2 ml of 5% bisulfite solution is added, the resulting solution is mixed, and 2 ml of 40% sodium hydroxide solution added, followed by 0.2 ml of 20% solution of salicylic aldehyde in ethyl alcohol. The total mixture is shaken, heated and maintained at 80 C for 15-20 minutes, and cooled. A bright yellow-orange complex is formed and the absorption determined colorimetrically. Acetone was found to interfere while other primary alcohols did not. The sensitivity was reported to be 0.002 mg in 2 ml of water.

In the Knipping-Ponndorf method, [89] isopropyl nitrite, formed by reaction with sodium nitrite, is removed with carbon tetrachloride. Nitrous acid is then liberated from isopropyl nitrite by reaction with sulfuric acid, a known excess of potassium permanganate, and manganous sulfate solution. The unreacted potassium permanganate liberates iodine from potassium iodide. The iodine is then titrated with sodium thiosulfate solution. The amount of isopropyl alcohol can then be calculated from the

amount of sodium thiosulfate used. Data on the specificity, accuracy, precision, and sensitivity of either of these methods have not been found in the literature.

Other analytical methods that may be used are infrared spectroscopy and gas chromatography. These methods are especially useful when the samples are collected on charcoal or silica gel. However, infrared analysis is a qualitative rather than a quantitative technique. [90] Gas chromatography offers the greatest specificity and sensitivity and is suitable for analyzing grab samples and samples collected on charcoal. The advantage is that interferences are minimal. If they do occur, they can generally be eliminated by altering the instrumental conditions. [87] The retention time of isopropyl alcohol in a carbowax-chromosorb column is reported to be 12.8 minutes, while for an amine-carbowax-Teflon column it was 9.8 minutes. [91] A detection limit of 2 ppm has been reported for a 4-ft long chromosorb column at 94 C. [92] Gas chromatography can also be used for the simultaneous analysis of 2 or more solvents suspected to be present in the same sample by converting from an isothermal to a temperature-programmed mode of operation. Details of this method are given in Appendix II.

Detector tubes are used frequently for a quick, direct detection of the isopropyl alcohol concentration in air. [93] However, the British Occupational Hygiene Society considers the detector tubes as unreliable and does not recommend them. [93] Information on the accuracy and precision of detector tubes has not been found in the literature. They have been shown to measure total alcohol concentrations ranging from 100 to 3,000 ppm. [94] These tubes may be useful for detecting leaks in closed systems and testing

for the presence of isopropyl alcohol vapor in confined spaces. They may also be used to make a rough estimate of the air concentration of isopropyl alcohol. Based on this estimate, decisions on what volume of air to sample can be made.

The charcoal tube-gas chromatographic method is the method of choice, and details are given in Appendices I and II. Other sampling and analytical methods equivalent in accuracy, precision, and sensitivity may be used.

Engineering Controls

A major use of isopropyl alcohol is as a solvent in operations that may involve spraying, surface coating, pouring, mixing, and oven-drying (Stanford Research Institute, written communication, February 1975). Most of these operations are open to the air, and isopropyl alcohol vapor may be released into the atmosphere. The principles set forth in Industrial Ventilation - A Manual of Recommended Practices, published by the American Conference of Governmental Industrial Hygienists Committee on Industrial Ventilation, [95] and Fundamentals Governing the Design and Operation of Local Exhaust Systems, Z9.2-1971, [96] published by the American National Standards Institute, should be applied to control atmospheric concentrations of isopropyl alcohol. Application of surface coatings such as shellacs, lacquers, or varnishes can produce high atmospheric levels of solvent vapor. In enclosed areas, the concentrations can exceed the lower explosive limit, particularly if application is by spraying. [97] Such operations should always be ventilated by portable blowers and correctly positioned portable ducts. As far as possible, the alcohol vapors should

be controlled at the source rather than by general ventilation. Operations involving the use of isopropyl alcohol at an elevated temperature, such as drying, evaporation, etc, may require special attention in the placement of local ventilation controls. Such controls must be explosion-proof (Stanford Research Institute, written communication, February 1975). Since other substances are present where isopropyl alcohol is used, special care must be taken to make sure that substances that form explosive mixtures are not vented into the same system.

Closed systems using isopropyl alcohol are more successful in controlling isopropyl alcohol vapor in air. However, frequent tests should be conducted for leaks. Based on the data obtained during field visits, the major isopropyl alcohol-manufacturing processes in the US are currently closed processes (Stanford Research Institute, written communication, February 1975).

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The present federal standard (29 CFR 1910.1000) for isopropyl alcohol exposure is an 8-hour TWA of 400 ppm. It was based on the recommendation first made in 1959 by the American Conference of Governmental Industrial Hygienists (ACGIH). [98] The ACGIH based this recommendation on the human experiment reported in 1943 by Nelson et al [34] who found that at 400 ppm, isopropyl alcohol caused mild irritation of the eyes, nose, and throat. A concentration of 200 ppm or less was estimated by the exposed subjects to be most suitable for an 8-hour exposure period. The results of this very simple and subjective study have been widely adopted as a basis for isopropyl alcohol standards.

