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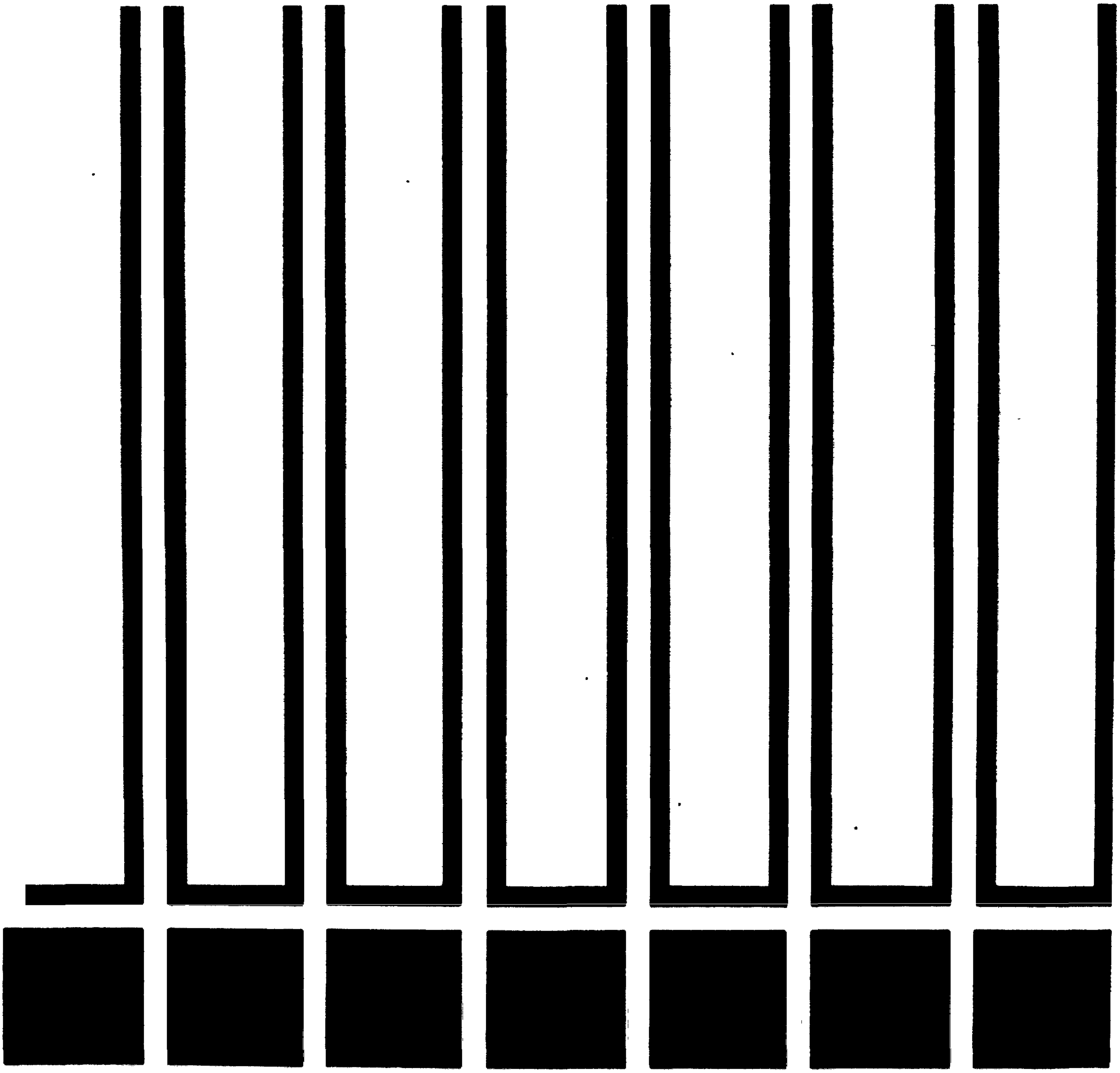

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service Center for Disease Control

criteria for a recommended standard....

OCCUPATIONAL EXPOSURE
TO
FORMALDEHYDE

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health
DECEMBER 1976

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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 formaldehyde by members of the NIOSH staff and the valuable, constructive comments by the Review Consultants on Formaldehyde, by the ad hoc committees of the American Conference of Governmental Industrial Hygienists and the American Academy of Occupational Medicine, 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 formaldehyde. Lists of the NIOSH Review Committee members and of the Review Consultants appear on the following pages.

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The Division of Criteria Documentation and Standards Development, National Institute for Occupational Safety and Health, had primary responsibility for development of the criteria and recommended standard for formaldehyde. The Division review staff consisted of J. Henry Wills, Ph.D., Chairman, and Richard A. Rhoden, Ph.D. Bert J. Vos, M.D., Ph.D., served as a special reviewer. The Department of Environmental and Industrial Health, School of Public Health, University of Michigan, developed the basic information for consideration by NIOSH staff and consultants under contract No. HSM-99-73-31. Earl S. Flowers, Ph.D., had NIOSH program responsibility and served as criteria manager.

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CRITERIA DOCUMENT: RECOMMENDATIONS FOR AN OCCUPATIONAL EXPOSURE STANDARD FOR FORMALDEHYDE

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I. RECOMMENDATIONS FOR A FORMALDEHYDE STANDARD

The National Institute for Occupational Safety and Health recommends that employee exposure to formaldehyde in the occupational environment be controlled by compliance with the following sections. The standard is designed to protect the health and to provide for the safety of employees for up to a 10-hour workday for a 40-hour week over a working lifetime. Compliance with the standard should prevent adverse effects of exposure to formaldehyde. This recommended standard is not designed to protect an individual already sensitized to formaldehyde. Such individuals should not be exposed to formaldehyde. The standard is measurable by techniques that are valid, reproducible, and available to industry and government agencies. Sufficient technology exists to permit compliance with the recommended standard. The standard will be subject to review and revision as necessary.

Occupational exposure to formaldehyde is defined as exposure to formaldehyde in air at a concentration in excess of 0.6 mg/cu m (0.5 ppm), based on a 30-minute sampling period, or by contact with formaldehyde in liquid or solid form. Adherence to all provisions of Sections 3-6 is required in occupational environments where formaldehyde is used regardless of the concentration of airborne formaldehyde. Medical surveillance and environmental monitoring are required as specified in Sections 2 and 8, respectively.

Section 1 - Environmental (Workplace Air)

(a) Concentration

Exposure to formaldehyde shall be controlled so that no employee is exposed to formaldehyde at a concentration greater than 1.2 milligrams per cubic meter of air (1 ppm) for any 30-minute sampling period.

(b) Sampling and Analysis

Methods for calibration of equipment, air sampling, and analysis for formaldehyde shall be as provided in Appendices I and II, or by any procedure shown to be equivalent in precision, accuracy, and sensitivity to the procedures specified.

Section 2 - Medical

Medical surveillance shall be made available as outlined below to all workers subject to occupational exposure to formaldehyde.

(a) Preplacement examinations shall include at least:

(1) Comprehensive medical and work histories with special emphasis on any evidence of chronic inflammatory reaction of the respiratory tract, of skin reaction or hypersensitivity, or of such other allergic conditions as asthma, hayfever, and rose fever.

(b) An evaluation of the employee's ability to use positive and negative pressure respirators.

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

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

recommendations.

(4) In the event of an overexposure to formaldehyde, a physical examination as described in (1)(b) above shall be made available within a reasonable period of time.

(5) Pertinent medical records shall be maintained for all employees exposed to formaldehyde in the workplace. Such records shall be kept for at least 5 years after termination of employment. These records shall be made available to the designated medical representatives of the Secretary of Health, Education, and Welfare, of the Secretary of Labor, of the employer, and of the employee or former employee.

Section 3 - Labeling and Posting

(a) All containers of formaldehyde solutions shall bear the following information in addition to, or in combination with, label information required by other statutes, regulations, and ordinances:

FORMALDEHYDE SOLUTION (Percent formaldehyde by weight)
(MAY CONTAIN METHANOL)

WARNING: HARMFUL IF INHALED OR SWALLOWED. CAUSES IRRITATION OF SKIN, EYES, NOSE, AND THROAT.

Avoid prolonged or repeated breathing of gas or mist. Avoid prolonged or repeated contact with skin. Keep container closed. Use with adequate ventilation. Do not get in eyes, on skin, on clothing. Wash thoroughly after handling. Wash contaminated clothing before reuse. Destroy and discard contaminated shoes.

FIRST AID: CALL A PHYSICIAN

On contact, immediately flush skin or eyes with large amounts of water for at least 15 minutes; get medical attention. If inhaled, remove to fresh air, give artificial respiration if breathing has stopped.

IF SWALLOWED: Induce vomiting. If victim is unconscious, do not attempt to induce vomiting.

SPECIAL CONTAINER HANDLING AND STORAGE: Before moving a container, be sure closure is securely fastened. Loosen closure carefully. In case of spillage, flush with plenty of water.

(b) When environmental monitoring indicates that there is occupational exposure to formaldehyde, the following sign shall be posted in readily visible locations at or near entrances to the area and on or near process, storage, and other equipment utilizing or containing formaldehyde.

FORMALDEHYDE

WARNING: IRRITANT TO SKIN, EYES, NOSE, AND THROAT

Avoid prolonged breathing of formaldehyde.

Avoid prolonged or repeated contact.

(c) If formaldehyde concentrations in the air of a workroom or area exceed the recommended limit, the following statement shall be added in large letters to the signs as required in Section (b):

RESPIRATORY PROTECTION REQUIRED IN THIS AREA

(d) In any occupational environment or area where accidental or other release of formaldehyde vapor may cause an emergency requiring the use of respiratory protection, the signs required by Section (b) shall be supplemented by an additional sign giving: (1) the location of emergency respiratory protective equipment, and (2) instructions for evacuation from the area and emergency procedures.

(e) Signs shall be printed in English and in the predominant language of non-English-reading employees, if any, unless employers use equally effective means to ensure that non-English-reading employees know the hazards associated with formaldehyde and with areas where formaldehyde is used, handled, or stored.

Section 4 - Personal Protective Equipment and Protective Clothing

Engineering controls shall be used to maintain the concentration of airborne formaldehyde at or below the ceiling concentration of 1.2 mg/cu m. In some situations, the added protection of personal protective equipment and clothing shall be provided to prevent excessive contact with solutions and solids containing formaldehyde or inhalation of formaldehyde gas. Such protective equipment and clothing shall be furnished to employees or shall be readily available at convenient and appropriate locations. Emergency equipment shall be located at well-marked and identified stations and shall be adequate to the needs of all employees, either to escape from the area or to safely cope with the emergency. Safe work practices including use of protective equipment and clothing, shall also be used to control exposure.

(a) Protective Clothing

(1) Employees shall wear gloves made of rubber or of other impervious material when working with formaldehyde and when contact with the hands is likely.

(2) Employees shall wear protective sleeves, aprons, jackets, trousers, and caps as needed to protect them from skin contact

with formaldehyde. Protective garments shall be made of a material impervious to formaldehyde. In emergencies or other circumstances involving exposure to formaldehyde at high concentrations of vapor, mists, or dusts in the air, full body protection shall be worn. Emergency garments shall be of an impervious material, and shall fit snugly about the wrists, neck, waist, and ankles.

(3) Employees handling drums, cans, or other containers of formaldehyde shall wear leather or rubber safety shoes. Rubbers may be worn over leather safety shoes as protection from splashes or spills of formaldehyde.

(4) Protective garments shall be cleaned inside and out and well ventilated after each use, and particularly after contamination has occurred.

(b) Eye and Face Protection

(1) Cup-type or rubber-framed chemical safety goggles shall be worn by employees when there is any possibility of eye or facial contact with formaldehyde solutions. Goggles also protect eyes from contact with gas. In cases of excessive vapor concentrations, a full face mask respiratory protective device shall be required; this device may be substituted for cup-type or rubber-framed chemical safety goggles.

(2) Full-length, plastic face shields shall be required in addition to safety goggles for face protection when the work process involves risks of exposure to splashes of formaldehyde. Chemical safety goggles are required in addition to the face shield when there is danger of formaldehyde entering underneath or around the sides of the shield.

(3) The safety goggles, full-face masks, and shields shall

be thoroughly decontaminated after each use.

(4) Eye-protective measures and equipment shall conform with the provisions under 29 CFR 1910.133.

(c) Respiratory Protection

Respirators may be used for nonroutine operations, evacuation, or emergencies which may involve occasional brief exposures to formaldehyde at concentrations in excess of 1.2 mg/cu m. Such exposures may occur during the period necessary to install or test required engineering controls, or to take protective actions.

Appropriate respirators as described in Table I-1 may only be used pursuant to the following requirements:

(1) For the purpose of determining the type of respirator to be used, the employer shall measure the airborne formaldehyde concentration in the workplace initially, and thereafter whenever process, operations, worksite, climate, control, or other changes may occur which are likely to increase the airborne concentration of formaldehyde. This requirement does not apply when only positive pressure supplied-air respirators are used.

(2) The respirator and cartridge or canister used shall be of the appropriate class, as determined on the basis of the airborne concentration of formaldehyde. The employer shall ensure that no employee is exposed to formaldehyde in excess of 1.2 mg/cu m for any 30-minute period because of improper respirator selection, fit, use, or maintenance.

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

(4) The employer shall provide respirators in accordance

with Table I-1 and shall ensure that the employee uses the respirator properly.

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

(6) Respirators specified for use at greater airborne concentrations of formaldehyde may be used in lesser airborne concentrations of formaldehyde.

(7) Use of chemical cartridges and canisters more than once or for a period greater than that indicated in Table I-1 shall be prohibited.

(8) The employer shall ensure that respirators are adequately cleaned, maintained, and stored when not in use, and that employees are instructed on the use of respirators assigned to them and on how to test for leakage.

TABLE I-1

REQUIREMENTS FOR RESPIRATOR USAGE WHEN THE CEILING CONCENTRATION IS EXCEEDED

Formaldehyde Concentration	Respirator Type
Less than or equal to 2.4 mg/cu m	(1) Chemical cartridge respirator and organic vapor cartridge and full-face mask. Maximum service life of 3 hours (2) Type C supplied-air respirator, demand type (negative pressure), and full-face mask
Greater than 2.4 mg/cu m, up to 12 mg/cu m	(1) Chemical cartridge respirator and organic vapor cartridge and full facepiece. Maximum service life of 3 hours (2) Full-face mask, chin type, with organic vapor canister. Maximum life of 4 hours
Greater than 12 mg/cu m, up to 120 mg/cu m	(1) Full-face mask, chest- or back-mounted type, with industrial size organic vapor canister. Maximum service life of 2 hours (2) Type C supplied air-respirator, continuous-flow or pressure-demand type (positive pressure), with full facepiece, hood, or helmet
Greater than 120 mg/cu m	(1) Self-contained breathing apparatus with positive pressure in full facepiece. (2) Combination supplied-air respirator pressure-demand type with auxiliary self-contained air supply
Emergency or firefighting (no concentration limit)	(1) Self-contained breathing apparatus with positive pressure in facepiece (2) Combination supplied-air respirator, pressure-demand type, with auxiliary self-contained air supply
Evacuation or escape (no concentration limit)	(1) Self-contained breathing apparatus in demand or pressure-demand mode (negative or positive pressure) (2) Full-face mask, front- or back-mounted type with industrial size organic vapor canister.

Section 5 - Informing Employees of Hazards from Formaldehyde

(a) At the beginning of employment or assignment in areas that may involve exposure to formaldehyde and annually thereafter, each employee shall be informed of the hazards of his occupation and of possible injuries. He shall be instructed in the proper procedures for the safe handling and use of this compound, in the operation and use of protective systems and devices, and in appropriate emergency procedures.

(b) Instruction shall include the pertinent information in the Material Safety Data Sheet (Appendix III). In addition, employees shall be informed that repeated or prolonged contact with formaldehyde may result in sensitization and that excessive exposure may cause irritation of the skin, eyes, and respiratory tract. This information shall be posted in the work area and kept on file, readily accessible to employees at all worksites where exposure may occur. Employees shall be apprised of the location and availability of this information.

(c) A continuing education program, conducted by a person or persons qualified by experience or special training, shall be instituted to ensure that all employees have current knowledge of job hazards, proper maintenance procedures and cleanup methods, and that they know how to use respirators correctly. The instructional program shall include a description of the general nature of the medical surveillance procedures and why it is advantageous to employees to undergo these examinations.

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

Section 6 - Work Practices and Engineering Controls

(a) Appropriate protective clothing and equipment (goggles, face shields, gloves, etc), as described in Section 4, shall be worn by each employee engaged in the transfer of formaldehyde solution or in any other task in which splashes, spills, or other circumstances likely to involve contact with the solution may occur. When working with formaldehyde-generating solids, protective garments shall be worn to prevent contact of the solids or dust with the eyes or skin.

(b) Appropriate respiratory protective devices, as described in Section 4, shall be worn by all exposed employees in any operation or area for which the airborne concentrations of formaldehyde vapor or formaldehyde-generating substances are determined to be likely to cause exposure in excess of the recommended limit. Suitable respiratory protection shall be worn by all employees in emergency exposure situations.

(c) Systems or processes using or handling formaldehyde shall be enclosed to the extent that is feasible for the necessary operations.

(1) Total enclosure is most desirable, with provision for venting of excess gas without allowing it to enter the air of the workplace.

(2) When total enclosure is not possible, processes shall be designed and operated to limit occupational exposure of employees by contact with, or inhalation of, any gas, liquid, splash, or mist. Such installations shall be adequately ventilated to ensure that formaldehyde concentrations in the workroom air will not exceed the recommended limit.

(3) Enclosed process equipment which must be opened periodically to charge or discharge materials shall be provided with a

system of venting or ventilation such that employees are protected from exposures to formaldehyde concentrations in excess of the recommended limit.

(d) Formaldehyde solutions and formaldehyde-generating substances shall be stored in securely closed containers in a storage area which is adequately ventilated to ensure that airborne concentrations of formaldehyde will not exceed the limit specified in Section 1(a).

(1) Bulk storage tanks for formaldehyde solution:

(A) Shall have vents of such size and design as to permit the safe venting of tanks for the purpose of pressure and vacuum relief. The vents must be easily cleared and shall be regularly inspected and cleaned. Formaldehyde gas shall be vented in such a manner that excessive exposure of employees or other individuals cannot occur.

(B) Each storage tank shall have one or more manholes to allow for inspection and cleaning of the tank.

(C) Each tank shall be equipped with positive sealing connections for filling and draining the tank.

(D) All such tanks shall be adequately grounded to discharge static electricity.