In 1945, Cook [99] reviewed a list of maximum allowable concentrations of various contaminants recommended by the US Public Health Service and the American Standards Association. A value of 400 ppm for isopropyl alcohol was referred to as an "accepted and tentative" value. Altman and Dittmer [100] indicated that, in 1962, the US Navy established 400 ppm as the maximum acceptable concentration in a submarine. In 1961, the Hygienic Guides Committee of the American Industrial Hygiene Association [101] also accepted a minimum concentration of 400 ppm of isopropyl alcohol for a TWA concentration for a normal workday.

Documents on standards established in other countries were not found in the literature. Elkins (written communication, August 1975) reported

that the MAC for isopropyl alcohol in Czechoslovakia is 205 ppm and the USSR limit is 80 ppm. Reports on the basis for these standards have not been found.

Basis for the Recommended Environmental Standard

It is evident from the chapter on Biologic Effects of Exposure that there are few toxicologic data over wide exposure ranges suitable for establishing a standard for isopropyl alcohol in the occupational environment. For example, in one study [45] four out of 6 rats inhaling isopropyl alcohol at 16,000 ppm for 8 hours died within 14 days. In another study [47] no adverse effects were observed in men ingesting daily doses of 2.6 mg/kg and 6.4 mg/kg for 6 weeks. Irritation of the eyes, nose, and throat occurred in people inhaling isopropyl alcohol at 400 and 800 ppm for 3-5 minutes. [34] Thus, a TWA of 400 ppm for 8-hour exposure periods accompanied by a ceiling value of 800 ppm has been recommended on the following basis. The present Occupational Safety and Health regulation classifies isopropyl alcohol as a flammable liquid of Class IB in 29 CFR 1910.106(a)(19)(ii). The lower explosive limit of isopropyl alcohol is 2% by volume or 20,000 ppm. Since an accepted margin of safety for fire and explosion protection is 10 (29 CFR 1917.11(a)(2) and 29 CFR 1915.11(a)(2)), a level of isopropyl alcohol below 2,000 ppm would make the atmosphere safe from fire hazard. However, mild irritation of eyes, nose, and throat has been reported at levels of isopropyl alcohol at about 400 ppm, and even at 800 ppm, these effects were not severe. [34] While it is recognized that the report by Nelson et al [34] is inadequate as the sole basis for a standard, it is only used to substantiate the need for a workplace exposure

limit where minimal irritation occurs. A TWA of 400 ppm is therefore recommended with a ceiling level of 800 ppm at which minimal irritation occurs.

Special medical surveillance, including preplacement and annual physical examinations, is recommended for employees engaged in isopropyl alcohol manufacture. An epidemiologic investigation by Weil et al [39] established that a carcinogen was present in the original isopropyl alcohol-manufacturing process. The present manufacturing process differs from the one examined by Weil et al [39] in that dilute, rather than concentrated, sulfuric acid is used, the reaction conditions are different, and the resulting oils differ in composition. It cannot be assumed that these changes in the 2 processes have been sufficient to eliminate the carcinogen. However, no other epidemiologic study has been reported in the new process. Therefore, special medical surveillance, engineering controls, and work practices have been recommended for employees working in isopropyl alcohol-manufacturing plants. Because of the suspected presence of a carcinogen, it is recommended that records of medical and environmental data be kept for 30 years.

Use of respirators as a means of control is not recommended. Respirators must be used only when both the engineering and the administrative controls are inadequate to protect the employee from isopropyl alcohol exposure. Table I-1 lists the types of respirators that should be used at various concentrations of isopropyl alcohol. Because there is a distinct odor of isopropyl alcohol at both the recommended action level and the TWA, [35,36] employees should change the cartridge or the canister immediately after detecting the odor of isopropyl alcohol.

However, the maximal service life for an organic vapor cartridge is 40 minutes at 1,000 ppm; for a full facepiece with chin-style canister, it is 10 minutes at 5,000 ppm; and for a full facepiece with front- or back-mounted chest-type canister, it is 10 minutes at 20,000 ppm. [102,103] An air-purifying respirator is not recommended for entry into areas where the concentration of the vapor exceeds the lower explosive limit. Self-contained breathing apparatus must be used in such atmospheres.

Sampling and analytical methods described in Appendices I and II have been tested by NIOSH and found suitable for monitoring isopropyl alcohol. [87]

It is recognized that many employees handle small amounts of isopropyl alcohol. Under these conditions, it is not necessary to comply with all provisions of the recommended standard. However, concern for employee health requires that protective measures be instituted below the enforceable limit to ensure that exposures stay below that limit. Therefore, environmental monitoring and recordkeeping are recommended for those work situations which involve exposure above 200 ppm. Occupational exposure is hence defined as exposure to isopropyl alcohol at or above the action level of 200 ppm.

VI. WORK PRACTICES

Work practices and safety precautions for handling isopropyl alcohol are the subject of numerous reports. [1,104-108] Reports of work practices designed for the prevention of isopropyl alcohol exposure are not available. In general, good engineering controls should be used to control continuous low-level exposures and to minimize excursions.