(2) Drums and barrels of formaldehyde solution shall be stored with the bungs up and tightly placed.

(3) When drums, barrels, carboys, or other such containers of formaldehyde solutions are placed in a storage room, trapped floor drains shall be provided, and the floor shall be pitched toward the drains.

(e) When handling containers of formaldehyde solutions (carboys, drums, barrels, etc), suitable methods and procedures shall be used to prevent contact with formaldehyde or inhalation of formaldehyde at airborne concentrations in excess of the recommended limit.

(1) Carboys shall be handled with special care to prevent breakage.

(2) All such containers shall be securely closed or sealed when being moved or handled, except for the transfer of the solution.

(3) When transferring solution from such containers, pumps should be used when practical. If the solution is removed by tilting, a supporting device (inclinator) shall be used for all containers of more than 2-gallon capacity. Transfer operations shall be accomplished in a manner and by methods which will not result in contact or inhalation exposures in excess of the recommended limit. Transfer shall be made only with adequate ventilation for control of the gas concentrations.

(4) Carboys, drums, and barrels shall be completely drained before being returned for reuse. These containers may not be used for any other material until cleaned.

(f) When solutions of formaldehyde or formaldehyde-yielding substances are used in open or unsealed containers, the containers shall be kept covered as much as possible and provided with general or local exhaust ventilation adequate to control emission of gas or dust.

(g) The transfer of formaldehyde solution to or from tank trucks or tank cars may be done only in areas and at facilities designed and specified for these operations. The area should be level and the wheels of the vehicle shall be blocked. Connections must be compatible and specifically identified. Only trained persons may carry out the procedures.

(1) No such transfers may be made unless authorized by the

responsible supervisor.

(2) The area shall be posted and unauthorized persons shall be excluded from the area during such transfers.

(h) Cleaning, maintenance, and repair of tanks and process equipment or lines may be done only by properly instructed and trained personnel under responsible supervision. When possible, such work shall be accomplished from the outside. Entry into confined spaces such as tanks, pits, tank cars, barges, process vessels, and tunnels shall be controlled by a permit system. Permits shall be signed by an authorized representative of the employer certifying that preparation of the confined space, precautionary measures, and personal protective equipment are adequate, and that precautions have been taken to ensure that prescribed procedures will be followed.

(1) Tanks, equipment, lines, pumps, and valves shall be drained, then thoroughly flushed with water and drained again before any work is done on them. All spillage shall be flushed to the drain with large amounts of water. Contact with drainage liquid shall be avoided.

(2) Prior to entry, the atmosphere in any tank or equipment to be entered for such work shall be tested and found to have adequate oxygen and to be free of excessive formaldehyde concentrations for work contemplated and equipment worn.

(3) No employee shall enter any tank or equipment which does not have a manhole or entry large enough to admit an employee equipped with safety harness, lifeline, and emergency respiratory equipment. The employee shall be able to leave the tank or vessel by the same opening.

(4) A person shall be stationed at the entry to keep employees under constant observation and one or more other persons shall be

readily available in case of an emergency requiring rescue of the employee(s). A supplied-air or self-contained breathing apparatus with safety harness and lifeline shall be located outside the tank or vessel for emergency use.

(5) Prior to entry, provision shall be made for adequate ventilation of the tank or vessel to provide sufficient oxygen for the employees inside and to remove or flush any airborne formaldehyde in excess of the recommended limit.

(6) Before work in or on any tank, line, or equipment is started, provision shall be made to prevent inadvertent entry of formaldehyde solution or vapor into the work area.

(7) Exterior work involving cutting, chipping, riveting, and welding on a tank, vent, or equipment may not be started until the item has been cleaned and purged of formaldehyde gas, solutions, or formaldehyde-yielding solids, and until a test has been made to ensure that formaldehyde concentrations are below the lower flammable limit.

(j) Employers shall ensure that waste of formaldehyde solutions or formaldehyde-yielding substances is disposed of by methods and procedures which will prevent exposure of employees and other persons.

(k) Eye-flushing stations and showers shall be provided in any area where contact of the eyes or the skin with formaldehyde or formaldehyde-yielding substances is likely to occur.

(l) All leaks and spills of formaldehyde solution and/or formaldehyde-generating substances shall be cleaned up immediately. When the quantities involved are likely to produce exposures exceeding the recommended limit, the employees at such cleanup operations shall wear suitable respiratory protection and protective clothing.

(m) Plans and procedures to meet emergency situations shall be formulated and all personnel shall be trained in their effective use.

(1) All employees shall be thoroughly instructed in emergency procedures and in the proper use of emergency equipment.

(2) Appropriate emergency equipment including protective clothing, emergency and rescue breathing apparatus, and first-aid supplies shall be located in each area where an emergency could occur. Locations of such emergency stations shall be prominently and clearly posted in the work areas.

(3) During emergency situations, all personnel shall be evacuated from the area except the trained and equipped emergency teams.

(n) Protective clothing, respirators, goggles, and other personal protective gear which have been contaminated by contact with formaldehyde or formaldehyde-yielding substances shall be thoroughly washed or cleaned before reuse by the employee.

Section 7 - Sanitation

(a) Eating and food preparation or dispensing (including vending machines) shall be prohibited in formaldehyde work areas.

(b) Smoking shall not be permitted in areas where formaldehyde is used, transferred, stored, or manufactured.

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

(d) Waste material contaminated with formaldehyde shall be disposed of in a manner not hazardous to employees and in compliance with local regulations.

Section 8 - Monitoring and Recordkeeping Requirements

(a) Workroom areas shall not be considered to have formaldehyde exposure if airborne concentrations of formaldehyde, as determined on the basis of annual industrial hygiene surveys, do not exceed a ceiling concentration of 1.2 mg/cu m (1 ppm) and if there is no occupational exposure to formaldehyde solutions. Records of these surveys, including the basis for concluding that the airborne concentration of formaldehyde does not exceed either half of the ceiling concentration limit, or the ceiling concentration limit, shall be maintained.

(b) Employers shall maintain records of exposures to airborne formaldehyde based upon the following sampling and recording schedules:

(1) The first workplace environmental survey shall be completed within 6 months of the promulgation of a standard incorporating these recommendations.

(2) Workplace environmental surveys shall be conducted within 30 days after installation of a new process or any process changes.

(c) Should environmental sampling indicate airborne formaldehyde concentrations between half of the ceiling concentration limit and the ceiling concentration limit, the following requirements shall apply: Samples shall be collected at least semiannually in accordance with Section 1(b) for the evaluation of the workplace environment with respect to the recommended standard. Each employee or employee location shall be evaluated at least once every year. Samples shall be collected in accordance with Appendix I and analyzed in accordance with Section 1(b) for the determination of the airborne 30-minute ceiling concentrations of formaldehyde.

(d) When employee exposure exceeds the 30-minute ceiling limit, environmental controls shall be applied. Monitoring and recordkeeping shall be repeated on a weekly basis until two consecutive sampling periods have demonstrated that corrective measures have decreased airborne formaldehyde concentrations at or below the limit.

(e) Records of all sampling and analysis of airborne concentrations of formaldehyde shall be retained for at least 5 years. Records shall indicate the type of personal protective devices, if any, in use at the time of sampling. Records shall be maintained and classified so that an employee shall be able to obtain information about his or her own present and past workplace exposures to formaldehyde.

(f) Access to records

(1) All records required to be maintained by this section shall be made available upon request to authorized representatives of the Assistant Secretary of Labor for Occupational Safety and Health and to the Director of the National Institute for Occupational Safety and Health.

(2) Employee exposure determination and exposure measurement records required to be maintained by this section shall be made available to employees and their designated representatives.

(3) Without interfering with the measurement, observers shall be entitled to receive an explanation of the measurement procedure, visually observe all steps related to the measurements that are being performed at the place of exposure, and record the results obtained.

II. INTRODUCTION

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

The National Institute for Occupational Safety and Health (NIOSH), after a review of data and consultation with others, formalized a system for the development of criteria upon which standards can be established to protect the health and provide for the safety of employees by limiting their exposure to hazardous chemical and physical agents. Criteria for a standard should enable management and labor to develop better engineering or administrative controls, resulting in more healthful work practices and mere compliance with the recommended standard should not be regarded as a final goal.

The criteria and recommended standard for formaldehyde are a part of a continuing series of documents published by NIOSH. The proposed standard applies only to the processing, manufacture, and use of formaldehyde as applicable under the Occupational Safety and Health Act of 1970.

The standard was not designed for the population-at-large, and any extrapolation beyond the occupational environment is not warranted. It is intended to (1) protect against injury from formaldehyde, (2) allow measurement by valid, reproducible procedures available to industry and official agencies, and (3) be attainable by using existing technology.

For the purpose of this standard, formaldehyde is defined as monomeric formaldehyde, HCHO. Sources of formaldehyde include aqueous solutions, such as formalin (37 to 42% formaldehyde), and formaldehyde-yielding substances, such as trioxane, paraformaldehyde, polyoxymethylene, and hexamethylenetetramine.

There is a need to obtain more information on possible chronic effects produced by prolonged exposures to formaldehyde at low concentrations. Information on the solution chemistry of formaldehyde and its reactive derivatives would be useful in developing sampling and analytical procedures. The formation of bis-chloromethyl ether, a potent carcinogen, from the reaction of formaldehyde with chlorides appears unlikely at low concentrations of formaldehyde in air, but additional research on this topic is desirable.

III. BIOLOGIC EFFECTS OF EXPOSURE

Extent of Exposure

Formaldehyde, HCHO, and its derivatives are chemicals used in numerous industrial operations involving the manufacture, formulation, commercial distribution, and production of a variety of products [1]. Selected chemical and physical properties of formaldehyde monomer (FM) are listed in Table XII-1. The utilization of formaldehyde in the United States is summarized in Table XII-2. Clearly, formaldehyde is an important industrial chemical, so that demand, production, and use of formaldehyde should increase.

In the vapor phase, formaldehyde exists as a monomer FM, whereas the chemistry of formaldehyde in aqueous solutions is more complex [1]. An understanding of the basic chemistry of formaldehyde and its derivatives, shown schematically in Figure III-1 and described in Table XII-3, is essential to any discussion of biologic effects.

Reactions of FM with itself, as described by Walker [1], depend primarily upon temperature and concentration. The presence of small amounts of water, metals, or other impurities may significantly accelerate reactions. The anhydrous gas (FM) is stable in the gas phase over the temperature range of 80-100 C, but undergoes polymerization upon condensation and cooling. Formaldehyde in alcohol and/or water solutions (FS) slowly polymerizes, forming paraformaldehyde and amorphous higher polymers of polyoxymethylene (PF). Amorphous polyoxymethylenes containing 100 residues or more are derived from FM and are regarded as alpha-polyoxymethylenes (PO alpha). PO alpha may be formed by addition of sulfuric acid to FS or PF.

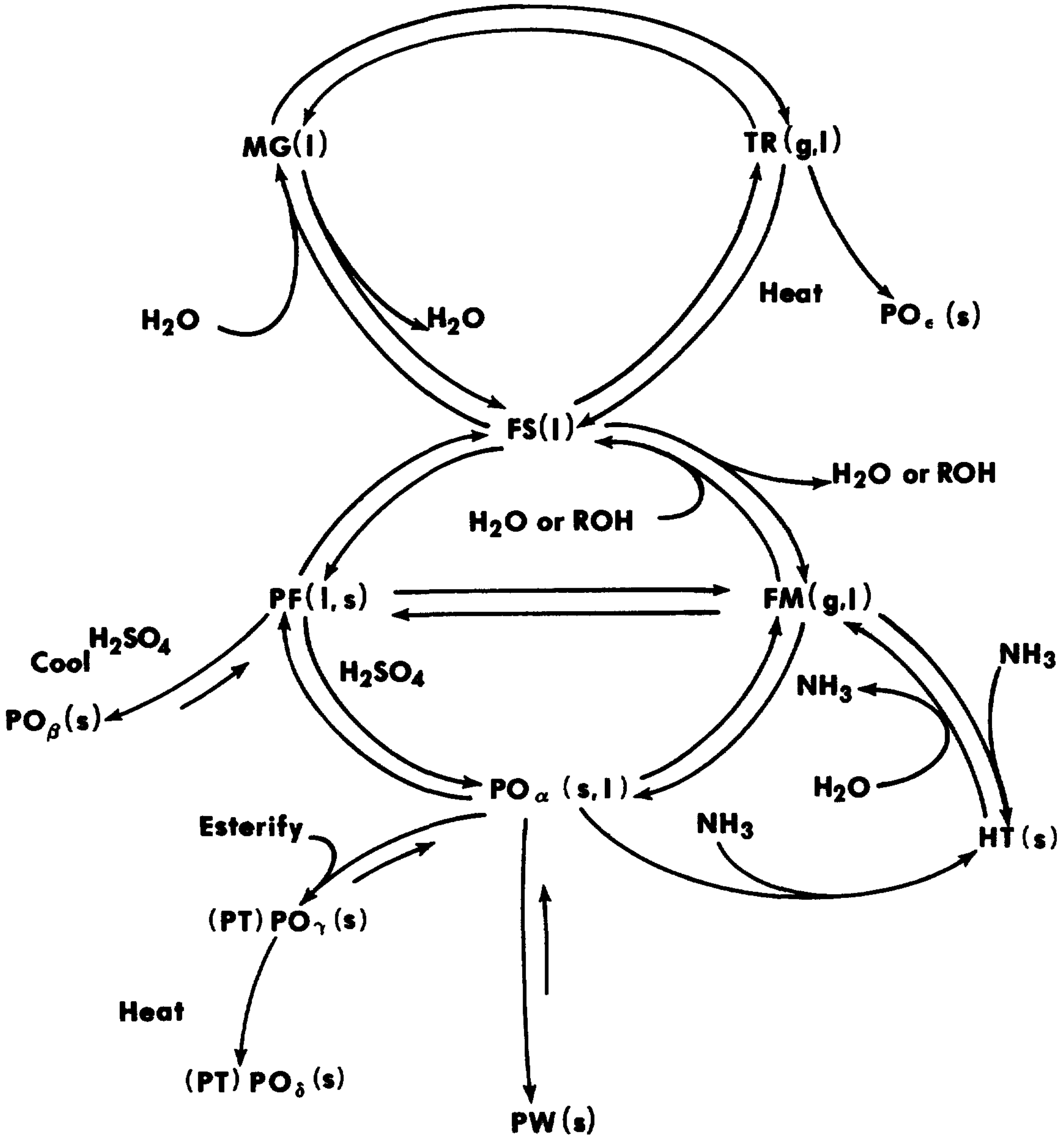

FIGURE III-1

FORMALDEHYDE REACTIONS AND PRODUCTS

FM - Formaldehyde monomer
FS - Formaldehyde in solution
MG - Methylene glycol
PF - Paraformaldehyde
TR - Trioxane
HT - Hexamethylene tetramine
PO - Polyoxymethylenes
PT - Polyoxymethylenes modified
PW - Polyoxymethylenes, high polymers

Slow addition of H_2SO_4 at 0-5 C produces a highly ordered clear-crystalline polyoxymethylene (PO beta). Esterification of PO alpha yields a relatively stable amorphous product which undergoes rearrangement on heating to various temperatures and forms polymeric ethers and esters (PT), including PO delta. With continued reaction, higher molecular weight insoluble polyoxymethylenes may be formed and are designated as PW. Repeated distillation of the cyclic trimer, trioxane, yields a polyoxymethylene residue, PO epsilon. PO alpha is labile to degradation yielding FM on destructive distillation or on dissolving in alcohol or water. Other PO derivatives are more resistant to degradation and are not generally regarded as sources of FM.

Formaldehyde exists in freshly prepared aqueous solutions as a monohydrate form, methylene glycol (MG) (See Figure III-1). Depending on the age and concentration of the solution, a series of paraformaldehyde and low molecular weight polyoxymethylene glycols (PF) having the typical formula, $HO(CH_2O)_xH$, may be present. Lower concentrations of formaldehyde favor formation of methylene glycol as the principal molecular species while higher concentrations and aging of the solutions favor formation of polymeric forms of formaldehyde (PO, PT, PW). Aqueous solubility of the higher polymers decreases with increasing molecular weight, resulting in precipitation of the higher polymers (PO, PT, PW) from solution. To prevent or retard continued polymerization, methanol or other alcohols may be added to formulations as stabilizers. Aqueous solutions of formaldehyde generally contain less than 0.1% FM. However, distillation of such solutions yields a vapor that consists primarily of unhydrated FM in equilibrium with a low concentration of MG vapor [1]. Although FM is not found in significant amounts in solid or liquid products, formulations, or derivatives, vapor produced by, or evolved from, such materials may contain significant amounts of FM gas. Distillation of an alkaline solution containing polymeric aldehydes derived from formaldehyde is a fundamental process for obtaining or recovering FM.

The number of employees engaged in the direct production of formaldehyde monomer, supplied as an anhydrous product or in solution, has been estimated by NIOSH to be 8,000. Formaldehyde is used (see Table XII-4) in the manufacture of a variety of derivatives, including phenolic resins, urea-formaldehyde resins, polyacetal resins, melamine, pentaerythritol, hexamethylenetetramine, fertilizers, and acetylene derivatives. Some of these materials may contain unreacted formaldehyde residues or yield formaldehyde on decomposition. The population of employees potentially exposed to formaldehyde or substances acting as sources of formaldehyde is uncertain. Although an estimated 8,000 employees may be at risk of exposure to the high concentrations found in industrial synthesis, formulation, and distribution of concentrated products, the numerous uses of formaldehyde and its derivatives indicate that a substantially larger population of employees may be at risk from intermittent exposures to products containing sources of formaldehyde or its congeners and derivatives.

Commercial production of formaldehyde is accomplished by a variety of techniques, including controlled oxidation of low molecular weight aliphatic petroleum hydrocarbons [2] and oxidation of methanol in the presence of a metal catalyst [1,3,4,5]. Two basic techniques for the production of formaldehyde by oxidation of methanol are operation of the process in either a fuel-rich mode or a fuel-lean mode. Other variations in the oxidation processes are related to differences in catalyst and the extent to which off-gases are recirculated.

Formaldehyde gas has a characteristic pungent odor. The pure, dry gas is stable in the temperature range of 80-100 C [1]. At usual room temperatures, polymerization occurs slowly and produces a white film of polyoxymethylene on the walls of containers, while cooling to temperatures between -20 to -80 C can cause condensation and more rapid polymerization. Table XII-3 lists the composition, properties, and structures of various formaldehyde polymers described by Walker [1]. Stability of the monomer depends on purity. Even traces of polar compounds (water, acids, or bases) can accelerate polymerization [2]. Water is a usual contaminant.