The flash point (closed cup) of isopropyl alcohol is 53 F (11.6 C). It is therefore classified as a flammable liquid of Class IB in 29 CFR 1910.106(a)(19)(ii). The lower and upper explosive limits in air at 20 C are 2.0% (20,000 ppm) and 12.0% (120,000 ppm) by volume. [2,104] The Bureau of Explosives classifies isopropyl alcohol as an "inflammable liquid." [107] The Manufacturing Chemists Association cautions that isopropyl alcohol vapors mixed with air at ordinary temperatures are explosive within certain limits. [1] Hence, fire and explosion are the principal safety hazards of isopropyl alcohol. Engineering controls should prevent the accumulation of explosive concentrations of isopropyl alcohol in the air. Such control equipment must be sparkproof. Recommended work practices are intended to ensure that no flames or other sources of ignition, such as smoking, be permitted in the area where isopropyl alcohol is stored or handled. Since the accepted margin of safety for flammable substances is a factor of 10 (29 CFR 1917.11(a)(2) and 29 CFR 1915.11(a)(2)) precautions against the fire and explosion hazards must be taken whenever isopropyl alcohol vapor may accumulate and exceed 10% of the lower explosive limit (2,000 ppm). Special precautions are necessary for entering a vessel which may contain isopropyl alcohol [105,109] and for

flame- and spark-generating operations, such as welding, cutting, and transferring the alcohol. [1,104] Moreover, smoking must also be prohibited.

Since the presence of a carcinogen is suspected in the isopropyl alcohol-manufacturing area, [39] and since the identity of the carcinogen is not known, it is necessary to protect the employees from all agents in this area. Routine checks must be done to ensure that the process is completely enclosed. If leaks occur, these must be promptly corrected, regardless of the isopropyl alcohol concentration in the environment. If employees must withdraw samples from the process, an impervious suit including gloves, boots, and air-supplied hood must be worn. Any waste or residues produced in the isopropyl alcohol-manufacturing area shall be collected in an impervious container with an appropriate label and incinerated properly so that no carcinogenic products are released in the air.

Isopropyl alcohol is a moderate eye irritant. [55] In view of this, use of personal protective equipment, such as safety glasses or goggles, is recommended when isopropyl alcohol contact with the eyes is likely. Isopropyl alcohol is usually not a skin irritant, as is obvious from its extensive use as rubbing alcohol. Protective clothing is normally not required for operations involving the use of isopropyl alcohol. If an employee's clothes become contaminated with isopropyl alcohol, a change of clothing shall be made available as a good hygiene practice. Although it is not required, it has been observed that some employers do provide fire-retardant clothing to employees (Stanford Research Institute, written communication, February 1975).

Safety showers, eyewash fountains, and fire extinguishers shall be located in or near areas where isopropyl alcohol splashes are likely to occur and shall be properly maintained.

Handwashing facilities, soap, and water must be available to the employees. As a good hygiene practice, it is recommended that any spills on the body be promptly washed, and that employees wash their hands before eating.

In summary, precautions must be exercised against the fire hazard of isopropyl alcohol. It is also important that employees be informed before job placement of hazards associated with the use of isopropyl alcohol and when any changes are made in the process that may alter their isopropyl alcohol exposure. Appropriate emergency procedures should be stressed. Recommended labels and posters must be displayed. The US Department of Labor "Material Safety Data Sheet," or a similar OSHA-approved form, must be filled out. In addition, all employees in the isopropyl alcohol area should know where the safety sheet is posted. If all of these work practices are observed and good engineering controls are installed, employees working with isopropyl alcohol should be adequately protected from overexposure, fire, explosion, and other hazards associated with isopropyl alcohol.

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VIII. APPENDIX I

METHOD FOR SAMPLING ISOPROPYL ALCOHOL IN AIR

The sampling and analytical methods presented in Appendices I and II are based on that described in the Method No. S65 of the Physical and Chemical Analysis Branch of NIOSH. [87]

General Requirements

Isopropyl alcohol concentrations shall be determined within the employee's breathing zone and shall meet the following criteria in order to evaluate conformance with the standard:

(a) Samples collected shall be representative of the individual employee's exposure.

(b) Sampling data sheets shall include:

(1) The date and time of sample collection.

(2) Sampling duration.

(3) Volumetric flowrate of sampling.

(4) A description of the sampling location.

(5) Other pertinent information such as temperature and pressure.

Recommended Method

The following method of sampling is recommended. If other methods can be proved to be equivalent, they may be used.

(a) Personal samples shall be collected in the breathing zone of the employee without interfering with his freedom of movement and shall characterize the exposure from each job or specific operation in each production area.

(b) A portable, battery-operated personal sampling pump whose flow can be accurately controlled to within 15% at 200 ml/minute, and an activated charcoal tube should be used to collect the samples.

(c) The activated charcoal tube should be attached to the employee. The shirt collar is convenient for this purpose.

(d) The sampler shall be operated at a flowrate of 0.20 liter/minute or less. It should be noted that some pumps are designed for high flowrates and some for low. Care should be taken to use the proper pump with proper flowrate, eg, up to 200 ml/minute flow range.

(e) Breathing zone samples shall be collected to permit calculation of a ceiling exposure for every operation involving exposure to isopropyl alcohol.

(f) At least one unused activated charcoal tube from the same batch shall be provided to the analytical laboratory to determine the blank correction.

Equipment for Air Sampling

(a) Battery-operated personal sampling pump: It should have a clip for attachment to the employee. All pumps and flow meters must be calibrated using a calibrated test meter or other reference, as described in the section of this appendix entitled Calibration of Equipment.

(b) Charcoal tubes: Glass tubes with both ends flame-sealed, 7 cm long with a 6-mm outer diameter and a 4-mm internal diameter, containing 2 sections of 20/40 mesh activated coconut-shell charcoal separated by a 2-mm portion of polyurethane foam. The adsorbing section contains 100 mg of charcoal, the backup section 50 mg. A 3-mm portion of the polyurethane foam is placed between the outlet end of the tube and backup section. A plug of silylated glass wool is placed in front of the adsorbing section.

Calibration of Equipment

Since the accuracy of an analysis can be no greater than the accuracy with which the volume of air is measured, the accurate calibration of a sampling pump is essential to the correct interpretation of the volume indicated. The frequency of calibration is dependent upon 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, it should be calibrated more frequently if necessary. Regardless of use, 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 upon where the calibration is to be performed. For laboratory testing, standards such as a spirometer or soapbubble meter are recommended, although other standard calibration instruments such as a wet test meter or dry gas meter can be used. The actual setups will be similar for all instruments.

The calibration setup for personal sampling pumps with a charcoal tube is as shown in Figure XII-1. If another calibration device is selected, equivalent procedure should be used. Since the flowrate given by a pump is dependent on the pressure drop of the sampling device, in this case a charcoal tube, the pump must be calibrated while operating with a representative charcoal tube in line. Instructions for calibration with the soapbubble meter are as follows:

(a) The voltage of the pump battery is checked with a voltmeter to ensure adequate voltage for calibration. The battery is charged if necessary.

(b) The tips of a charcoal tube are broken to produce openings of at least 2 mm in diameter.

(c) The sampling train is assembled as shown in Figure XII-1.

(d) The pump is turned on and the inside of the soapbubble meter is moistened by immersing the buret into the soap solution and drawing bubbles up the inside until they are able to travel the entire length of the buret without bursting.

(e) The pump flow controller is adjusted to provide the desired flowrate.

(f) The water manometer is checked to ensure that the pressure drop across the sampling train does not exceed 2.5 inches of water at 200 ml/min.

(g) A soapbubble is started up the buret and the time it takes the bubble to move from one calibration mark to another is measured with a stopwatch.

(h) The procedure in (g) is repeated at least twice, the results averaged, and the flowrate calculated 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 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 2 preselected marks divided by the number of strokes.

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

Collection of Samples

(a) Both ends of the charcoal tube are broken to provide openings of at least 2 mm, which is 1/2 of the internal diameter of the tube. A smaller opening causes a limiting orifice effect which reduces the flow through the tube.

(b) The smaller section of charcoal in the tube is used as a

backup section and should therefore be placed nearest the sampling pump. Tubing may be used to connect the back of the tube to the pump, but no tubing must ever be put in front of the charcoal tube. The tube shall be supported in a vertical position for sampling to prevent channeling. After the sample is collected, the tube must be capped; caps are provided with commercially available tubes.

(c) The recommended sampling flowrate is 0.20 liter/minute or less. A 3-liter sample is normally adequate. The calibrated flowrate should be set as accurately as possible using the manufacturer's directions. The temperature and pressure of the atmosphere being sampled must be recorded.

(d) The initial and final counter readings must be recorded. The sample volume can be obtained by multiplying the number of counter strokes times the volume cc/stroke factor.

(e) Immediately after sampling, the charcoal tubes should be capped with the plastic caps supplied by the manufacturer. Masking tape is the only suitable substitute for sealing the tubes. Rubber caps must never be used.

(f) One charcoal tube should be treated in the same manner as the sample tubes (break, seal, ship), except that no air is drawn through it. This tube will serve as a blank.

Special Consideration

(a) Where 2 or more compounds are known or suspected to be present in the air, such information, including their suspected identities, should

be conveyed with the sample.

(b) Pump must not be operated for more than 8 hours without recharging the battery.

(c) If high humidity or water mist is present, breakthrough volume can be severely reduced. If condensation of water occurs in the tube, isopropyl alcohol will not be trapped quantitatively. Therefore, in high humidity, the volume sampled should be reduced.

(d) The desorption efficiency of charcoal varies from batch to batch. Therefore, all the tubes used to collect a set of samples must contain charcoal from the same batch. Several unused charcoal tubes should accompany the samples. Information on the batch number of the charcoal must be supplied.