Commercial preparations of formaldehyde are available in grades of methanol free, methanol stabilized (NF), or reagent. In addition to methanol or other alcohols, commercial preparations may contain formic acid [6]. Aqueous solutions consist of 0-15% alcohol (methyl, propyl, n-butyl, or isobutyl) [7,2,6] in water containing 30-50% dissolved formaldehyde by weight, which is introduced as a gas consisting of FM. Formaldehyde solutions are supplied in glass carboys of 5- to 13-gallon capacity, lined steel drums of 5- to 50-gallon capacity, 55-gallon stainless steel drums, lined wooden barrels, stainless steel or lined tank trucks of 2,000- to 3,000-gallon capacity, or 8,000- to 10,000-gallon tank cars. In the industrial setting, it is possible to encounter formaldehyde in a variety of containers, processes, and products. One product, hexamethylenetetramine (HT), (CH2)6N4, which is formed by reaction of formaldehyde with ammonia, reacts as formaldehyde in many instances and is regarded as a special form or source of formaldehyde in industrial use [1]. Occupational groups at risk from formaldehyde exposure are listed in Table XII-5.

Although a substantial number of individuals may be intermittently exposed to formaldehyde or substances acting as a source of formaldehyde gas, a relatively smaller number of employees engaged in primary production, formulation, and distribution operations are at comparatively higher risk of incurring occupational exposure by either inhalation or skin and eye contact.

Historical Reports

The preparation and identification of several aldehydes had been elucidated by mid-19th century but the first member of the aldehyde family was unknown. Butlerov prepared formaldehyde in 1859 while attempting a synthesis of MG through hydrolysis of methyl acetate [1]. He also prepared polyoxymethylene using two procedures: by reaction of either methylene iodide with silver oxalate or of methylene iodide with silver oxide. Reaction of the polymeric products with ammonia yielded a crystalline product, hexamethylenetetramine (HT). However, Hofmann [8] reported the direct synthesis and definite identification of formaldehyde in 1867, when he passed a mixture of methanol and air over a heated platinum spiral. This method is a direct forerunner of a modern method of manufacture.

In 1913, Brunnthaler [9] noted that as early as 1893 Blum [10] had shown that formaldehyde combines with proteins. Subsequently, other investigators, Benedicenti [11] in 1897, Sollmann [12] in 1902, Kendall [13] in 1927, Gubareff and Bystrenin [14] in 1932, and Zipf and Bartscher [15] in 1933 demonstrated that formaldehyde combines with specific amino acids.

Formaldehyde reacts with terminal hydrogen atoms, particularly in free amino groups of amino acids. Hydroxymethylated derivatives are formed, which then may interact with other terminal hydrogen atoms by elimination of water and crosslinking in protein chains [16,17]. Stewart [18] showed that red blood cells treated with formaldehyde at 0.2% in solution lost the ability to take up oxygen but retained normal permeability to ammonium chloride and normal impermeability to sodium chloride. A more concentrated solution of formaldehyde (4%) destroyed the selective permeability of the red blood cells presumably produced by crosslinking of protein chains and opening pores in evelopes of the red blood cells.

Ingestion of formaldehyde has resulted in headache, upper gastrointestinal pain [19-23], allergic reactions [19], damage to tissues of the upper gastrointestinal and respiratory tracts [21, 22,24,25], systemic damage [22-24], and death [21,22,26].

In 1904, Levison [26] reported that a person who swallowed 2-3 oz of a "commercial" formaldehyde solution collapsed and died 20 minutes later. At autopsy, the mucosa of the lower esophagus, stomach, and duodenum were dark brown and hardened, and there was an excessive amount of mucus in the bronchi.

The US Department of Agriculture [19] investigated the use of formaldehyde as a food preservative in 1909. Eleven male volunteers received daily 100 mg of formaldehyde in milk for 5 days followed by daily doses of 200 mg of formaldehyde in milk for the next 10 days. During the 15-day test period, one subject stopped taking the formaldehyde after the 11th day, when he took a 100-mg dose, while two others took only 100 mg on the 14th day and nothing on the 15th. Ten of the 11 subjects complained of stomach or intestinal pain and headache during the test period and for 10 days after their last dose. A burning sensation in the throat and a slight decrease in body temperature were noted in "the majority of cases." A distinct itching rash appeared on the chest and thighs of four of the subjects. This observation was perhaps the earliest evidence of a systemically induced skin reaction to formaldehyde.

In 1909, Bower [23] reported a case involving a 20-year-old woman who swallowed about 0.5 oz of formalin (37-40% aqueous formaldehyde solution). A stomach lavage was performed before the victim collapsed and lost consciousness. The woman regained consciousness after administration of strychnine and later complained of pain in the throat and paroxysmal pain in the stomach. Kidney damage, as evidenced by analysis and physical appearance of the urine, was slight. A diuretic mixture containing about 130 mg each of potassium acetate and potassium citrate was given every 2-4 hours. Recovery was complete after 4 days.

Ely [21] reported in 1910 a case of formaldehyde poisoning that resulted in the death of a child who had ingested a few drops of a 40% formaldehyde solution. At post-mortem examination, the mucous and submucous coatings of the epiglottis, larynx, and trachea were thickened. Upper respiratory tract damage appeared to be a result of direct contact of formaldehyde with tissues at the juncture of the epiglottis and the esophagus and infiltration of the irritant into the trachea.

Earp [24] in 1916 reported three cases of formaldehyde ingestion involving adults. One man who drank 1.5 oz of formalin became cyanotic and cold and vomited. Mucous membranes of the mouth and throat were dry and white. The patient had a weak, irregular pulse, and his respiration was shallow. He was given a quart of milk and periodic injections of various respiratory and cardiac stimulants. Recovery occurred in 4 days. Ingestion of 0.5 oz formalin by another man produced very little cyanosis, and only a dry, sore throat, and vomiting. The victim recovered after a stomach washing with milk of magnesia, dilute ammonia water, and later a quart of milk administered by means of a stomach tube. A woman who attempted suicide by drinking 4 oz of formalin showed signs of cyanosis, reduced body temperature (96 F), shallow respiration, and a weak, rapid, and irregular pulse. She improved rapidly following administration of an oral dose of dilute ammonia water and injection of strychnine sulfate. Recovery occurred in 4 days.

In 1925, Kline [22] presented 12 fatal case histories from his own files and from those of other physicians, listing clinical treatments and pathologic changes as a result of formaldehyde ingestion. The amount of formaldehyde ingested varied from "a few drops" to 7.5 oz of solutions containing various concentrations of formaldehyde. Pathologic examinations revealed damage that was severe in the lower esophagus and even more extensive in the stomach. Damage produced in these organs varied from hardening of the tissue to extreme corrosion. Congestion, edema, tissue erosion, and hemorrhage were frequently observed, particularly in the lower esophagus. The author noted that, in cases in which victims died 13 hours or more after ingestion of formaldehyde, degenerative changes involving slight cloudy swelling, fatty degeneration, and necrosis in the parenchymatous organs were seen.

Vinson and Harrington [25] reported a case of corrosive stenosis of the stomach in a 59-year-old man caused by the accidental ingestion of formaldehyde. He experienced severe epigastric pain for 2-3 hours after swallowing the solution and was able to ingest only soft foods for about 10 days after the accident. Thereafter, swallowing even of fluids became impossible for 4 days before he entered the hospital. Surgery was performed to bypass the pyloric sphincter and to form an opening into the stomach near the cardiac sphincter. After 2 months of treatment to dilate a stricture below the cardia, the patient was able to swallow any type of food and was permitted to return home. The authors commented that additional dilations of the stricture just below the cardia probably would be needed.

Inhalation of formaldehyde has caused severe irritation of the upper respiratory tract [27,29] and death [27]. In 1934, Böhmer [27] reported that exposure to high concentrations of formaldehyde gas may lead to pulmonary edema. In one case, respiratory paralysis and death occurred within 15 minutes after drinking a 30% solution of formaldehyde. Pulmonary edema from inhalation of formaldehyde appears to be an uncommon response. Respiratory embarassment from acute inflammatory edema of the larynx is the most usual result [28].

In a 1935 report, Krans [29] described a case of chronic exposure to fumes and vapor produced during hot molding of formaldehyde-base synthetic resins. During the parting of 2-piece molds, a cloud of dense, acrid fumes containing "various amounts" of formaldehyde gas was released and, at times, caused immediate throat irritation. Airborne formaldehyde concentrations, durations of exposure, and analyses for other irritants were not reported. Six years earlier, Krans had encountered a man who had been working a short time in a hot molding operation and had acquired a slight cough. Over the next few months, the worker developed a typical bronchial cough. Between 1929 and 1932, the coughing gradually worsened. In 1932, he was suddenly taken ill with what the attending physician diagnosed as pneumonia. The author concluded that the condition was actually secondary bronchopneumonia caused by the progressive irritant damage resulting from the prolonged mixed exposure to vapor and dust containing formaldehyde at excessive concentrations. Airborne formaldehyde and dust concentration in the plant were not reported.

Prior to 1945, the bulk of the literature describing the effects of short- and long-term contact of the skin with formaldehyde was published in Germany [30-40]. The dangers resulting from the contact of formaldehyde with the skin and nails were summarized in a review article by Chajes [41] published by the International Labour Office in 1930. Individual differences in susceptibility to formaldehyde were noted. Some individuals adapted to exposure, others became progressively more sensitive. Prolonged use of 2-10% formaldehyde solutions produced eczema on the fingers and hands which were covered with vesicles, fissures, and ulcerations; these could eventually extend to the skin of other parts of the body [41]. Erythematous rash and urticaria were reported in some cases. Chajes mentioned a 1922 report from the Medical Inspector of Factories in Great Britain in which dermatitis was said to appear among workmen polishing celluloid substitutes containing 0.015% formaldehyde. Similar cases arising from the industrial use of dilute (less than 0.5%) formaldehyde solutions and pastes were noted. Fingernails, after prolonged contact with formaldehyde, showed a tendency to become brown, to soften, and to decay, while the skin folds of the fingers became inflamed, with suppuration at the site. In other cases, nails became scaly and friable prior to the appearance of inflammation. Occasionally, the fingertips developed a sensitivity which was accompanied by a "tightening pain," extending up to the arms in some cases.

Effects on Humans

(a) Respiratory Tract Irritation

Respiratory tract irritation has been observed after inhalation [42-54] and ingestion [55,56] of formaldehyde. Irritation after inhalation has produced localized effects in the nose [42-47,57-59], the throat [42-45,47-51], and tracheo-bronchial tree [43,47,48,59]. Cases involving respiratory irritation following ingestion [55,56] were due to invasion of the formaldehyde via the glottis.

Ettinger and Jeremias [44] noted eye, nose, and throat irritation in cutters, sewers, and other employees handling nylon fabric coated with urea-formaldehyde resins. These symptoms were attributed primarily to formaldehyde gas present in the workroom in concentrations of 1-11 ppm and secondarily to the contamination of employees' hands with tiny flakes of resin during handling. In the latter case, subsequent rubbing of the eyes with the hands caused irritation and conjunctivitis. In such cases, flakes which had become imbedded in the skin had to be removed by a physician. They also noted that gaseous formaldehyde was released from the fabric during curing and storage, but airborne concentrations of formaldehyde were not reported. The authors concluded that the ideal method for the elimination of the health hazard was improvement of the curing system to achieve complete polymerization in as short a time and at as low a temperature as possible.

In 1957, Zannini and Russo [48], as part of a study of irritant gases, examined a man who had undergone a single acute inhalation of formaldehyde. The patient complained of dyspnea, asthma attacks, asthenia, weight loss, and nervousness. An initial chest radiograph showed accentuated bilateral bronchiovascular markings. Clinical examination revealed pulmonary edema with diffuse harsh respiration, a 40% decrease in vital capacity, a maximum loss of pulmonary ventilation of 45%, an enlarged left atrium, an accentuated second pulmonary sound, and hyperthyroidism. A second radiograph made 5 months later revealed that the left and right atria and the right ventricle were enlarged. Diaphragmatic hypomobility was also noted at this time. An electrocardiogram showed slight signs of atrial overloading and an intraventricular conduction defect.

Sim and Pattle [46] reported the effects of possible smog irritants on 12 male subjects, all healthy and ranging in age from 18 to 45 years. The men were exposed simultaneously to 13.8 ppm (17.0 mg/cu m) of formaldehyde for 30 minutes in a 100-cu m chamber. No restrictions were placed on their activities; they were allowed to walk around and smoke if they wished to do so. Airborne formaldehyde was generated by bubbling air through a formaldehyde solution. The concentration of formaldehyde in the chamber air was determined as total aldehydes by passing air from the chamber through hydroxylamine hydrochloride at pH 4.5 and determining the amount of HCl liberated by titration with base back to pH 4.5. Formaldehyde at 13.8 ppm produced considerable nasal and eye irritation when the men first entered the chamber, but produced no severe effect despite continued slight lacrimation. The eye irritation was not severe and wore off after about 10 minutes in the chamber. Thus, this study provided some evidence of short-term human adaptation to an irritant stress.

Bourne and Seferian [42] in 1959 reported complaints of burning and stinging eyes, headaches, and nose and throat irritation by customers and employees in several dress shops. The odor was described as suffocating. Complaints were most numerous when the ambient temperature was the highest.

Air sampled in the dress shops was found to contain 0.13-0.45 ppm formaldehyde. Samples of apparel from these same shops contained 5-8 mg of formaldehyde for each 10 g of rayon textiles and 3.4 mg/10 g of cotton, while a wool dress was found to be formaldehyde-free. The authors recommended a ventilation rate of 15 air changes/hour for the shops to remedy the situation.

Glass [49] reported in 1961 that breathing-zone concentrations of 16-30 ppm formaldehyde, as determined by detector tubes, produced irritation of the throat and smarting of the eyes in an unspecified number of the 60 employees in a resin-manufacturing and paper plant. Sixteen workers also had dermatitis with marked erythema of the face and neck. Five of the 16 had edema of the eyelids. Two of these five did not handle the resin but were exposed to both airborne resin dust and formaldehyde gas.

In 1961, Morrill [50] published the results of a study of exposure to formaldehyde in a paper-conditioning installation. Two employees were exposed to airborne formaldehyde released from paper treated with either urea-formaldehyde or melamine-formaldehyde resin. Samples of air taken in the area of the employees' breathing zone contained 0.9-1.6 ppm formaldehyde. No further details as to the number of air samples or the analytical methods used were reported. The employees complained of itching eyes, dry and sore throats, disturbed sleep, and unusual thirst upon awakening in the morning. This report does not take into account, however, the fact that during the work operation one employee stood partially in a ventilated booth housing the paper dryer which may have altered that employee's exposure.

Hovding [45] reported complaints of dryness and irritation of the nose and throat, a burning sensation in the eyes, and itching eruptions of the skin of the face, neck, and forearms in four women exposed to pyrolysis products generated by thermocutting of polyethylene. The four women presented mild dermatitis, primarily in the vicinity of the eyes, and also on the neck and volar areas of the forearms. Formaldehyde and acrolein were identified as two of these pyrolysis products. The employees also noted feelings of drowsiness and headache at the end of the working day. These last two symptoms and the nose, throat, and eye irritation disappeared during absences from the workplace, but recurred on resumption of work. The employees had been engaged in thermocutting for 1.5 years. They had no histories of previous skin diseases. Occasionally, other employees in the room complained of discomfort from the smoke, so that the cutting operation had to be stopped. One woman working next to the cutting machine showed no clinical signs of dermatitis but, along with the four women employed at the thermocutting operation, gave a positive patch test to a 4% formaldehyde solution.

In 1968, Shipkovitz [58] reported the findings of an investigation of eight textile plants in which formaldehyde was released from fabrics treated with formaldehyde-containing resins. Thirty-two samples of air were examined for formaldehyde by drawing air through fritted bubblers containing sodium bisulfite at the same times that air was drawn through 32 detector tubes. All but two of the detector tube samples failed to detect any formaldehyde (limit of detection either 0.5 or 2 ppm, depending upon which tube was used); the two positive tubes yielded results that were considerably different from those obtained with the bubbler samples. Bubbler samples were analyzed for total aldehyde by iodometric titration, using a method which has a limit of detection of 0.5 ppm but which is not specific for either formaldehyde or total aldehyde. Shipkovitz reported airborne formaldehyde concentrations of 0-2.7 ppm, with an average of 0.68 ppm. Annoying odor, constant prickling irritation of mucous membranes, heavy tearing, wheezing, excessive thirst, and disturbed sleep were reported by the employees. Based upon "composite estimates" obtained from plant records, interviews with plant foremen, management, and several employees at each plant, the prevalence of respiratory illness and complaints was over 15% for four plants and 5-15% for the other four. The author [58] also mentioned that upon entering certain plant areas an odor was detected immediately which would decrease in intensity as he spent time in the area, but would occur again the next day. This report of olfactory adaptation to formaldehyde is consistent with the observations of Sim and Pattle [46].

In 1975, Kerfoot and Mooney [52] surveyed six funeral homes using formaldehyde and paraformaldehyde in the embalming process. The average concentrations in the air of the embalming rooms were 0.25-1.39 ppm formaldehyde while the total range for all samples was 0.09-5.26 ppm. Formaldehyde exposures were determined by sampling air at a rate of 1.5 liters/minute through a single midget impinger containing 10 ml of 0.1% chromotropic acid in concentrated sulfuric acid until a purple color was obtained. The color intensities of the sampling solutions were read on a recording spectrophotometer. This method is specific for formaldehyde but may have been in error on the low side because the paraformaldehyde could have dissociated to formaldehyde before collection. No prefilter was used. Separate samples of airborne paraformaldehyde dust were collected with a thermal precipitator, and dust particles were sized microscopically. The airborne dust was found to have a geometric mean particle size of 1.6 μm. The investigators noted eye and upper respiratory tract irritation in some employees at "most" establishments, but this may have been due partly to paraformaldehyde and partly to formaldehyde adsorbed on the dust. The investigators also experienced irritation which wore off within an hour while they remained in the room but reappeared after lunch away from the establishment or upon returning to it on the next day.

The authors also noted that employees other than the embalmers might be severely irritated when entering a room in which an embalmer was working. The investigators suggested that the embalmers become "inured to the vapor" as concentrations gradually increased with time, and that such chronic exposures may contribute to lung diseases. However, they offered no proof for the latter hypothesis.