Shipping of Samples

Capped charcoal tubes should be packed tightly and padded before they are shipped to minimize tube breakage during shipping. Bulk samples must be submitted in addition to charcoal tubes. Bulk samples and charcoal tubes must be shipped in separate containers.

IX. APPENDIX II

ANALYTICAL METHOD FOR ISOPROPYL ALCOHOL

Principle of the Method

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

(b) The charcoal in the tube is transferred to a small, graduated test tube and desorbed with carbon disulfide containing 1% 2-butanol.

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

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

Range and Sensitivity

(a) This method has been validated over the range of 505-1,890 mg/cu m (206-769 ppm) in a test-atmosphere at a temperature of 25 C and pressure of 747 mmHg, using a 3.0-liter air sample. [87] With a sample size of 3.0 liters, the probable range of this method is 100-2,500 mg/cu m (approximately 40-1,000 ppm) at detector sensitivity that gives nearly full deflection on a strip chart recorder for a 6.0-mg aliquot. The method is capable of measuring much smaller amounts, such as 10 ppm, if the desorption efficiency is adequate. Desorption efficiency must be determined over the range used.

(b) The upper limit of the range of the method is dependent on the adsorptive capacity of the charcoal tube. This capacity varies with the

concentrations of isopropyl alcohol and other substances in the air.

Interferences

(a) When the amount of water in the air is so great that condensation actually occurs in the tube, organic vapors will not be trapped. Preliminary experiments indicate that high humidity severely decreases the amount of organic vapor which can be collected before breakthrough of the primary adsorbing section occurs. Therefore, in case of high humidity, a low volume of air must be sampled. The capacity of the charcoal tube for adsorption of isopropyl alcohol may also be reduced by the presence of another organic vapor in high concentration.

(b) Any compound which has about the same retention time as that of isopropyl alcohol at the gas chromatographic conditions described in this method will interfere with the analysis. This type of inteference can be overcome by changing the operating conditions of the instrument, usually the column and/or the column temperature.

Precision and Accuracy

(a) The precision and accuracy values for the analysis of isopropyl alcohol vary from one laboratory to another and from one set of equipment to another.

(b) A desorption efficiency of 96.7% from 1 lot of coconut shell charcoal has been reported. If any other type of charcoal is used, the desorption efficiency must be determined.

Apparatus

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

(b) Column (10 ft x 1/8 inch) with 10% FFAP stationary phase on 80/100 mesh, acid-washed DMCS Chromosorb W solid support. Other columns such as K-20M carbowax capable of performing the required separations may be used.

(c) A mechanical or electronic integrator or a recorder and some other method for determining the peak area.

(d) Glass glass-stoppered test tubes or the equivalent.

(e) Microsyringes: 10 μl and other convenient sizes for making standards.

(f) Volumetric flasks: convenient sizes for making standards.

(g) Pipets.

Reagents

(a) Carbon disulfide, containing 1% 2-butanol, reagent grade.

(b) Isopropyl alcohol.

(c) Internal standard n-Undecane (99+%) or other suitable standard.

(d) Purified nitrogen.

(e) Purified hydrogen.

(f) Filtered compressed air.

Analytical Procedure

(a) Cleaning of equipment

All glassware used for laboratory analysis should be washed in detergent followed by tap and distilled water rinses.

(b) Analysis of samples

(1) Preparation of samples: Each charcoal tube, including the blank from field samples, is scored with a file in front of the first section of charcoal and broken open. The glass wool is removed and discarded. The charcoal in the first (larger) section is transferred to a small stoppered test tube. The separating section of foam is removed and discarded; the second section is transferred to another test tube. These 2 sections are analyzed separately.

(2) Desorption of samples: Prior to analysis, 1.0 ml of carbon disulfide is pipetted into each test tube to desorb the isopropyl alcohol from the charcoal. For the internal standard method, a 0.5% solution of internal standard in carbon disulfide is used.

> 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.

Tests indicate that desorption is complete in 30 minutes if the sample is stirred occasionally during this period. The use of graduated glass-stoppered, microcentrifuge tubes is recommended so that any apparent change in volume during the desorption process can be observed.

(3) Gas chromatographic conditions: The typical operating conditions for the gas chromatograph are:

(A) 30 cc/min (80 psig) nitrogen carrier gas flow.

(B) 30 cc/min (50 psig) hydrogen gas flow to detector.

(C) 300 cc/min (50 psig) airflow detector.

(D) 200 C injector temperature.

(E) 300 C manifold temperature (detector).

(F) 70 C column temperature.

(G) Isothermal oven, unless temperature programming is necessary to separate interfering substances.

(4) Injection: The first step in the analysis is the injection of the sample into the gas chromatograph. The solvent flush injection technique is employed. This eliminates difficulties arising from blowback or distillation within the syringe needle, thus increasing the accuracy and reproducibility of the injected sample volume. The 10.0 μl-syringe is first flushed with solvent several times to wet the barrel and plunger, then 3.0 μl of solvent are drawn into the syringe. Next, the needle is removed from the solvent and the plunger is pulled back about 0.2 μl to separate the solvent flush from the sample with an air pocket to be used as a marker. The needle is then immersed in the sample and a 5.0-μl aliquot is withdrawn, taking into consideration the volume of the needle, since the sample in the needle will be completely injected. After the needle is removed from the sample and prior to injection in the gas chromatograph, the plunger is pulled back a short distance to minimize sample evaporation from the needle tip. Duplicate injections should be made of each sample and of the standard. No more than a 3% difference should result in the peak areas that are recorded.

Calibration and Standards

It is convenient to express the concentration of the standards in terms of mg/ml of eluent. A series of standards of various concentrations over the range of interest is prepared and analyzed under the same gas chromatographic conditions and during the same time period as the unknown samples. Standard curves are established by plotting concentration in mg/ml carbon disulfide versus the ratio of peak area of isopropyl alcohol to peak area of the internal standard.

Determination of Adsorption and Desorption Efficiencies

This section describes a method for determining adsorption and desorption efficiencies. It must be kept in mind that the desorption efficiency is a function of the amount of isopropyl alcohol for each sample, and that it is not constant for isopropyl alcohol. Hence, if possible, the measured concentration of isopropyl alcohol used should be similar to the concentration expected in the test situation. Unused charcoal tubes from the same batch as that used in obtaining samples in the work area are to be used in this determination. A measured volume of isopropyl alcohol is injected into a bag containing a known volume of air. The bag, made of a material that will not absorb the alcohol, should have a gas sampling valve and a septum injection port. The concentration of isopropyl alcohol in the bag may be calculated, if the temperature and pressure in the bag are known. A measured volume is then drawn through a charcoal tube. At least 5 tubes are prepared in this manner. Desorption and analysis are done in the same manner as the sample. Samples taken with

a syringe from the bag are also injected into the gas chromatograph to confirm the actual concentration in the bag.

$$\frac{\text{Quantity of isopropyl alcohol desorbed from charcoal}}{\text{concentration of isopropyl alcohol in bag}} \times \frac{100}{\text{volume of air drawn through tube}} = \% \text{ Efficiency}$$

Calculations

(a) The weight in mg of isopropyl alcohol, corresponding to each peak area, is read from the standard curve. No volume corrections are needed, because the standard curve is also based on a mg/ml eluent and the volume of sample injected is identical to the volume of the standards injected.

(b) Corrections for the blank must be made for each sample. The weight of isopropyl alcohol determined for the front section of the blank tube is subtracted from the weight determined for the front section of the sample tube. A similar procedure is followed for the back section.

(c) The corrected amounts present in the front and back sections of the same sample tube are added to determine the total measured amount in the sample.

(d) This total weight is divided by the determined desorption efficiency to obtain the total weight of isopropyl alcohol in mg that was present in the air volume sampled.

(e) Milligrams/cubic meter are converted into parts per million by volume of isopropyl alcohol in the air sampled assuming isopropyl alcohol is an ideal gas, using the following equation:

$$\text{number of parts/million} = \frac{\text{number of mg}}{\text{cu m}} \times \frac{24{,}450}{MW} \times \frac{760}{P} \times \frac{T + 273}{298}$$

where:

P = pressure (mmHg) of air sampled

T = temperature (C) of air sampled

MW = molecular weight (g/mole) of isopropyl alcohol

24,450 = molar volume (ml/mole) at 25 C and 760 mmHg

760 = standard pressure (mmHg)

298 = standard temperature (K)

X. APPENDIX III

MATERIAL SAFETY DATA SHEET

The following items of information which are applicable to a specific product or material shall be provided in the appropriate block of the Material Safety Data Sheet (MSDS).

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

(a) Section I. Product Identification

The manufacturer's name, address, and regular and emergency telephone numbers (including area code) are inserted in the appropriate blocks of Section I. The company listed should be a source of detailed backup information on the hazards of the material(s) covered by the MSDS. The listing of suppliers or wholesale distributors is discouraged. The trade name should be the product designation or common name associated with the material. The synonyms are those commonly used for the product, especially formal chemical nomenclature. Every known chemical designation or

competitor's trade name need not be listed.

(b) Section II. Hazardous Ingredients

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

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

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

Toxic hazard data shall be stated in terms of concentration, mode of exposure or test, and animal used, ie, "6.8 ml/kg LD50-oral-rat," "16.4 ml/kg LD50-skin-rabbit," or "permissible exposure from 29 CFR 1910.93," or if not available, from other sources of publications such as the American Conference of Governmental Industrial Hygienists or the American National Standards Institute Inc. Flammable or reactive data could be flash point,

shock sensitivity, or other brief data indicating nature of the hazard.

(c) Section III. Physical Data

The data in Section III should be for the total mixture and should include the boiling point and melting point in degrees Fahrenheit (Celsius in parentheses); vapor pressure, in conventional millimeters of mercury (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 flash point and autoignition temperature in degrees Fahrenheit (Celsius in parentheses); flammable limits, in percent by volume in air; suitable extinguishing media or materials; special firefighting procedures; and unusual fire and explosion hazard information. If the product presents no fire hazard, insert "NO FIRE HAZARD" on the line labeled "Extinguishing Media."