In a 1966 study [53] of a clothing store, the California Department of Public Health reported airborne work zone concentrations of 0.9-3.3 ppm formaldehyde. The investigators sampled for formaldehyde in air with fritted midget absorbers, containing a solution of 3-methyl-2-benzothiazolone hydrazone hydrochloride (MBTH), for 15-minute periods and analyzed the contents colorimetrically. This method is sensitive to formaldehyde at low concentrations but responds also to other aldehydes. The only aldehyde likely to have been present was formaldehyde. Odors attributed to formaldehyde were noticeable and were accompanied by complaints of mild eye irritation. The investigators postulated that allergies, chronic respiratory diseases, or any preexisting respiratory ailments in employees might be aggravated by such airborne exposures to aldehydes.

The California Department of Public Health conducted another occupational health study [54] in the same year at a textile garment factory where "perma-press" clothing was manufactured. The odor of formaldehyde was readily noticeable to the observers and was accompanied by eye and upper respiratory tract irritation. Air was drawn through Greenburg-Smith impingers containing sodium bisulfite solution. The method of analysis used, given the large volume of air required in using Greenburg-Smith impingers, provided adequate sensitivity but was a measure of total aldehyde. Again, formaldehyde was probably the only aldehyde present. The airborne formaldehyde concentrations ranged from 0.9 to 2.7 ppm. The greatest discomfort, tearing of the eyes and irritation of the nasal passages and the throat were reported by the employees in areas where the largest quantities of partially completed garments were accumulated. The irritant effects were greatest at the beginning of the workday and after the lunch period. Irritation lasted for about 15-20 minutes during these two periods after which the formaldehyde became tolerable. This study reinforces the observations of Shipkovitz [58] and Kerfoot and Mooney [52] that any "acclimatization" to formaldehyde lasted for no more than a few hours and that irritation returned after a 1-2 hour interruption of exposure.

Porter [59] experienced acute respiratory distress after working with formalin. As a neurology resident, he spent 2 hours preparing brain specimens and inhaled high concentrations of formaldehyde gas. The previous week, he had been exposed to formaldehyde gas for 15 hours. After his more recent exposure of 2 hours, he developed dyspnea and tightness of the chest which became progressively worse during a 15-hour period. His wife noticed an odor of formaldehyde on his breath. Immediately before onset of respiratory distress, there were unpleasant effects on the conjunctivas and nasal mucosa. On hospitalization, the patient was dyspneic. A radiograph of his chest was interpreted to indicate an inflammatory reaction in his lungs with early edema. Isolated occasional rhonchi where noted and soft diffuse rales were heard over both lung fields. Porter was known to be atopic to a wide range of allergens, and the respiratory distress could have been due to a hypersensitivity reaction but more likely was an acute chemical pneumonitis provoked by formaldehyde. The author suggested that inhalation of formaldehyde gas may entail serious danger to susceptible individuals.

In a study reported by both Yefremov [47] and Zaeva et al [51], 278 employees working in wood-processing plants were examined medically. One hundred twenty-nine (78%) were found to have signs of upper respiratory tract irritation, including hypertrophic, inflammatory, subtrophic or atrophic rhinitis. Airborne formaldehyde concentrations of 2.6-11 mg/cu m (2.1-8.9 ppm), with a maximum of 36.3 mg/cu m (31.2 ppm), produced illness in 39.1-66.2% of those exposed. [51] Airborne formaldehyde concentrations of generally 0.6-4.1 mg/cu m (0.5-3.3 ppm), with a maximum of 8.8 mg/cu m (7.1 ppm), produced an illness rate of 14.6-37.5% [51]. A control group of 200 individuals of corresponding ages had an incidence of respiratory catarrh of 8.9% [51]. Yefremov [47] further noted that signs of chronic respiratory tract irritation were most pronounced in persons 30-59 years of age and in those who had worked for less than 5 years. He further noted that pronounced morbid states developed from inflammatory phenomena in the mucosa of the upper respiratory tract consequent to inhalation of formaldehyde vapor. Initial signs indicating onset of inflammatory pneumonia were: (1) increased travel time of carbon particles from the nares to the nasopharynx (2) more rapid absorption of noratropine from a tampon inserted into the nasal cavity, and (3) decreased olfactory activity for such substances as rosemary, thymol, camphor, and tar.

Zaeva et al [51] also mentioned a study by A. K. Sgibnev without stating where the original information was published. Sgibnev's study reported that particularly sensitive individuals exposed to 1 mg/cu m (0.8 ppm) formaldehyde developed irritation of the mucous membranes of the upper respiratory tract and eyes, respiratory disorders, changes in the function of the autonomic nervous system and enhancement of the alpha-rhythm of the EEG. All perceived the odor.

In 1971, Kratochvil [43] evaluated the health status of employees engaged in the processing of textiles impregnated with urea-formaldehyde and melamine-formaldehyde resins. Airborne formaldehyde concentrations in the workshop did not exceed 5 mg/cu m. The employees complained of irritation of the conjunctivas, nasopharynx, and skin. Objective findings were catarrhal conjunctivitis in 72% of the employees, inflammatory rhinitis in 28%, slightly reddened, dry facial skin in 11%, and chronic bronchitis in 22% of the employees. The author stated that the frequency of occurrence of bronchitis did not differ from that in the general population.

(b) Gastrointestinal Irritation

Ingestion of formaldehyde solutions has caused irritation [55,56,60-62] and damage [55,56,61,62] to the tissues of the gastrointestinal tract and has been responsible for at least 13 deaths [15,21,26,55].

Rathery et al [55] reported in 1940 that a 27-year-old man died 45 minutes after the drinking of 150 cc of 40% formaldehyde. Death was caused by edema of the glottis and by consequent asphyxia despite medical efforts to save the victim. At autopsy, intense edema and congestion of the pharyngeal, laryngeal, esophageal, and gastric mucous membranes were apparent. Multiple congestions and hemorrhagic suffusion were noticed in all viscera and serous membranes, as well as in the heart and lungs.

Roy et al [56] observed the effects produced by ingestion of 240 ml of 37% formaldehyde in a 41-year-old man. Because of severe stomach pains, the man reported to the hospital within 45 minutes of the draft. Ulcerations were noted in the oropharynx and hypopharynx, and the epiglottis was red and edematous. A tracheostomy was done on the day of admission. The patient was subsequently released, but was readmitted about 6 weeks later because of excessive vomiting, loss of weight, and weakness. Because of stenosis and gastric lesions produced by chemical corrosion, a subtotal gastrectomy was performed, and the duodenum was connected to the small portion of the healthy fundus that remained. The patient recovered but subsequently complained of regurgitation and difficulty in swallowing.

In 1941, Yonkman et al [60] described giving two male subjects 22 mg of pure formaldehyde in water/day for 14 days. Thereafter, every 7 or 14 days the dosage was increased until a dose of 200 mg/day was consumed during the 13th week. Periodic blood samples revealed no significant changes in the concentration of hemoglobin in the red and white cell counts, or in the appearances of these cells. All urine specimens were negative when tested for free formaldehyde and albumin by unspecified methods. One subject complained of mild gastric and pharyngeal discomfort when the formaldehyde reached a concentration of about 0.029%; another voiced similar complaints when a concentration of about 0.04% was attained. This discomfort was alleviated by dilution. The authors also commented that the feeding of formaldehyde-containing foods to rats confirmed the low oral toxicity of this aldehyde.

Corrosive gastritis caused by the accidental ingestion of 100 cc of a solution of formaldehyde was reported by Heffernon and Hajjar [61] in 1964. Severe epigastric pain occurred immediately after ingestion and the patient collapsed. He awakened several hours later, vomited blood, and passed black stools. Following hospitalization, his general condition improved, but dysphagia continued and he suffered a progressive weight loss of 50 pounds. A subtotal gastrectomy was performed and microscopic study of the specimen confirmed an extensive chemical corrosion of the distal part of the stomach. The patient gradually improved and was discharged, but later had to be treated for a stricture in the esophagus.

In 1968, Bartone et al [62] performed a total gastrectomy on a woman 3 months after she ingested an estimated 120 cc of a 10% solution of formaldehyde. There was an extreme degree of gastric shrinkage, tissue damage, and contracture.

(c) Effects on the Eye

Exposure to airborne formaldehyde [42-47,49-54,63,64] or to airborne dusts carrying absorbed formaldehyde or composed of formaldehyde-yielding materials [44,49,52] has been shown to produce not only respiratory irritation [42-47,49-54] but ocular damage as well. Saury et al [63] observed a case of optical atrophy in a worker employed in a textile factory producing resin-coated fabrics. Ophthalmoscopic examination showed a bilateral papillitis with congestion, but without any edema of the papilla. The condition resulted in repeated short episodes of blurred vision. The authors commented that this optic neuritis was difficult to attribute to occupational intoxication, but that a toxic etiology appeared to be the only one that could be considered seriously.

Schuck et al [64] reported a study of the ocular effects of low concentrations of smog components generated by the photooxidation of either ethylene or propylene within a 520-cu ft smog chamber with welding masks mounted in its sides to allow exposures of human eyes to the atmosphere within the chamber. Formaldehyde concentrations were determined by a modified chromotropic acid procedure, specific for formaldehyde, with a sensitivity of 0.01 ppm. The subjects reported their feelings of eye irritation in terms of 4 standard descriptions during 5-minute exposures. Exposure to the photooxidation products of ethylene caused somewhat more eye irritation at a given concentration of formaldehyde in the air of the chamber than to those of propylene. The concentration-response relation for subjective irritation of the eyes was linear for propylene oxidation products but became linear for ethylene oxidation products only after concentrations of formaldehyde exceeded 0.3 ppm. The subjects were said to experience equivalent irritations at formaldehyde concentrations of 0.05 and 0.5 ppm. The differences between concentration-response curves for formaldehyde in the presence of the photoxidation products of ethylene and propylene emphasize the importance of other components in the gas mixtures studies. The blinking rate of the eyes, which was used as an objective measure of irritation, was variable for any given subject and passed through several cycles of waxing and waning during a 5-minute exposure period. The authors further reported that the eyes of human subjects could readily detect, by the sensation of irritation, some gas mixtures containing as little as 0.01 ppm formaldehyde.

(d) Skin Effects

Two skin hazards are associated with exposure to formaldehyde: primary irritation [65,66] and allergic dermatitis [43,45,49,67-83]. Primary irritation has resulted from direct skin contact with formaldehyde solutions [65, 66], and exposure to gaseous formaldehyde [65]. Allergic dermatitis has been produced by direct skin contact with formaldehyde solutions [65,68,71, 73,74,78,79], the handling of formaldehyde-containing textiles [67,69,76,77,80, 81,83], skin contact with formaldehyde from formaldehyde-containing resins [44,65,72,75,82], and exposure to gaseous formaldehyde [43,45,49,65,79,84].

Cases involving primary skin irritation by contact with formaldehyde or its formulations include a case of hyperkeratotic palmar and plantar eczemas in a 63-year-old seamstress who ironed permanent-press cloth with a steam iron [66], dermatitis in a hairdresser who used a hair-waving solution containing 3% formalin (about 1% formaldehyde) [65], red and blistered hands in a pathologist [65], and an irritant dermatitis in fourteen workers using a vegetable glue containing 0.25 - 1% formalin (.09 - .4% formaldehyde). One glue worker after 0.5 - 1 year of exposure became so sensitized that inhaling formaldehyde caused a recurrence of her dermatitis [19]. Patch testing of these people with 4% formalin (1.5% formaldehyde) produced positive reactions. In addition, the seamstress reacted positively to permanent press cotton cloth and reacted slightly to permanent press wool cloth [66]. Pirila and Kilpio [65] also reported observing an irritant dermatitis in two lithographers who handled egg-albumin solutions containing formalin as a preservative. In these incidents of primary skin irritation, repeated exposures to formaldehyde led to development of hypersensitivity in some individuals.

In 1934, Horsfall [79] presented the results of a detailed study of the effects of formaldehyde on a single hypersensitive individual. He investigated cutaneous hypersensitivity, specificity of sensitivity to formaldehyde, cutaneous hypersensitivity reactions after the inhalation of formaldehyde, humoral manifestations, and cutaneous hypersensitivity to formalinized proteins. Following intradermal injections of 0.02 cc, the back of the hand in the subject was found to respond to solutions as dilute as 1:8,000,000 while the skin of the forearms reacted only to solutions of 1:4,000,000 or less dilution. Aqueous and saline solutions of formaldehyde produced nearly identical results. Horsfall observed a latent period of 15-40 hours between injection and response, which in general was directly related to the amount of formaldehyde injected but had a long plateau between dilutions of 1:640,000 and 1:20,000. In addition, the effects of immersing fingers of either hand, singly or in a pair, in solutions as dilute as 1:8,000,000 were investigated. Here, the greatest dilution producing a positive response was 1:5,000,000 for both the aqueous and saline solutions; latent periods were 16 and 20 hours, respectively for these two solvents. Four control subjects did not react to intradermal injections of 0.02 cc 1:10,000 formaldehyde solutions and three controls had no positive responses to immersion in a 1:1,000 solution. Tests using similar procedures for evaluation of sensitivity to acetaldehyde, propionaldehyde, and paraldehyde produced no positive reactions. In addition, immersions of fingers in solutions of formic acid, hexamethylenetetramine, and methanol failed to elicit any positive reaction. Positive reactions were defined as papules greater than 3 mm in diameter after intradermal injection and swelling of the skin of the finger or fingers, circumferential erythema and itching, and vesiculation after immersion.

Rostenberg et al [68] reported the development of eczematous sensitivity to formalin in five nurses after 2-3 months of handling thermometers kept immersed in a 10% solution of formaldehyde. Papules and vesicles developed on the fingers and, in a few, on the face. When use of the formaldehyde solution was discontinued, the nurses reported no further trouble. Positive sensitivity reactions to formaldehyde were obtained in all five subjects using patch-testing with formaldehyde solutions from 0.2 to 5% in concentration. The smallest concentration of formaldehyde inducing a positive response was 0.5%; all 5 nurses gave positive responses to formaldehyde at a 5% concentration. Four of the subjects also showed positive reactions after intradermal injections of formaldehyde solutions and formalinized protein. The fifth nurse was not tested in this way. The reactions to injections of formalinized proteins were less pronounced than those to a solution of formaldehyde believed to contain aldehyde in a concentration equal to that in the solution of formalinized human serum albumin.

A case report involving a severe reaction to the formaldehyde component of a nail hardener was published by Lazar [71] in 1966. The distal phalanges in a 58-year-old woman became edematous, red, and scaling, and a bluish discoloration could be seen through the nails. The severe reaction first appeared 2 days after a chemical nail hardener had been applied by a manicurist; no other skin trouble was present. Patch tests with the nail hardener and a 5% aqueous solution of formaldehyde were both positive, producing edema, erythema, and vesiculation. Patch tests with nail polish were negative. Two control subjects did not react to any test materials. The author [71] subsequently observed five other people with similar fingernail damage who had positive reactions to nail hardeners containing formaldehyde. Danto [73] reported a similar effect in a woman whose fingernails became opaque with subungual hyperkeratosis and distal separation from the nail bed following the use of a formaldehyde-containing hardener.

Sneddon [74] reported the outbreak of a sensitization dermatitis in 6 of 13 members of a nursing staff working in a hemodialysis unit. A 2% formalin solution was used daily to sterilize the open tanks in which the dialysis solution was prepared. The solution was allowed to stand in the tanks for several hours, during which considerable formaldehyde gas was released into the air of the room. Six months after the opening of the unit, the first case occurred, followed by five others within an unspecified number of weeks. The dermatitis affected the face, neck, arms, and hands. Patch tests with a 3% formalin solution were positive for three of the five nurses; one who did not react when patch tested, later suffered a severe reaction upon accidental exposure, which according to Sneddon confirmed her sensitivity to formaldehyde. With substitution of another sterilizing agent for formalin, all skin lesions attributable to formaldehyde improved. The nurses may have received a mixed cutaneous and inhalation exposure. The type of exposure which was primarily responsible for the observed dermatitis cannot be absolutely identified, but exposure to gaseous formaldehyde seems to be the most likely cause.

Guyot [78] reported that the use of a formaldehyde solution of unknown strength applied to the pulp cavity of a tooth of a 9-year-old boy led to urticaria which disappeared on removal of the solution by flushing the cavity.

Exposure to gaseous formaldehyde [43,45,49,65,74,79] has been implicated as a cause of allergic skin reactions in sensitized people. Lesions observed included drying and reddening of the skin of the face, neck, or arms [43,65,49], and itching eruptions of the face, neck, arms, or hands [45,65,74,79]. In yet another study, Harris [84] reported a tingling of the face and lips with a rapid development of an acute papulovesicular eczema of the whole face, the neck, and the elbow flexures, with subsequent edema of the eyelids and lips, in a man engaged in the breaking up lumps of a urea-formaldehyde resin. The condition developed after exposure to an atmosphere containing about 30 ppm formaldehyde and recurred after he returned to work.

Individuals sensitized to formaldehyde have been shown to develop allergic contact dermatitis from textiles treated with formaldehyde containing resins [67,69,76,77,80,81,83]. In most cases [67,76,80,81], patients reacted positively to patch tests performed with the resin-treated textiles which were the apparent cause of their dermatitides. In two studies [69,77], patch tests with the textile were negative, but patch tests with formaldehyde were positive. Subjects with latent hypersensitivity to formaldehyde, or with sensitivity to formaldehyde due to causes and sites of application not related to textiles, did not react to the swatches but did react to formaldehyde itself [81].

In contrast to results reported by Peck and Palitz [76], Fisher et al [77] reported in 1962 that formaldehyde-sensitive individuals (12 women and 8 men) did not show any positive skin reaction when patch tested with textiles and paper containing free formaldehyde. Samples of various textiles and papers which had been impregnated with certain formaldehyde resins were tested for free formaldehyde using a method advocated by Marcussen [85]. The resins consisted of urea-formaldehyde, melamine-formaldehyde, and phenol-formaldehyde polymers. All tested samples contained free formaldehyde according to this analytical method.

In 1964, Berrens et al [69] reported analyses of over 600 samples of clothing from patients with nonoccupational formaldehyde contact dermatitis who gave positive patch tests with solutions of 3% free formaldehyde. Very sensitive patients gave positive patch test reactions to 0.3% formaldehyde and some even to 0.03%. Samples of the fabrics were used for patch tests and also for estimation of formaldehyde content. Nearly 57% of the samples contained less than 0.05% free formaldehyde. Patch tests with these samples were negative. Withdrawal of the clothing made from cloth containing free formaldehyde was followed almost always by disappearance of the dermatitis, however. The authors concluded that patch testing using patients clothing found to contain free formaldehyde is of little clinical value.