(e) Section V. Health Hazard Information

The "Health Hazard Data" should be a combined estimate of the hazard of the total product. This can be expressed as a 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.

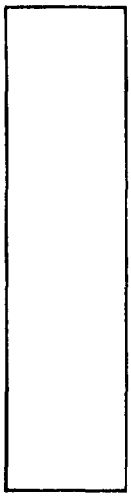
(i) Section IX. Special Precautions

"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 isopropyl alcohol. 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 _____

XI. APPENDIX IV

OCCUPATIONAL RESEARCH PRIORITIES FOR ISOPROPYL ALCOHOL

(1) Acute Effects of Inhalation of Isopropyl Alcohol in Humans

Additional studies should be performed to elucidate the acute effects of isopropyl alcohol inhalation in humans. These studies should be designed to determine whether isopropyl alcohol produces significant skin and eye irritation, changes in respiratory parameters, and liver pathology at various concentrations. Tolerance to these effects should also be evaluated.

(2) An Epidemiologic Study

Since the first study conducted by Weil et al [39] regarding the old process, no epidemiologic studies have been made to see if a high incidence of paranasal sinus cancers prevails in the new process. The need for an epidemiologic study is urgent. A retrospective cohort study would be an important tool in determining whether the cancer rate has significantly changed in the present isopropyl alcohol manufacturing plants.

(3) Chronic Animal Exposure Studies

Exposure of rodents to several concentrations of isopropyl alcohol up to the maximum tolerated concentration, 8 hours/day, 5 days/week, for 18 months is recommended to investigate the possible carcinogenic action of the alcohol and effects of long term exposure. Two types of studies should

be involved, one a dermal application study and the other inhalation.

(4) Acute Animal Exposure Studies

As stated previously, there are numerous information gaps on biochemical effects of isopropyl alcohol at levels that might be encountered in the workplace environment. In this regard, acute animal experiments using levels up to 800 ppm of isopropyl alcohol are essential.

Accumulation of liver triglycerides has been caused by isopropyl alcohol and this phenomenon has been the basis for inferring that fatty liver is produced. [61,62] In light of these effects, additional data are needed to answer two basic questions:

(a) Is there a dose-response relationship for these effects?

(b) Is there any histological evidence for isopropyl alcohol-induced fatty liver?

(5) Effect of Isopropyl Alcohol on Chlorinated Hydrocarbon Toxicity

It has been established that isopropyl alcohol intake in large amounts 16-20 hours prior to inhalation of carbon tetrachloride, can increase the toxicity of carbon tetrachloride. [65-67] Again, further studies of animal exposure by inhalation must be done to answer three basic questions:

(a) Does inhalation of isopropyl alcohol at low levels (below 800 ppm) followed by inhalation of carbon tetrachloride at low levels (below 10 ppm) augment the toxicity of the latter?

(b) Does isopropyl alcohol potentiate the toxicity of other chlorinated hydrocarbons as well?

(c) Is isopropyl alcohol, or acetone, or any other metabolite, the potentiator of carbon tetrachloride toxicity in vivo?

XII. TABLES AND FIGURE

TABLE XII-1

PROPERTIES OF ISOPROPYL ALCOHOL

Appearance	Colorless
Odor	Acrid
Molecular formula	$CH_3CHOHCH_3$
Formula weight	60.09 g
Boiling point	82.3 C
Freezing point	-89.5 C
Specific gravity	0.7861 at 20 C
Solubility	Miscible with water, ethyl alcohol, and ethyl ether
Flash point	12 C (closed cup)
Ignition temperature	399 C
Lower explosive limit	2%
Relative vapor density	2.07 (air = 1.00)
Vapor pressure	44 mmHg at 25 C 59.1 mmHg at 30 C 105.6 mmHg at 40 C 176.8 mmHg at 50 C
Conversion factors at standard temperature and pressure	1 ppm = 2.46 mg/cu m 1 mg/liter = 407 ppm

Derived from references [1] and [2]

TABLE XII-2

EFFECTS OF ISOPROPYL ALCOHOL IN ANIMALS*

Species	Route of Exposure	Dose	Effects	Reference
Rats	Inhalation	16,000 ppm	Death of 4 of 6 after a single 8-hour exposure	45
"	"	8.13 ppm	Continuous exposure: increased BSP retention, leukocyte counts, abnormal fluorescent leukocytes, changed latent period of unconditional reaction, statistically significant	47
"	"	1.02 ppm	Continuous exposure: same as effects as at 8.13 ppm, not statistically significant	47
"	"	0.24 ppm	Continuous exposure: no effect.	47
Rabbits	Oral	6.5-8.0 ml/kg	Death of 34 of 36 within 80 hours	50
Rats	"	6 g/kg (7.63 ml/kg)	Accumulation of liver triglycerides	61, 62
Rats, Older adult	"	6.8 ml/kg	LD50	52
Rats, Young adult	"	6.0 ml/kg	"	52

TABLE XII-2 (CONTINUED)

EFFECTS OF ISOPROPYL ALCOHOL IN ANIMALS*

Species	Route of Exposure	Dose	Effects	Reference
Rats, 14-day-old	Oral	5.6 ml/kg	LD50	52
Rats	"	3.0 g/kg (3.82 ml/kg)	Accumulation of liver triglycerides	63
"	"	2.58 g/kg (3.28 ml/kg)	Narcosis	51
"	"	2.34 g/kg (2.98 ml/kg)	16-18 hours after alcohol administration, inhalation of CC14 at 1,000 ppm for 2 hours resulted in increased SGOT level.	65
Rabbits	"	2.5 ml/kg	Narcosis	50
Mice	"	"	Single doses (0.05-2.5 ml/kg) of 4 chlorinated hydrocarbons were administered 18 hours after alcohol: augumented hepatoxticity of 3 hydrocarbons.	68
Rabbits	Dermal	16.4 ml/kg	LD50	45

*Results of additional cancer studies on animals are included in Chapter III

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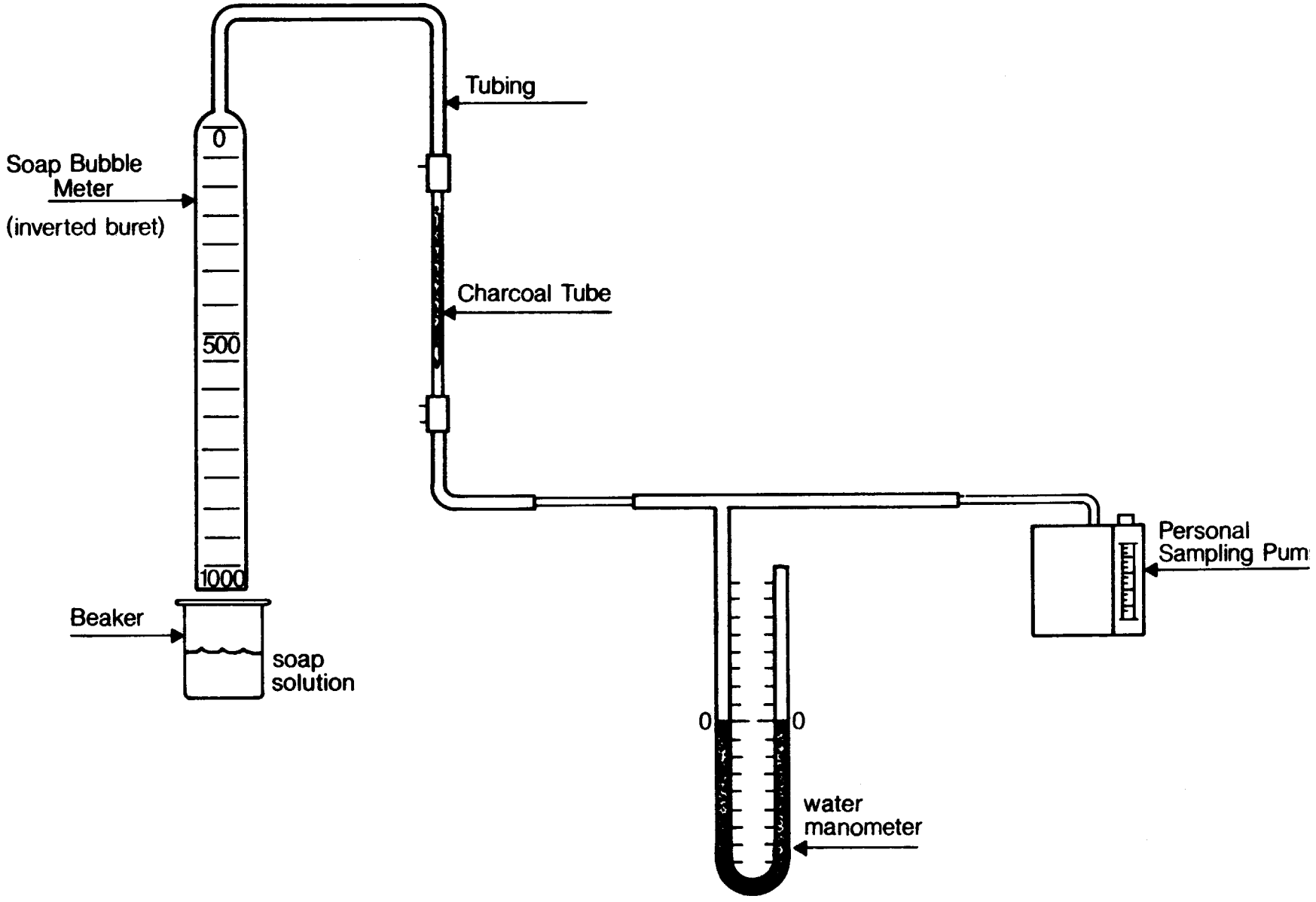
FIGURE XII-I

CALIBRATION SETUP FOR PERSONAL SAMPLING PUMP WITH CHARCOAL TUBE



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