O'Quinn and Kennedy [67] noted three cases in which diagnoses of contact dermatitis due to formaldehyde in textiles were established, using the criteria proposed earlier by Fisher [77], the paper or fabric was shown to contain free formaldehyde, the patient gave a positive patch-test reaction to 2-5% formaldehyde a positive patch test was obtained with the formaldehyde resin-impregnated material, and the use or wearing of the fabric or tissue produced clinical dermatitis [67].

In 1966, Shellow and Altman [80] reported the single case of an adolescent man with a 2-year history of a pruritic eruption which began in the antecubital fossae and gradually spread to involve the trunk, extremities, and face. The patient had a history of hay fever and of allergic reactions to 50 commercial allergens. Textiles in his clothing contained free formaldehyde. Although patch tests with some of these textile samples gave positive reactions, others did not.

Skogh [83] noted that 19 cases of formaldehyde eczema in women due to wearing permanent press clothing were all of axillary eczemas. The patients often suffered from recurrences of their conditions, which sometimes spread to other parts of the body. The author reported one typical case in detail. This started with itching under the arms, shortly thereafter, the axillary skin became covered with a weeping, papular rash.

These localized effects reappeared intermittently for about 1 year. Three years after onset, the eczema still persisted and had spread to other areas of the body.

In 1944, Keil and Van Dyck [72] studied 26 cases of nail polish dermatitis in which patch tests with toluene sulfonamide-formaldehyde resin, melamine-formaldehyde resin, toluene sulfonamide-formaldehyde dimer, toluene sulfonamides, and formic acid were performed. The toluene sulfonamide-formaldehyde resin was applied as a 30% solution in acetone. Although no primary irritation occurred in 15 control subjects, 25 of the 26 subjects with a history of nail polish dermatitis gave intense positive patch tests to the toluene sulfonamide-formaldehyde resin; 10 of 11 reacted positively to the malamine-formaldehyde resin, but less vigorously than to the toluene sulfonamide-formaldehyde one. Of 11 subjects with nail polish dermatitis, 8 reacted to the toluene sulfonamide-formaldehyde dimer. By comparison 7 of 16 gave definitely positive reactions to toluene sulfonamide, while only 1 of 13 subjects showed a mild primary irritation to formic acid. These last data are at variance with the idea that hypersensitivity to formaldehyde depends on formation of formic acid.

Kamchatnov and Gayazova [86] studied thermal asymmetry (right side vs left side), measurements of the temperature of the surface of the skin being made on the forehead, the chest, and the forearms, in 99 women, aged 25-40, working in the formalin-using departments of a sheepskin-dyeing factory. An aqueous solution containing 40% formalin solution (500 ml/l), ethanol (250 ml/l), and monochloroacetic acid (40 ml/l) was painted on the sheep skins, which were then calendered with rollers heated to 190-210 C. The air in the breathing zone of the women contained not only gaseous formaldehyde (5-78 mg/cu m) but also methanol vapor (2.1-7.5 mg/cu m), and ethanol vapor (47.5-110 mg/cu m). In the exposed group of workers, before the start of a shift, 8.3% of the women had equal overall skin temperatures on the two sides of their bodies, 43.3% had "physiological" temperature asymmetry (difference of 0.1-0.5C), and 48.4% had "morbid" asymmetry (difference of 0.6-2.2C). Corresponding percentages for the control group were 69.8%, 27,2%, and 3.0%, respectively. At the end of the shift, the percentages for these types of temperature asymmetry were 7%, 33%, and 60% for the exposed group and 56.9, 34.5, and 8.6% for the control group. These values indicate that exposed women had 3 times the incidence of preshift asymmetry when compared with the controls but that exposure during the shift had a greater proportional effect in shifting workers from the symmetric to the asymmetric state in the control group than in the exposed but produced a greater absolute shift in the exposed group than in the control. Kamchatnov and Gayazova attributed these differences to CNS effects, and complaints of persistent headache, vertigo, and a tendancy to weep were probably related to CNS disturbances as well. No evaluation of possible contribution by methanol or ethanol to the observed effects appears to have been attempted.

Kachlik [87] described an episode involving 63 cases (5.25% of the total number of employees) of occupational skin disorders and irritation of the upper respiratory tract which developed within a 1-year period among employees in a plant processing mainly crease-resistant materials. Complaints were a tightness in the skin, pruritus (particularly of the face), and burning of the eyes and tongue. Redness of the skin and face, swelling of the eyelids, irritation of the throat, and irritation of the nasal mucosa were evident. Free formaldehyde was detected in the fabrics, lint from which often covered the workers clothing and exposed skin by the end of their shift.

In 1964, Frenk [82] reported the simultaneous appearance in 26 of 120 foundry employees of itching red macules, sometimes with wheal and flare, in or near. the areas of skin rubbed by the clothes. Appearance of these eruptions coincided with periods of inadequate ventilation of the workshop. Frenk thought it likely that these eruptions arose from a combination of mechanical irritation from the foundry dust and a chemical irritation from formaldehyde emanating from furan resins. Both the air and the dust of the foundry were found to contain free formaldehyde.

Logan and Perry [75] reported in 1973 six cases of allergic contact dermatitis from plaster casts containing a melamine-formaldehyde resin. In four of the six patients, a skin reaction developed within 7 days after the application of the resin-containing plaster. In the other two cases, four weeks passed before signs and symptoms developed. The patients all gave positive reactions in patch tests with formaldehyde-containing resins.

Of the numerous additional studies of dermatitis which involved the use or handling of formaldehyde-containing resins [49,70,72,82,88-91], few implicated free formaldehyde as the primary causative agent [49,65,75, 82]. Most concluded that either the parent resin [44,65,70,88-91] or some other substance was the primary causative agent [70,72,82,88,91].

(e) Thresholds of Response

Responses by people to formaldehyde have been by its odor [42,57,58,92-94], upper respiratory tract irritation [42,50, 58], eye irritation [42,46,58,64], and changes in cerebral electrical activity [57,93]. Further, the perception of formaldehyde by odor [58] and eye irritation [46] have been shown to become less sensitive with time as one adapts to formaldehyde.

Aside from the reports described previously [42,58], Leonardos et al [94] have defined the formaldehyde odor threshold to be 1.0 ppm using an odor panel. This threshold represents the lowest concentration to which all 4 trained panelists, selected from a pool of 15 experienced odor panelists, responded positively. At least five different concentrations of formaldehyde were tested.

Freeman and Grendon [92] investigated two laminating plants using four different phenol-resorcinol glues which released formaldehyde upon curing. Air samples were collected at each plant on different days between May 1968 and July 1969 using their modification [92] of the chromotropic acid method following collection of formaldehyde in a fritted gas bubbler containing distilled water. Using a 30-minute sampling period and the modified method, airborne formaldehyde concentrations of 0.04-8 ppm could be determined. Increasing sampling time allows determination of lesser concentrations. Formaldehyde concentrations were 0.04-4.2 ppm in the first plant and 4.2-10.9 ppm in the second. The concentrations varied as a function of the operation of the process at different times of day and of the specific glue being used. The authors reported that employees objected whenever the airborne formaldehyde concentration exceeded 1 ppm, and that the odors in areas found to contain 4.2-10.9 ppm were considered to be unbearable without respiratory protection.

Melekhina [57] subjected 12 persons, aged 19-64, to breathing of various concentrations of formaldehyde in studying the odor threshold and the effects of formaldehyde on the central nervous system. The gas was generated from a glass aspirator, containing 5 ml of formalin through which air was blown. The volume of liquid within the aspirator was kept constant by replacing the formalin as it evaporated. Formaldehyde concentrations were verified by collection into water in a U-shaped fritted absorber followed by spectrophotometric measurement of the chromophore formed with chromotropic acid. Optical chronaxie determinations were made by using a chronaximeter every 3 minutes during a 15-minute period of breathing formaldehyde-containing air. Optical chronaxie, expressed in microfarads, was measured by the duration of an electrical discharge at a voltage twice the rheobase required to produce the sensation of a flash of light. The airborne formaldehyde concentrations varied from 0.07-1.59 mg/cu m (0.06-1.29 ppm) for each of a large series of tests. Formaldehyde at 0.068 to 0.075 mg/cu m had no effect on rheobase or chronaxie. At 0.084 mg/cu m (0.07 ppm), formaldehyde decreased the chronaxie in two test subjects and increased it in one. Maximal changes for these subjects occurred after breathing formaldehyde-containing air for 9 minutes. This formaldehyde gas concentration decreased the electrical chronaxie from 0.06-0.23 μF. The most pronounced changes were noted at concentrations of 0.2 and 1.59 mg/cu m (0.16 and 1.29 ppm), but for the 3 subjects for whom data are available, two had decreases of 0.10 and 0.22 μF at 0.2 mg/cu m, and of 0.08 and 0.23 μF at 1.59 mg/cu m, whereas the third had increases of 0.09 and 0.39 μF at these two formaldehyde concentrations. The odor panel tests established that 0.11 mg/cu m (0.09 ppm) was the threshold concentration for odor perception of formaldehyde gas for all the test subjects.

In another experiment, [57] the same 12 individuals adapted to a dark, noise-free, odor-free environment during a 5-day training period. Initial curves of responses in receptors in the upper respiratory passages were established for the inhalation of fresh air. They were then exposed to 0.06, 0.07, 0.098, 0.2, 0.3, and 1.7 mg/formaldehyde gas/cu m of air for 4-5 minutes. Under these conditions, the threshold of perception of formaldehyde by odor was 0.07 mg/cu m for all the subjects. The sensitivity of the eyes to light was increased in 2 subjects by formaldehyde at 0.098 mg/cu m, and was decreased in all 3 subjects tested by formaldehyde at 0.25 to 1.7 mg/cu m.

Fel'dman and Bonashevskaya [93] reported the biologic effects of low airborne concentrations of formaldehyde on humans and rats in 1970. Methods of generation and measurement of formaldehyde concentration were the same as those used by Melekhina [57]. Effects on humans were evaluated by determining olfactory thresholds and changes in cerebral biopotentials. Fifteen healthy human subjects were exposed to formaldehyde at four concentrations between 0.054 and 0.09 mg/cu m. After numerous observations, seven subjects were found to be unable to detect 0.054 mg/cu m of formaldehyde by odor but were able to detect 0.073 mg/cu m of formaldehyde. Four other subjects were unable to detect 0.074 mg/cu m of formaldehyde but were able to detect 0.08 mg/cu m of formaldehyde. The remaining four subjects did not smell 0.08 mg/cu m but could detect 0.09 mg/cu m of formaldehyde. The five most sensitive subjects, as determined by the olfactory threshold tests, were monitored by an EEG during further exposures. A concentration of 0.053 mg/cu m produced statistically reliable ($p \pm 0.05$) changes in cerebral electrical activity in all the subjects, whereas 0.04 mg/cu m produced no effects in any of the subjects. The odor threshold measurements of these authors agree reasonably well with those of Melekhina [57], but EEG appears to be a more sensitive indicator of an effect than either optical chronaxie or the sensitivity to light of a dark-adapted eye used by Melekhina.

Epidemiologic Studies

Several epidemiologic studies involving formaldehyde have described and enumerated cases of dermatitis [84,95,96,97] and upper respiratory tract irritation [47,51,58].

In 1936, Schwartz [95] reviewed the occurrence of dermatitis in the manufacture of synthetic resins. Both phenol-formaldehyde and urea-formaldehyde resin-manufacturing processes described in a companion paper [98] were investigated. Schwartz described one phenol-formaldehyde factory with about 400 employees, where 27 (7%) cases of dermatitis occurred in an 8-month period. Patch tests with powdered hexamethylenetetramine and a 4% formaldehyde solution were positive for 8 of the 10 employees tested from among the 27 cases. Schwartz observed that the dermatitis was more prevalent in winter because then employees did not shower after their shifts. In a urea-formaldehyde resin manufacturing plant, Schwartz reported four (2%) cases of dermatitis, all due to hypersensitivity to formaldehyde, among 190 employees during a 2-year period. In a urea-formaldehyde resin-molding plant, 26 (9%) cases among 300 employees were reported in 10 months of 1934. Half the employees in another urea-formaldehyde resin-molding plant were said to have developed dermatitis in the hot months of 1935. Schwartz believed the observed dermatitis in such cases was due to a mixed exposure involving skin contact with the resins and the inhalation of gaseous formaldehyde. Poor ventilation, poor housekeeping, and a lack of personal cleanliness were also contributing factors.

In a 1943 report based upon studies of seven plants using either urea-formaldehyde or phenol-formaldehyde glues for laminating wood or fabrics, Schwartz et al [96] summarized their observations regarding resin glue dermatitis. They concluded that the actual cause was complex and that formaldehyde may have been only one of many factors in some cases. In one factory laminating plywood for planes and gliders, 600 (75%) cases of glue dermatitis occurred among 800 employees during the first 6 months of operation. In a factory making tool handles using a phenol-formaldehyde glue, 40 (40%) cases of dermatitis occurred among 100 employees during the first 6 months of operation. No incidence ratios were indicated for the other five plants.

In 1943, Markuson et al [97] studied four industrial plants employing 2,370 employees, 355 (15%) of whom had developed dermatitis because of skin contact with phenol- and urea-formaldehyde resins. The onset of dermatitis usually occurred 3-6 weeks after the initial exposure to the formaldehyde-containing resins. The large majority of employees developed a mild-to-moderate form of dermatitis, characterized by a fine rash, an itching sensation, and redness of the skin. The rash occasionally extended beyond the initially involved area. Recurrence of the same type of dermatitis was common. If contact with the resinous material continued, the exposed skin surfaces, which were already irritated, were subjected to further injury, and a more severe type of dermatitis resulted. Regional distribution was as follows: face, 70%. side of the neck, 73%. chest, 32%, back, 19%, abdomen, 10%, forearms, anterior surface, 72%, posterior surface, 65%, hands, anterior surface, 54%, posterior surface, 62%, legs, anterior surface, 31%, posterior surface, 32%. The investigators concluded that the distribution of the dermatitis on the body surface gave direct evidence of areas in contact with the material while working, or areas touched by hands coated with the resin. Some individuals reportedly developed a mild-to-severe form of skin rash which later subsided. On continued contact with the resinous material, such individuals generally did not develop dermatitis. The investigators concluded that, if workers should "lose their immunity" at some later period and develop severe dermatitides, the resulting incapacitation would require removal of the employee from working with resins. Occasionally, individuals were reportedly sensitive to formaldehyde itself, so that small amounts of formaldehyde emitted from the resin may have caused the dermatitis. However, the cause of this type of dermatitis, characterized by edema about the eyes and face and marked redness of the face, was not verified by the investigators, but the explanation presented above is consistent with the observations of Harris [84].

Harris [84] reported four (16%) cases of dermatitis among 25 men employed in a small factory manufacturing urea-formaldehyde resin. All 25 had been employed for a minimum of 5 years. All airborne formaldehyde concentrations in the plant were said to be below 30 ppm while in most parts of the plant concentrations were well below 10 ppm, but no details of the type or number of samples or of the analytical method were given. The 25 men had chest radiographs, complete blood counts, and blood pressure readings. Radiographs were completely normal in 14 (56%), signs of old pulmonary lesions were evident in 6 (24%), cardiac enlargement in three (12%), and increased vascular shadows in two (8%). White blood cell counts were elevated in six (24%) men, but those for five of these men (20%) had returned to normal upon recheck. Four of the men complained of mild dyspnea, but one of these had hypertension (blood pressure of 160/115) and another had suffered from asthma for several years.

In 1968, Shipkovitz [58] published the results of a study of eight textile plants in which formaldehyde was released from fabrics treated with formaldehyde-containing resins. Thirty-two samples for formaldehyde in air were taken with fritted bubblers containing sodium bisulfite and 32 detector tube samples were collected at the same locations. All but two of the detector tube samples failed to detect any formaldehyde (limit of detection either 0.5 or 2 ppm, depending upon which tube was used) and the other two gave considerably different estimates of the concentration of formaldehyde than those obtained from the bubblers. The bubbler solutions were analyzed for total aldehyde by iodometric titration using a method which had a limit of detection of 5 ppm. Airborne formaldehyde concentrations of 0-2.7 ppm, with an average of 0.68 ppm, were reported. Complaints of annoying odor, constant prickling irritation of mucous membranes, heavy tearing, wheezing, excessive thirst, and disturbed sleep were noted. Based upon "composite estimates" obtained from plant records, interviews with foremen, management, and several employees at each plant, the prevalence of respiratory illness and complaints were over 15% at four plants and 5-15% at the other four. The author [58] also mentioned an immediate perception of odor upon entering certain plant areas. Perception would diminish as he spent time in the areas, but would increase again the next day. This account of olfactory acclimatization is consistent with the observations of Sim and Pattle [46].

Other epidemiologic investigations which have been discussed previously under skin effects were the Kerfoot and Mooney [52] survey of funeral homes, the two studies by the California State Department of Public Health [53,54] on formaldehyde in the garment industry, and the Yefremov [47] and Zaeva et al [51] studies of a wood-processing industry.

Animal Toxicity

(a) Metabolism and Retention

Pohl [99] in 1893 administered formaldehyde subcutaneously (sc) to a dog, and sodium hydroxy methane sulfonate, which hydrolyzes to formaldehyde in alkaline solution, also sc, to another dog, and measured the formate excreted in the urine before and after the doses. The first dog excreted excess formate equivalent to about 2.4% of the formaldehyde dose as formate, and the second dog excreted 4% of its potential dose of formaldehyde as formate. There is an apparent minor oxidation of formaldehyde just to formic acid in the dog. In vitro, liver (horse and pig) was found to have a slight ability to oxidize formaldehyde but skeletal muscle (dog) did not. Lutwak-Mann [100] in 1938 and Kendal and Ramanathan [101] in 1952, using in vitro liver preparations, observed that formaldehyde can undergo dismutation to form formic acid and methanol. Malorny et al [102] verified the oxidation to formic acid and formates in vivo in dogs. The latter investigators [102] also showed the possible involvement of liver aldehyde dehydrogenase and nicotinamide adenine dinucleotide (NAD) in this oxidation and further esterification to methyl formate. In vitro experiments [102] with human blood showed that formaldehyde was quickly oxidized to formic acid after its absorption by erythrocytes.

According to Williams [103], the major route of biotransformation of formaldehyde in the body is oxidation to formic acid. He further characterized formaldehyde as a compound which reacts rapidly with the amino groups of proteins and amino acids and presented a plausible scheme of metabolic reactions of formaldehyde. Figure XII-1 shows such a scheme.

In 1972, Egle [104] published a study of the retention of inhaled formaldehyde in which tracheotomized and untracheotomized mongrel dogs were exposed to formaldehyde at 150-350 ppm in an effort to determine the retentions of formaldehyde in the upper, the lower, and the entire respiratory tract. Formaldehyde gas was generated by forcing air through a formaldehyde solution at room temperature. Samples of gases were analyzed for formaldehyde by the colorimetric method of Sawicki et al [105], using 3-methyl-2-benzothiazolone hydrazone hydrochloride, modified by the addition of sulfamic acid in the oxidizing step [106]. The experiments involved animals inhaling via the nose, through a tightly fitted rubber mask for total-tract experiments and via an endotracheal tube for the lower-tract experiments, and from a spirometer. The animals exhaled into a collection bag. The two types of upper-tract experiments involved severing the trachea just above the bifurcation and passing dilute formaldhyde gas from the spirometer through the tract to this point by means of a mask. In the "1-way" experiments, the vapor passed into a collecting bag at the lower end of the trachea and was not returned, whereas in the "2-way" experiments the vapor was returned upward by means of a 2-liter syringe attached to the lower end of the trachea. At least four dogs were used in each type of experiment.

The total-tract retention was nearly 100% regardless of the ventilatory rate, formaldehyde concentration or tidal volumes measured. In the 2-way upper tract retention studies, the uptake of formaldehyde was 100% at all rates. The retention of formaldehyde was slightly lower with a single pass through the upper tract, but still exceeded 95%. The results of exposure of the lower tract alone showed over 95% uptake of formaldehyde. Thus, for the range of concentrations studied, both the upper and the lower parts of the respiratory tract were shown to be effective absorbers of formaldehyde.

(b) Acute Exposures

The LD50 for formaldehyde was shown by Skog [107] to be 300 mg/kg in mice, and 420 mg/kg in rats following sc injections of 150-460 mg/kg in 72 mice and 300-640 mg/kg in 64 rats. Skog further found the LC50 of formaldehyde for rats to be 1000 mg/cu m (810 ppm) air based upon 30-minute exposures at 600-1,700 mg/cu m (490-1400 ppm) in a total of 72 rats. These values were determined in groups of eight animals for each dose (mg/kg body weight or mg/cu m of air). The exposure time for inhalation was 30 minutes. The animals were kept under observation for up to three weeks after completion of exposures. Determinations for gaseous formaldehyde in air were made as total aldehydes, using a method based on the sodium sulfite reaction. The formaldehyde solutions used had the following concentrations: for injections, 35.5% for rats and 2% for mice; for inhalation, 35.5% for rats and mice.

With subcutaneous administration, the animals became listless and showed lacrimation and increased secretion from the nose. Respiration was accompanied by a whining and rattling sound; with each breath the animals gaped and turned their heads backward. All deaths of rats occurred within 68 hours, and those of the mice within 20 minutes. The survivors recovered after 2-3 days. Autopsy findings were bronchitis and slight pulmonary hyperemia with small hemorrhages and edema being visible around some vessels. Hyperemia was noted in the liver and kidneys also, with no changes in other organs.

Signs which appeared after SC administration appeared also after inhalation and were considerably more pronounced. Respiratory difficulty lasted several days after exposure and, in some rats, for as long as 2 weeks afterwards. The last death occurred on the 15th day after the exposure. Microscopic changes in the lungs included hemorrhages and intra-alveolar and perivascular edema. Hyperemia, perivascular edema, and necroses were found in the livers; perivascular edema was found in the kidneys. No changes were noted in other organs. (The rat that died on the 15th day had also purulent bronchitis and diffuse bronchopneumonia.)

In 1911, Iwanoff [108] exposed 2 groups of 2 cats each and 1 group of 3 cats to increasing concentrations of formaldehyde. As seen in Table XII-6, formaldehyde concentrations of 260-820 mg/cu m (211-667 ppm) for 3.5-hours produced temporary irritation of the mucous membranes and slight dyspnea in both cats, which recovered after 2 days. The two cats exposed to 820 mg/cu m (664 ppm) for 8-8.7 hours died on days 4 and 6, respectively, after profuse salivation, pronounced dyspnea, and vomiting. The three cats exposed at 2,010-9,630 mg/cu m (1628-7800 ppm) for 3-4.7 hours died. One died during the exposure; another died 20 minutes after the end of the exposure; and the third died 4 days later. All three experienced hypersalivation, pronounced dyspnea, vomiting, and general cramps. At autopsy, the five cats in the two higher-exposure groups had pulmonary edema, hyperemia, and hemorrhages of the lungs, pus in the trachea and bronchi, and hyperemia of the kidneys.

Carpenter et al [109] exposed groups of six Sherman strain rats weighing 100-150 g to formaldehyde, for periods of 4 hours and observed the death rates in these groups for 14 days. Calculated airborne formaldehyde concentrations were generated from a formalin solution introduced into a heated tube at a constant rate from a motor-driven syringe, air being passed through the tube in a countercurrent direction and into the exposure chamber. No analysis of chamber air was made. Exact details of death were not given, but exposures to formaldehyde at 250 ppm killed 2, 3, or 4 of the 6 rats in the exposed groups prior to the end of the observation period.

Murphy et al [110] exposed eight rats to formaldehyde at 35 ppm for 18 hours. The formaldehyde concentrations were generated by metering the gases through a dilution system and into a chamber ventilated at the rate of 2 cubic feet/minute. Air concentrations of formaldehyde in air were verified by the method of Altshuller et al [111]. A control group of eight rats received clean air only. All animals in both groups were killed 24 hours after the start of exposure, and their organs were subjected to gross pathologic examination and biochemical analysis. As seen in Table XII-6, the exposed rats had dyspnea, eye and nasal irritation, and significantly higher (p ± 0.01) liver alkaline phosphatase activities than the controls.

In 1960, Salem and Cullumbine [112] reported a study of the inhalation toxicity of formaldehyde for 2 groups each of 50 mice, 20 guinea pigs, and 5 rabbits. The animals were exposed for up to 10 hours in a 1 cu-m dynamic chanber made of plate glass. One group was exposed to formaldehyde at 20 mg/cu m as an aerosol of formalin and the other group to formaldehyde at 19 mg/cu m as a gas. The aerosol had a mean particle diameter of 0.7 µm. The formaldehyde gas was introduced into the same apparatus by gentle bubbling of air through formalin, which was held at 50 C in a water bath. Aerosol and gas concentrations were analyzed quantitatively after sampling into impingers containing hydroxylamine hydrochloride. As summarized in Table XII-6, 48 (96%) of 50 mice died during or shortly after exposure to the aerosol while 17 (34%) of the 50 mice exposed to the gas died during a similar time period. Only 1 (5%) of the 20 guinea pigs exposed to the aerosol died, but 8 (40%) of those exposed to the gas succumbed. One (20%) of the rabbits exposed to the aerosol died while three (60%) of those rabbits exposed to the gas were killed. At autopsy, all animals had expanded, edematous, and hemorrhagic lungs with distended alveoli, and most had ruptured alveolar septa.

In two studies [113,114], Amdur exposed guinea pigs for periods of 1 hour to formaldehyde at various concentrations and other irritants with and without simultaneous exposure to an aerosol of NaCl. Intrapleural pressure, tidal volume and into and out of the respiratory system were monitored by the methods of Amdur and Mead [115]. A dynamic exposure chamber was used for all exposures. Concentrations of formaldehyde in air were prepared by passing air through a sintered glass bubbler containing a 37% formaldehyde solution and diluting the resultant stream with air prior to introduction into the chamber. The aerosol of NaCl was generated by aerosolizing a 1% NaCl solution in a Dautrebande generator. The formaldehyde concentrations were measured by the Schiff's reagent method suggested by Elkins [116], or, for low concentrations, by the chromotropic acid method of MacDonald [117]. The geometric mean particle size of the NaCl aerosol was found by electron microscopy to be 0.04 μm with a geometric standard deviation of 3.3. The concentration of NaCl in the aerosol was determined by collection on a membrane filter, followed by soaking in demineralized water and measurement of the conductivity of the water. When the aerosol was used in combination with the formaldehyde, the filter preceded the midget impinger used for gas sampling. According to Amdur [113], an increase in the product of resistance and compliance suggested that bronchial constriction was the principal response to formaldehyde. When three guinea pigs were exposed to 50 ppm formaldehyde for 4 hours [113], the resistance increase produced by formaldehyde reached its maximum by the end of the first hour of exposure. During the second hour, the resistance decreased slightly, and then remained constant during the remaining 2 hours. Two hours after the end of the exposure, the resistance had decreased markedly but had not returned to the control value. Exposure to formaldehyde increased the amount of work required to overcome the increased elastic, resistive, and elastic plus resistive components of ventilatory recoil.

Amdur experimented further [113] by exposing normal and tracheotomized guinea pigs to formaldehyde and to formaldehyde in the presence of NaCl aerosol to bypass the scrubbing effect of the upper respiratory tract and study the effect of more direct access by formaldehyde to the lung parenchyma. A greater response was obtained for formaldehyde gas alone at a particular atmospheric concentration when the protective effect of the upper airway was eliminated. Untracheotomized animals exposed to formaldehyde and NaCl aerosols had additive effects of exposure. Figure XII-2 shows the effects of exposure to formaldehyde in combination with NaCl aerosols. The greatest changes were observed in tracheotomized animals receiving both formaldehyde and NaCl aerosol. All responses within an exposure group were proportional to the concentrations of formaldehyde, however.

In a second report [114], Amdur exposed normal guinea pigs to formaldehyde alone and to formaldehyde with NaCl aerosol, and tracheotomized guinea pigs to formaldehyde as above in concentrations from 0.9 to 50 ppm. In addition, the effects of adding the NaCl aerosol to the formaldehyde at various exposure concentrations were investigated. Methods used to generate formaldehyde and NaCl aerosol concentrations and techniques used to measure responses were identical with those previously used [113]. The results of these experiments, summarized in Table XII-10, were observations of increased resistances and decreased compliances after exposures to formaldehyde at 0.9, 5.2, 20, and 50 ppm and combined exposures to formaldehyde at 1.1 and 3.6 ppm in the presence of an aerosol containing 10 mg NaCl/cu m. Tidal volumes were unchanged by the exposures in all groups except those receiving formaldehyde at 5.2, 20, and 50 ppm and those receiving formaldehyde at 3.6 ppm in the presence of NaCl aerosol. Elastic work was increased significantly only in the group exposed to formaldehyde at 50 ppm.

As indicated in Figure XII-2, the conclusions made in Amdur's previous report [113] remained unchanged. The dose-response curves indicated that resistance was increased in accord with the concentration of formaldehyde, and that addition of aerosolized NaCl may have increased the effectiveness of formaldehyde in heightening resistance. Those untracheotomized guinea pigs receiving formaldehyde plus the aerosol were more severely affected than tracheotomized animals receiving formaldehyde alone, which, in turn, were more severely affected than untracheotomized animals receiving formaldehyde alone [113,114].

Murphy and Ulrich [118] subjected 10 and 9 guinea pigs to 1-hour exposures to formaldehyde at concentrations of 3.9 and 12.5 ppm, respectively, and monitored resistance to airflow, respiratory rate, and tidal volume. Formaldehyde concentrations were generated by an unspecified method and were introduced via a manifold through masks to individual guinea pigs housed in exposure-pneumotachygraph chambers, which restricted their movements. A plethysmograph was used to record respiratory rate and tidal volume. Total respiratory resistance to airflow was determined from the plethysmograph record and flow-calibrated pressure changes in the mask of each animal. Sequential measurements of respiratory rate, tidal volume, and resistance during expiration and inspiration were taken at 15-minute intervals and were reported as the average percentage of preexposure values. Formaldehyde concentrations of 3.9 and 12.5 ppm, as shown in Table XII-6, increased resistance to airflow by 69% and 81%, respectively, increased tidal volume by 29% and 36%, and decreased the respiratory rate by 27% and 37%.

In 1967, Davis et al [119] studied the respiratory effects during exposure of guinea pigs to airborne formaldehyde. Continuously measured responses included intrapleural pressure, respiration rate, and tidal volume in intact and tracheotomized animals. Formaldehyde was determined by the chromotropic acid method of Altshuller et al [120]. A t-test of paired data was used for statistical analysis, since each animal acted as its own control. Qualitatively continuous exposure for 60 minutes to formaldehyde at 50, 1,000, and 6,000 ppm resulted in increases in resistance, decreases in respiration rate, increases in tidal volume, decreases in minute volume, and no changes in compliance. In tracheotomized animals, formaldehyde did not produce changes in any of these areas. This data is summarized in Table XII-6. The authors concluded that these irritant responses were nonspecific and due to receptors present in the nasopharynx and larynx of the guinea pig which are stimulated by irritant and chemically inert substances, e.g., formaldehyde.

(c) Chronic Exposure

Coon et al [121] continuously exposed animals for 90 days via inhalation to formaldehyde at 4.6 mg/cu m by bubbling air through a 1.35% formaldehyde solution into modified Rochester-type exposure chambers.

Airborne formaldehyde concentrations were monitored continuously with a nondispersive infrared analyzer. Five species, including "15 male and female Sprague-Dawley and Long-Evans-derived rats, 15 male and female Princeton-derived guinea pigs," 13 male New Zealand albino rabbits, 3 male squirrel monkeys, and 2 purebred male beagle dogs were exposed to formaldehyde in the chambers. An unspecified number of control animals were maintained in similar dynamic chambers without contaminants and were handled in the same way as the experimental animals. As shown in Table XII-6, one of the 15 rats died during the continuous formaldehyde exposure, but none of the other animals showed any clinical signs of illness or toxicity. Hematic values were normal. On microscopic examination, the lungs of all species of exposed animals consistently showed varying degrees of interstitial inflammation, and the hearts and kidneys of guinea pigs and rats had focal chronic inflammatory changes. The investigators were uncertain whether these changes resulted from the inhalation of formaldehyde. Details of the microscopic examination of tissues and organs from the control animals were not reported.

In 1970, Fel'dman and Bonashevskaya [93] reported the effects of low airborne concentrations of formaldehyde on rats. Four groups of 25 male albino rats were exposed continuously for 3 months to air containing formaldehyde at 0.012, 0.035, 1.0, and 3.0 mg/cu m (0.0098, 0.029, 0.82, and 2.45 ppm) in a 100-liter dynamic exposure chamber. A fifth group of 25 served as controls. Microscopic studies of the lungs of animals exposed to formaldehyde at 1 and 3 mg/cu m (0.81 and 2.43 ppm) revealed proliferation of lymphohistiocytic elements in the interalveolar walls and in the peribronchial and perivascular spaces, against a background of moderate hyperemia. The liver exhibited nuclear polymorphism, a profusion of binuclear cells around the triads, focal hyperplasia and activation of the elements of the reticuloendothelial system. At the same time, the liver cells exhibited a moderate decrease in glycogen content and enlargement and rarefaction of RNA granules. The kidneys of rats in the groups exposed to formaldehyde at 1 and 3 mg/cu m exhibited somewhat dilated vessels in the juxtamedullary zone of the cortex. The parietal area of the cerebral cortex exhibited focal proliferation of the glial elements, with many satellites of oligodendrocytes and astrocytes. No structural histologic changes were in noted groups exposed to formaldehyde at lower airborne concentrations. No further details regarding the methods of generation of formaldehyde or of its analysis were reported.

Carcinogenicity, Mutagenicity, and Teratogenicity

Horton et al [122] in 1963 published a study in which mice with lower than usual incidence of pulmonary adenomas were exposed to inhalations of formaldehyde and coal tar at various concentrations in aerosols in an effort to determine whether formaldehyde would induce bronchogenic carcinoma, predispose mice to cancer if they were exposed to only enough to produce metaplasia of squamous epithelial cells, or render exposed animals more susceptible to cancer of the skin or lungs than control animals upon exposure to coal tar aerosol. Formaldehyde concentrations were generated in a 623-liter chamber from a heated 2:1 mixture of paraformaldehyde and white mineral oil through which air was aspirated and subsequently diluted with make-up air. The actual formaldehyde concentrations in the chamber were analyzed quantitatively prior to each exposure and at 30-minute intervals by a modification of the bisulfite method of Goldman and Yagoda

[123], in which sodium bisulfite was used instead of thiosulfate for the destruction of excess iodine. Coal tar aerosol was generated from a heated glass and stainless steel generator pressurized with preheated nitrogen, with subsequent cooling to 27-28 C and dilution with air prior to entry into the inhalation chamber. Particulate matter in the air of the chamber was collected periodically on a filter and analyzed for benzo(a)pyrene by the method of Tye et al [124]. Both the coal tar and the aerosol generated were found to contain 0.71% benzo(a)pyrene in terms of total tarry material.

In preliminary range-finding experiments, Horton et al [122] found that exposure of mice to formaldehyde at 900 mg/cu m (731 ppm) for 2 hours caused death from pulmonary hemorrhage and edema. Further tests at 40 mg/cu m (32 ppm) formaldehyde for 2 hours/day for 4 days failed to kill any of the test animals and produced no "substantial" distress or weight loss.

Following the range-finding experiments, another batch of mice was divided into five groups. One group of 59 mice received no formaldehyde exposure for 35 weeks; 26 were then killed for microscopic examination of lung sections. The remaining 33 mice were exposed to coal tar aerosol at 300 mg/cu m for 2-hour periods, three times/week, for 35 weeks. A second group, of 60 mice, was exposed to formaldehyde at 50 mg/cu m (41 ppm), 1 hour/day for 35 weeks, when 23 were killed for microscopic examination of lung sections. The 37 remaining mice were exposed to formaldehyde at 150 mg/cu m (122 ppm) for the next 35 weeks. During that time, one mouse died from causes unrelated to the experiment. A third group, of 60 mice, was exposed to formaldehyde at 100 mg/cu m (81 ppm), 1 hour/day, for 35 weeks. Thirty-four were then killed for microscopic examination. The remaining 26 were exposed for 2-hour periods, three times/week, for 35 weeks to coal tar aerosol at 300 mg/cu m. A fourth group, of 42 mice, was exposed a total of 11 times to formaldehyde at 200 mg/cu m (162 ppm) during a 4-week period, when the 35 surviving mice were killed for microscopic examination. Mice in the fifth group served as controls and were killed after 82 weeks. Early structural changes in respiratory tissue were observed, but no tumors were found. Further, preconditioning with sufficient formaldehyde to produce irritation of the airway did not predispose mice to pulmonary or epithelial cancer from subsequent exposure to coal tar aerosol.

In 1966, Gofmekler [125] carried out inhalation experiments in which pregnant rats were continuously exposed to formaldehyde. Three groups of 12 female rats each were placed in chambers in which they were exposed to formaldehyde for 10-15 days before impregnation. They were then caged with males for 6-10 days, taking into account the 5-day sexual cycle of the females. The average length of pregnancy was 22 days. Two groups were exposed to concentrations of formaldehyde of 1 mg/cu m (0.8 ppm) and 0.012 mg/cu m (0.01 ppm), respectively. Both groups showed evidence of affected embryonic development in that the mean duration of pregnancy was increased by 14-15% over that of the third group of 12 controls. There were 135 fetuses in the control group, 235 in the 0.012 mg/cu m exposure group, and 208 in the 1.0 mg/cu m exposure group. Total body weight and the weight of the adrenal glands for offspring of the dams exposed to formaldehyde at both concentrations were greater than those of the offspring of the control dams. The weights of the kidneys and thymus of the offspring from females exposed to formaldehyde at 1.0 mg/cu m were also greater than those of the offsprint of the control dams. In contrast, the lung and liver weights of the offspring of both exposure groups were less than those of offspring of the control group.

Formaldehyde can react with hydrogen chloride and inorganic chlorides to yield bis-chloromethyl ether (BCME) [7,126-131], which is a potent carcinogen according to 29CFR 1910.1008. The reaction occurs at high concentrations (500-3,000 ppm) of formaldehyde and chlorides [128] but Tou and Kallos [132] reported that at the low concentrations encountered in the industrial environment, no evidence of formation of BCME using several common chloride salts could be found when using an analytical method with a detection limit in the low parts per trillion range.

Correlation of Exposure and Effect

Principal hazards which have been associated with human exposure to airborne formaldehyde are irritation of the respiratory tract [29,30,42-52,58], of the eye [42-45,47,67-69,71-73,84], and of the skin [65,66]. The effects on the skin may be particularly offensive in individuals who have become sensitized to formaldehyde by prior exposure or by other means [43-45,47,67-69,71-73,84]. In addition, the odor of formaldehyde is perceptible and may be disturbing to individuals unaccustomed to it at concentrations of the aldehyde which will vary from one individual to another. These concentrations are generally at or below 1 ppm [42,92], 57,58,93,94]. Acute irritation of the human respiratory tract from inhalation of formaldehyde has caused pulmonary edema [27,48], pneumonitis [59], and death [27]. Damage to the lungs in animals, as seen in Table XII-6, has been found on exposure to formaldehyde at much lower airborne concentrations [93,110,112,113,121, 114,119,122,125]. Two cats were killed by inhalation of formadelhyde at about 667 ppm in 4 and 6 days, respectively [108]. As seen in Table III-1, irritation of the upper respiratory tract has been reported in workplaces with formaldehyde concentrations between 0.09 and 11 ppm [42-44,47,51,52,54]. Other studies [43,44,47,50-52,54] support the possibility that aldehyde concentrations of 1-2 ppm may be irritating to some individuals. This effect is evidently somewhat independent of becoming accustomed to it because some investigators [52,54,58] have noted that, although initial irritation subsides to some extent after 1-2 hours of exposure, it returns again after a lunch period or a time away from the workplace.

In addition, Russian investigators have noted altered visual sensitivity [51, 93] and changes in cerebral electrical activity in a preselected group exposed to formaldehyde at 0.8 ppm [93]. Moreover, other Russian investigators [57] have reported optical chronaxie changes after inhalation of formaldehyde for 9-10 minutes at concentrations from 0.07 to 1.3 ppm among individuals preselected on the basis of perceiving the odor of formaldehyde at a concentration of 0.06. Although detection of formaldehyde is possible apparently by some people by unusual means (altered chronaxie of the optic nerve), the application of this information to control of industrial exposures to formaldehyde is uncertain at present.

Once skin sensitization to formaldehyde has occurred, exposures to as little as 10.5 ppm for 10 minutes have caused definite skin reactions [79]. Furthermore, a slight reddening and drying of the skin has been noted in a group of employees with airborne exposure to less than 4 ppm formaldehyde [43]. In this case, however, the possibility of direct skin contact as a causal factor cannot be excluded.

Considering differences in body weights and respiration rates, animal data, summarized in Table XII-6, appear to support the observations made in humans with respect to the effects of airborne exposures to formaldehyde, but indicate adverse reactions in animals from exposures to formaldehyde at generally lower air concentrations than those that affect humans similarly. Formaldehyde at a concentration of 49 ppm for 1 hour, caused airway resistance changes in guinea pigs which persisted for more than 1 hour after cessation of exposure, whereas exposure to formaldehyde at 11 ppm for 1 hour produced transient changes in resistance to the flow of air into and out of the lungs which disappeared within 1 hour of cessation of exposure [113,114]. Monkeys, rabbits, guinea pigs, rats, and dogs exposed to concentrations of 3.7 ppm for 24 hours/day for 90 days developed interstitial inflammation of the lungs [121]. Slight changes in the structure of the lungs have been found after exposure of cats to as little as 0.8 ppm [93]. Amdur [113,114] found airway resistance changes after exposing guinea pigs to as little as 0.31 ppm formaldehyde for 1 hour. Such changes were more dramatic when aerosolized saline solutions were included with the formaldehyde in the atmosphere within the exposure chamber [114], as seen in Figure XII-2. Changes of airway resistance were observed in such experiments after 1 hour exposure to formaldehyde at as little as 0.11 ppm in the presence of an NaCl aqueous aerosol with a mass median diameter of 0.04 µm and a NaCl concentration of 3.9 mg/cu m [114]. Following continuous 24 hour/day exposure of pregnant rats to formaldehyde concentrations as low as 0.01 ppm, a change in gestation time and both increases and decreases in the organ weights were reported [125]. There was also an increase in litter size in comparison with that of controls.

There is no evidence that formaldehyde is a carcinogen [133], but it has produced some effect on rat fetuses [125]. The significance of observed increases in organ weights for the rat fetuses requires further study. BCME apparently does not form in detectable amounts (ppt) at the low concentrations found in industrial environments [132].

The principal hazards of formaldehyde [65,66,68,71,73,74,78,79] or formaldehyde-yielding substances [44,65,67,69,72,75-82,95,98] to the human skin are either primary irritation [65,66] or allergic contact dermatitis [65,68,71,73,74,78,79]. Primary irritation has been elicited when human skin has contacted solutions as dilute as 4% formaldehyde [65,66], while one sensitized individual showed an allergic reaction to formaldehyde solutions as dilute as 1:8,000,000 when 0.02 cc was injected intradermally or when fingers were immersed for 40 minutes in a 1:5,000,000 solution [79].

Tissue destruction produced by ingestion of formaldehyde has been demonstrated in accidents [22-24,55,61], in human experimental feeding studies [85, 60], and in attempted suicides [24,56,62]. Table III-2 shows that the ingestion of as little as 50 mg of formaldehyde was fatal to a 3-year-old child [22] while 330 mg caused the death of an adult [22]. Furthermore, an experimental dose of 100-200 mg taken daily in milk produced headache, stomach pain, a burning sensation in the throat, and a rash in 4 of 11 subjects so tested [19]. The rash could well have been due to prior sensitization. Gastric and pharyngeal discomfort were also reported from daily ingestions of 22-200 mg formaldehyde by another group [60].

To date, no LC50 for formaldehyde has been estimated for humans, although there have been at least two accidental deaths, one from a massive inhalation [41] and the other from inhalation of an uncertain amount [27]. Animal studies have shown a 30-minute LC50 of 1000 mg/cu m (810 ppm) for rats [107], and LD50's by subcutaneous injections of 0.30 g/kg for the mouse [107] and 0.42 g/kg for the rat [107]. However, inhalation studies have shown that 17 of 50 mice [112], 8 of 20 guinea pigs [112], and 3 of 5 rabbits [112] were killed by a 10-hour exposure to formaldehyde at a concentration of only 15.4 ppm. The lowest concentration of formaldehyde reported to kill 1 rat out of 15 was an inhalation of 3.7 ppm, to which rats were exposed 24 hours/day for 90 days [121]. However, death of this rat may have been due to other causes since there was no satisfactory evidence (gross and microscopic examinations) that changes typical of those induced by formaldehyde were responsible for the animal's demise. Because of insufficient data, one can conclude only that any concentration immediately hazardous to life would be an unbearable respiratory and eye irritant to any unprotected individual.

TABLE III-1

DOSE-RESPONSE RELATIONSHIPS FOLLOWING HUMAN EXPOSURE TO AIRBORNE FORMALDEHYDE

Concentration (ppm HCHO)	Duration of Exposure	N	Responses	Reference
41.7	10 min	1	Bilateral vesicle reaction on hands of hypersensitive person	79
16-30	8 hr/d	60	Eye and throat irritation, skin reaction	49
±10-30	Min	1	Skin and eye tingling in hypersensitized worker, progression to generalized skin reaction	84
13.8	30 min	12	Nose and eye irritation subsiding after 10 min in chamber	46
1-11	8 hr/d	>50	Eye, nose, and throat irritation	4
4.2-10.9	Min		Unbearable without respiratory protection	19
10.5	10 min	1	Bilateral vesicle reaction on hands of hypersensitive person	79
0.5-7.3	Daily	278	Increased occurrence of upper respiratory irritation	47 51
± 4	?	Several	Complaints of irritation of conjunctiva, nasopharynx, and skin; increased incidence of catarrhal conjunctivitis, slight reddening and drying of the skin	3
0.09-5.26 (with paraformaldehyde)	Hr	"	Eye and upper respiratory irritation; lessened during day, returned after lunch or next day	52
0.3-2.7	8 hr/d	"	Annoying odor, constant prickling irritation of the mucous membranes, disturbed sleep, thirst, heavy tearing (Odor subsided during day, but returned at start of next shift)	58

TABLE III-1 (CONTINUED)

DOSE-RESPONSE RELATIONSHIPS FOLLOWING HUMAN EXPOSURE TO AIRBORNE FORMALDEHYDE

Concentration (ppm HCHO)	Duration of Exposure	N	Responses	Reference
0.9-2.7	Hr	"	Tearing of eyes and irritation of nasal passages and throat (Irritant effects were greatest at very beginning of workday and after lunch)	54
0.9-3.3	Hr	Several	Mild eye irritation, objectionable odor	53
0.9-1.6	8 hr/d	2	Itching eyes, dry & sore throats, disturbed sleep, and unusual thirst upon awakening in the morning	50
1.0	Odor panel	4	Odor threshold	94
1.4	Min	12	Eye sensitivity to light lowered in unacclimated group	57
0.06-1.3	"	12	Optical chronaxy changes in unacclimated group	57
> 1.0	"	Several	Increased worker complaints	19
0.8	"	12	Altered functional state of cerebral cortex	93
0.8	Daily	?	Equilibrium and olfactory sensation shifts; irritation of upper respiratory tract and eyes in most sensitive individuals; enhancement of alpha-rhythms	51
0.3-0.5 (smog chamber)	5 min (eye only)	12	Increased blink rate, rate proportional to formaldehyde concentration	64
0.05-0.5 (smog chamber)	"	12	Eye irritation range in unacclimated group	64

TABLE III-1 (CONTINUED)

DOSE RESPONSE RELATIONSHIPS FOLLOWING HUMAN EXPOSURE TO AIRBORNE FORMALDEHYDE

Concentration (ppm HCHO)	Duration of Exposure	N	Responses	Reference
0.13-0.45	?	Several	Complaints of temporary eye and upper respiratory tract irritation	2
0.07	Min	15	Odor perception threshold for group	2
0.06	Min	12	"	57
0.05	"	5	No alteration of cerebral electrical activity in subjects most sensitive to odor	93

TABLE III-2

DOSE-RESPONSE RELATIONSHIPS FOLLOWING THE INGESTION OF FORMALDEHYDE BY HUMANS

Amount of HCHO Ingested (mg)	N	Time Before Treatment	Responses	Reference
10,000 (100 cc)	1	Several hr	Severe epigastric pain, passed black stool; dysphagia, stenosis and corrosive destruction of the stomach	61
8,800 (240 ml of 37%)	1	45 min	Severe pain, ulceration and stenosis of stomach, dysphagia	56
50-8214 (Few drops to 7.5 oz)	12	Various	Gastrointestinal pain, corrosion of tissues of contact organs, respira-	22
6,000 (150 ml of 40%)	1	Immediate	Death, edema of glottis, asphyxia	55
2,200-2,400	1	45 min	Cyanosis; low temperature; shallow respiration; weak, rapid and irregular pulse	24
1665 (1 1/2 oz formalin)	1	1 hr	Cyanosis, vomiting, dry mucous membranes in mouth and throat, weak and irregular pulse, shallow respiration	24
1200 (120 ml of 10%)	1	?	Gastric shrinkage and contracture after 3 mo	62
555-600 (0.5 ml of 37-40%)	1	24 hr	Coma, recovery with treatment	23
555-600 (1/2 oz formalin)	1	?	Dry and sore throat, vomiting	24
100-200 daily in milk for 3 weeks	11	--	Headache, stomach pain, burning sensation in throat, rash on chest and thighs in 4 of the 11	19
22-200 daily	2	--	Mild gastric and pharyngeal discomfort	60

IV. ENVIRONMENTAL DATA

Sampling and Analytical Methods

The sampling and analysis of air to determine its formaldehyde content has been a matter of concern to industrial hygienists for many years [123,134, 135,136] as a result of the extensive use of formaldehyde as an industrial chemical [137], and its formation by the incomplete combustion of various organic substances. Since about 1960, the desirability of being able to analyze urban air for formaldehyde and total aldehydes has stimulated the development of many new methods [111,138-145] capable of providing the required sensitivity for analysis of formaldehyde in the occupational environment. Formaldehyde has entered community air from sources such as exhausts from gasoline and diesel engines [111,144,145], effluents from incinerators [111,145], and assorted other industrial effluents [111,144,145]. Frequently, the requirements of air quality investigations are satisfied by analytical methods which determine total aldehydes [111,138,139,142,143,146,147] without specific determination of the quantity of formaldehyde present. As a result, many methods are available [105,106,111,138,139,142,143, 146-154] which are general aldehyde methods, performed with reagents capable of reacting with formaldehyde and other low molecular weight aliphatic aldehydes. Such methods may not be satisfactory for the specific determination of formaldehyde in the occupational environment, but may be used if it is known that the only aldehyde present is formaldehyde. Although not usually required, in some instances it may be necessary to perform qualitative analyses to identify the aldehydes actually present, particularly if a method no specific for the aldehyde of interest is used.

Methods for Total Aldehydes

One of the earliest methods [123] used for the estimation of total aldehydes in the air is generally known as the bisulfite method. It was first proposed for estimating formaldehyde in air by Goldman and Yagoda [123] in 1943. Subsequently, it was adopted by the American Conference of Governmental Industrial Hygienists and was published as a recommended method [55] in 1958. Although identified as a method for formaldehyde in air in both references [123,155], it is actually a nonspecific method for aldehydes and ketones [123,155]. The method relies upon the formation of a nonvolatile sodium formaldehyde-bisulfite complex which is stable in neutral or slightly acid solutions. The sampling solution used in impingers is ordinarily a 1% solution of sodium hydrogen sulfite, and the collection efficiency for aldehydes with a single midget impinger has been shown to be about 98% [118]. The reagent-aldehyde complex has the further advantage of being quite stable, thus permitting analyses to be performed several days after collection without loss of sample [123].

Analysis is performed by destroying the unreacted bisulfite with iodine at neutral pH, after which the solution is made alkaline, decomposing the addition compound. The liberated sulfite may then be titrated with a standard iodine solution to give an indirect measure of the quantity of aldehyde originally collected [123,155]. Although no longer considered the preferred method for aldehyde analysis, this method is quite satisfactory whenever formaldehyde is the only aldehyde present in the atmosphere [155], provided that a sufficient quantity of formaldehyde can be collected to allow the titrations to be performed.

In 1940, Kersey et al [134] suggested the use of Schryver's method as a technique for measuring atmospheric formaldehyde. Formaldehyde in air was collected by means of a Jena glass distribution tube in an absorption bottle containing a dilute solution of phenylhydrazine hydrochloride, thus forming formaldehyde phenylhydrazone [134]. Subsequently, the addition of hexacyanoferrate(III) in acid solution caused the formation of a pink or purple color which was proportional to the amount of formaldehyde present. Barnes and Speicher [135] subsequently modified the method of Kersey et al by collecting formaldehyde in air with a 1.5% solution of potassium hydroxide contained in a standard impinger. These investigators also pointed out that formaldehyde could not be determined specifically by this method in the presence of acetaldehyde and acrolein. Hence, this method is actually an aldehyde method and not a specific formaldehyde method [135]. Hanson et al [156] also recommended the use of phenylhydrazine hydrochloride as a sampling solution, with subsequent color development in the laboratory following addition of potassium hexacyanoferrate(III). A similar method was published in Australia by Lugg and Wright [157]. Fedotov, according to an article translated by Levine [158], used the phenylhydrazine method by impregnating silica gel and making indicator tubes which could be used to quickly estimate the concentration of aldehydes in the field without laboratory analysis.

One of the most useful agents developed for the determination of aliphatic aldehydes was first described by Sawicki et al [105]. The reagent known as 3-methyl-2-benzothiazolone hydrazone (MBTH) reacts [105] with aliphatic aldehydes in the presence of iron(III) chloride to form a blue cationic dye in acidic solutions. In the original paper, Sawicki et al [105] showed that although the reagent responded to a number of aldehydes, it was most sensitive to formaldehyde. Subsequently, Hauser and Cummins [106] modified the method to increase the sensitivity sufficiently to determine formaldehyde at concentrations as low as several ppb in ambient air. This version of the method was also included in a volume of Selected Methods for the Measurement of Air Pollutants published by the US Public Health Service [148] in 1969. Additional data concerning collection efficiencies and molar absorbtivities of several low molecular weight aldehydes were noted by Cohen and Altshuller [149]. Several papers [138,139,159] in which the MBTH method was used to obtain data on aldehyde concentrations in the atmosphere have been published. In 1970, the Intersociety Committee, an alliance of 10 professional societies, including the APHA, AIHA, and ACGIH, devoted to recommending standard methods of ambient air sampling and analysis, adopted the MBTH method as a tentative method [150] of analysis for formaldehyde and other aldehydes. Elfers and Hochheiser [151] described a modification of the MBTH method which made use of a visual color comparator with calibrated color filters. They noted good agreement between the estimates obtained with the comparator and those obtained with the spectrophotometer and suggested that field surveys could be made using the comparator.

Other methods [134,147,152,160] have been used for the estimation of aldehydes, but few of them [134,147] have found application to industrial hygiene sampling and analysis. Several good reviews [111,161-164] should be consulted for information concerning these methods.

Sampling and Analytical Methods for Formaldehyde

The wide usage and occurrence of formaldehyde have led to the development of numerous methods for its sampling and analysis without significant interference from other aldehydes. Although many of the methods previously described [123,134,135,155,157,161] have been called formaldehyde methods, they are nonspecific methods for aldehydes and are suitable only when no interfering substances are present. By contrast, a number of reagents have been developed [136,141,144,160,162,164,165,166,167,168,169,170,171,172,173,174, 175, 176] which respond only to formaldehyde, or else respond so weakly to other aldehydes that they may be considered as essentially specific for formaldehyde. The most widely used color-forming reagents for formaldehyde are Schiff's reagent, pararosaniline and sulfite [133,136,140,142,143,165,171,176], and chromotropic acid [117,144,153-155,178-180]; others [170,174] include 2-hydrazinobenzothiazole, J-acid (6-amino-1-naphthol-3-sulfonic acid), and phenyl J-acid (6-anilino-1-naphthol-3-sulfonic acid).

One of the earliest reagents for determining formaldehyde, generally referred to as Schiff's reagent [133], has been known since 1866, and one of the earliest uses of this reagent for air analysis was described by Zhitkova [177] in 1936. Versions of the same method were published by Blaedel and Blacet [136] and Ackerbauer and Lebowich [165]. Numerous modifications of the method have been published [140,142,143,160,166,167], but all use reagent mixtures of fuchsin or pararosaniline which, together with sulfite and formaldehyde, yield a rose-violet color. The method was adapted by Rayner and Jephcott [140] to the microdetermination of formaldehyde in urban air, the formaldehyde being collected in a standard impinger containing a 0.005 N hydrochloric acid solution. The Chief State Sanitary Inspector of the USSR has recommended [166] the use of Schiff's reagent, with distilled water as the absorbing medium. A method using a modified Schiff's reagent was published by Lyles et al [141] in 1965. The reagent is a mixture of dichlorosulfitomercurate(II) complex and acid-bleached pararosaniline hydrochloride. This method [141] is an outgrowth of the West-Gaeke method [181] for sulfur dioxide, in which basically the same chemical reactions occur except that the reacting mixture contains formaldehyde and withholds the sulfite ion. The authors [141] believed that the substitution of bleached pararosaniline hydrochloride for fuchsin improved the method considerably and made it more highly selective for formaldehyde. Essentially the same method was adapted by Yunghans and Munroe [142] and Cantor [143] to the determination of atmospheric formaldehyde by an automated analysis system. Other modifications of methods using Schiff's reagent include those of Brewer [167] and Knight and Tennant [160].

The analytical method which currently appears to be favored [180] for the determination of formaldehyde in air relies upon the production of a purple color by reaction between formaldehyde and 1,8-dihydroxynaphthalene-3,6-disulfonic acid (chromotropic acid) in sulfuric acid. The reagent was first proposed [178] in 1937 as a specific reagent for formaldehyde, and various investigators [182-187] have reported its use in the analysis of vital samples. MacDonald [117] was the first to suggest its usefulness for the analysis of formaldehyde in air in 1954, and developed the method in essentially the form in which it is commonly [155,179,180] used today. Altshuller et al [145] studied a modification of the method which was said to result in improved sensitivity, stability, and freedom from interference. Inasmuch as the recommended sampling method [145] used concentrated sulfuric acid as the collection medium, it is obviously impractical to apply the method to personal air sampling in the occupational environment, where there is a chance for contact of the employees with concentrated sulfuric acid. When sampling air pollution sources such as the effluents from incinerators, Cares [144] noted that oxides of nitrogen interfered with the color development, and recommended that samples be collected in bisulfite solutions to avoid this interference. Other attempts to minimize the effect of interfering substances have included the use of porous polymer adsorbents [168] and a gas chromatographic separation of styrene and cresols [169]. The Intersociety Committee adopted the chromotropic acid method as a tentative method for formaldehyde in 1970 [153]. Essentially the same method was recommended by Levaggi and Feldstein [154] and the Intersociety Committee [153] except that formaldehyde was determined in an aliquot of a sample collected in 1% sodium bisulfite solution in the former method.

Sawicki et al [170] compared the chromotropic acid method with the J-acid and phenyl J-acid methods and pointed out the potential interference from some formaldehyde-releasing compounds which would not normally be present in an occupational setting. They established that J-acid and phenyl J-acid are extremely sensitive and selective reagents that, in some ways, are superior to chromatropic acid [170,172,174]. Numerous papers have outlined the use of chromotropic acid to measure formaldehyde in either ambient air [139,145,146,159,188] or pollution [145] sources. Gladchikova and Shumarina [171] recommended the chromotropic acid method for use in the USSR.

Several color-forming reagents [170,172,174] other than those described have been reported to be useful for formaldehyde analysis, but do not appear to have gained wide acceptance. Acetyl acetone forms a colored compound with formaldehyde [172,189]; because this compound is fluorescent, it may be measured by fluorimetry with much greater sensitivity than by colorimetry [173]. Other formaldehyde reagents include 5,5-dimethyl 1,3-cyclohexanedione (Dimedone, Methone) [147,152], 2-hydroxycarbozole [175], paraphenylenediamine [176], and an equilibrium mixture of potassium tetracyanonickelate and dimethylglyoxime [190]. Descriptions of even more reagents may be found in the several review articles previously cited.

Barnes and Speicher [135] suggested in 1942 that formaldehyde could be determined conveniently by polarographic analysis, after collecting the samples in dilute potassium hydroxide solution, but the method does not appear to have found favor, as evidenced by a lack of polarographic or electrometric methods in general use since that time.

Although gas-liquid chromatographic (GLC) methods have attained great popularity for most substances, relatively few GLC methods for formaldehyde have been reported. A possible explanation for this lack of GLC methods may be gained from a report issued by the Los Alamos Scientific Laboratory [191] in 1973 in which various problems of interference and sensitivity that had been experienced with the chromatographic conditions tried were noted. A 1975 report by Wood and Anderson [192], stated that attempts to develop a GLC analysis method were unsuccessful. Various authors have described the determination of formaldehyde in various substances by GLC means [193,-197], but have not applied the procedures to the analysis of low concentrations in air. Levaggi and Feldstein [154] have described the determination of the C2-C5 aldehydes by a GLC procedure but did not recommend its use for formaldehyde.

Until recently, there was no published evidence that the collection of formaldehyde on solid adsorbents or absorbents could be relied upon, so that it was necessary to collect formaldehyde in aqueous medium and to rely on analysis by one of the methods stated to be specific for formaldehyde.

Wood and Anderson [192] have described a method of collection on alumina, however, with subsequent analysis by the chromatropic acid method. Because elution of formaldehyde from the alumina must be performed immediately to prevent loss of the aldehyde, this method may not be applicable to use in the field. The most widely used estimation of formaldehyde at this time [117,155,179,180] is the modified chromotropic acid method, which is the method included in NIOSH's 1973 Manual of Recommended Methods [180].

Engineering Control of Exposure

In the manufacture and use of formaldehyde and formaldehyde-yielding substances, the possible routes of exposure to formaldehyde are:

(1) inhalation of formaldehyde gas and/or formaldehyde-generating dust;

(2) contact of formaldehyde gas and/or solutions and of formaldehyde-yielding dust and/or solid with the skin, eyes, and mucosal surfaces; and

(3) fire or explosion of formaldehyde gas or of formaldehyde-yielding solids.

Ingestion would be a potential exposure hazard inasmuch as formaldehyde is toxic by the oral route. However, ingestion in an amount sufficient to be toxic to an adult would occur only by intentional action, extreme carelessness, or an unusual accident. These sources of poisoning can be minimized by informing all employees of the danger and the need for exercising care [198].

Total enclosure of process and materials is the preferred means of control to prevent contact with, or inhalation of, formaldehyde or formaldehyde-yielding substances [6,97,198]. When total enclosure is used, provision must be made for its safe venting for pressure or vacuum relief. Vents should be designed for easy cleaning to remove any polymeric products which tend to accumulate [6]. Flame arrestors in the vent lines are recommended when concentrations of formaldehyde gas in the flammable range are expected [6,198,199].

When totally enclosed systems must be opened for either service or maintenance, provisions must be made for the exhausting of formaldehyde emissions either by prior purging of the system, by suitable ventilation, or by a combination of techniques, or by providing proper protective clothing and devices.

Total enclosure also applies to the storage of formaldehyde solutions and formaldehyde-yielding substances, whether in small containers, such as, carboys, drums, and barrels, or in tanks for bulk storage. Small containers should be securely closed and have sufficient strength to withstand likely differential pressure between outside and inside. The bulk tanks should be safely vented.

Storage areas should be adequately ventilated to remove any emissions which may arise from transfer operations or spills. Because formaldehyde gas is flammable and explosive, the storage areas should have sprinkler systems or other suitable automatic fire control facilities.

Storage areas should also be temperature-controlled to maintain the temperature always well below the flashpoint of all materials stored within [200]. The flashpoint of 37% formaldehyde solution with 15% methanol stabilizer is 50 C (122 F) and is higher for solution with less methanol [6]. Temperature in storage areas should not exceed 40 C (104 F) and preferably should be lower.

Storage of formaldehyde solutions should be in securely sealed containers. Large vessels or tanks should be safely vented for relief of pressure or vacuum.

Partial enclosure of process equipment, machinery, and containers will restrict the emission of gases or dust, but must be supplemented by ventilation to prevent the dissemination of vapors or dust into the air of the workroom.

Airborne concentrations of formaldehyde gas and of formaldehyde-generating substances can be controlled and kept below the recommended concentration limits by properly designed ventilation systems of adequate capacity [6,97,198-200]. General dilution ventilation can be used in many instances to reduce the airborne concentrations in a workroom to a level well below the recommended limit. Removal of the gas or dust by local exhaust ventilation close to the source of emission is preferred for control by ventilation. Local exhaust ventilation can prevent the emissions from reaching the employees and from being disseminated, even at low concentrations, throughout the work area. In employing exhaust ventilation for such control, certain recommended practices [201] and design and operating fundamentals should be followed [202]. Regular inspection and maintenance of the ventilation system is necessary for its continued effectiveness [97]. Recirculation of exhaust ventilated air in the workplace is prohibited.

Resins derived from formaldehyde, such as melamine-formaldehyde, urea-formaldehyde and phenol-formaldehyde resins, will begin to decompose rapidly with the release of formaldehyde (FM) at temperatures above 250 C (482 F). [203] Such temperatures may occur in injection molding of these resins. Sawing of sheets of these resins by high speed saws will produce sufficient heat to cause such release of formaldehyde (FM); sawing will also emit formaldehyde-contaminated dust. These and other operations with formaldehyde-derived polymers should be provided with local exhaust ventilation to remove gas and/or dust [97,203].

Waste disposal shall be by burial, flushing, or chemical deactivation. Burial of waste must be in an area of restricted access and where seepage is not likely to produce exposure of employees or other individuals. Small quantities (not more than several gallons) of waste may be flushed down the drain with large quantities of water (in excess of 20 times the volume of waste). Formaldehyde spills may be inactivated by reaction with aqueous solutions of sodium sulfite or bisulfite.

V. DEVELOPMENT OF STANDARD

Basis for Previous Standards

The United States of America Standards Institute (now the American National Standards Institute Inc) established a standard for formaldehyde in 1967 [204]. The standard specified that:

(1) Acceptable maximum for peaks, undefined, above the acceptable ceiling concentration for continued exposure is 10 ppm for a total of no more than 30 minutes during an 8-hour work period.

(2) Acceptable ceiling concentration for limitation of discomfort exposure is 5 ppm for an 8-hour work period.

(3) Acceptable 8-hour TWA within limits of Sections (1) and (2) above is 3 ppm. However, persons who have been previously sensitizied to formaldehyde may experience an allergic reaction when exposed to concentrations lower than 3 ppm.

(4) Minimum level for sensory detection qualified as to tolerance (sensory fatigue) for warning value is as follows:

1 ppm	Odor detectable [205]
2 or 3 ppm	Slight discomfort [205]
13 ppm	Eye irritation that wore off in 10 minutes [46]

(5) Acceptable concentration to avoid discomfort is 3 ppm.

This standard is based largely upon the personal observation of Fassett [205] and the work of Sim and Pattle [46] and was reaffirmed most recently in 1973.

The American Conference of Governmental Industrial Hygienists (ACGIH) has recommended an 8-hour ceiling limit of 2 ppm (approximately 2.5 mg/cu

m) for formaldehyde. A TWA limit of 10 ppm was first established in 1946 and was changed to 5 ppm in 1948. In 1963, ACGIH introduced the ceiling limit concept and established a ceiling limit for formaldehyde of 5 ppm which was decreased to the present limit of 2 ppm in 1973. In 1971, the ACGIH supported its limit in their Documentation of the Threshold Limit Values for Substances in Workroom Air [206] as follows: Formaldehyde irritates the eyes, respiratory tract, and skin [116,207]. Elkins [116] suggested that employees develop tolerance to these irritant effects, but Henderson and Haggard [207] noted that persons may also become more susceptible on repeated exposure. The latter authors cited data that indicate that a threshold limit value of 20 ppm would be appropriate. Elkins [116], however, reported complaints from persons exposed to an atmosphere in which the maximum concentration was 5-6 ppm; eye irritation was noted in unaccustomed persons exposed to much lower concentrations. He indicated that regular employees can tolerate without difficulty concentrations that are intolerable to outsiders, and suggested that the maximal acceptable concentration might be based on cutaneous rather than on pulmonary effects.

The threshold limit value of 5 ppm was expected to be low enough to prevent respiratory injury, but not necessarily to prevent subjective evidence of irritation. Irritation, in the form of itching eyes, dry and sore throat, disturbed sleep, and unusual thirst on awakening, has been reported in a few workers at levels of 1-2 ppm formaldehyde [42,50]. The threshold limit of 5 ppm obviously did not prevent irritation in all exposed individuals.

A recent study [58] of formaldehyde gas emissions in the permanent-press fabrics industry (8 plants) made after complaints of workers revealed formaldehyde concentrations between 0.3 and 2.7 ppm (sewing area), with an average of 0.68 ppm. Employees complained of annoying odor (odor threshold, below 1 ppm) [205], constant prickling irritation of the mucous membranes, and disturbed sleep. Formaldehyde dermatitis was not mentioned as a problem in the report.

Because of complaints of irritation by exposure to formaldehyde at concentrations well below 5 ppm, the ACGIH recommended in 1971 that the TLV be lowered to 2 ppm. The latter figure was entered in the list of adopted values for TLV's 1973. In 1976, a tentative short-term exposure limit (STEL) for formaldehyde also at 2 ppm was appended to the TLV. Although the reports of Bourne and Sefarian [42] and Shipkowitz [58] were the primary references cited for the new TLV, the former authors studied concentrations of formaldehyde in air at 0.13-0.45 ppm, which were associated with complaints of irritated eyes, headaches, and irritated nose and throat. Shipkovitz [58] reported that concentrations of 0.3-2.7 ppm of formaldehyde were found in 8 factories manufacturing permanent-press and crease-resistant clothing and were accompanied by numerous and bitter complaints of irritation.

The present federal standard, adopted from the American National Standards Institute limit [204], specifies an 8-hour TWA limit of 3 ppm formaldehyde, an acceptable ceiling concentration of 5 ppm formaldehyde, and an acceptable maximum peak above the acceptable ceiling concentrations of 10 ppm for a total of no more than 30 minutes during an 8-hour shift.

Other countries and various states in the United States have set standards for formaldehyde. These standards are listed in Table XII-7.

In evaluating the literature, the Czechoslovak Committee of MAC in their Documentation of MAC in Czechoslovakia [208] presented the table shown in Table XII-8. The basis for the Czechoslovak MAC can be stated as follows: in formaldehyde, the irritating effect predominates. This is the primary reason for establishing of a maximum allowable concentration (MAC). The mean MAC should therefore lie below the limit of irritation, and the peak concentration below the limit of damage or of severe irritation. The conclusion of the Czechoslavak Committee was that the concentration of formaldehyde in industrial environments then accepted as the MAC in the USSR of 1 mg/cu m was too strict and could be adherred to by Czechoslovak plants only with difficulty. Accordingly, a ceiling concentration of 2 ppm with a short-term peak concentration of 5 ppm was established.

Writing in support of the Italian standard for the Clinica del Lavoro, Vigliani and Zurlo [209] suggested 5 mg/cu m formaldehyde and noted the problem of setting standards for accustomed and nonaccustomed employees. However, they do not say for which group their standard applies and do not offer any supporting argument for the limit selected.

In 1967, Zaeva et al [51] submitted to the Ministry of Public Health of the USSR a recommendation that the maximum permissible concentration of formaldehyde in air of factories be decreased from 1 mg/cu m to 0.5 mg/cu m. This recommendation was based largely on published reports of disturbed sleep and irritation of the eyes and throat after exposures to formaldehyde at 1-1.9 mg/cu m [50], of irritation of the membranes of the orbit and upper airway at 1-9.6 mg/cu m [50], of chronic rhinitis and illness in workers exposed to formaldehyde at 0.6-36.3 mg/cu m [51], and of irritation of the membranes of the upper airway and orbit, respiratory disorders, changes in autonomic nervous system function, and altered alpha-rhythm of the EEG in some degree after exposure to formaldehyde at 1 mg/cu m [A.K. Sgibneyeu, quoted in 51]. In addition, the recommendation was based on a finding by the Ivanosk Institute of Labor Protection [quoted in 51] that most workers complained of upper airway irritation on exposure to formaldehyde at 2-3 mg/cu m in air. This recommendation by Zaeva et al [51] was apparently accepted, as the MAC listed for the USSR in 1968 [210] was that recommended by Zaeva et al [51].

Basis for the Recommended Standard

The recommended workplace environmental standard will protect all but the sensitized worker from the adverse health effects associated with exposure to formaldehyde, ie, monomeric formaldehyde, HCHO, and its aqueous solutions. Formaldehyde gas may be generated from a variety of materials, which include, but are not limited to, trioxane, paraformaldehyde, polyoxymethylene, and hexamethylenetetramine. The latter materials are included in this standard to the extent that they act as sources of formaldehyde (FM) exposure.

The odor of formaldehyde is perceptible to previously unexposed individuals at concentrations varying from one individual to another but generally at or below 1 ppm [42,57,58,92-94]. The lowest concentration at which formaldehyde was perceived by odor was 0.06 ppm [57] Although perception does not necessarily signify an adverse health effect, studies defining the odor threshold serve as indications of environmental concentrations which are below the threshold of irritation, whereas an annoyance may occur at any concentration at or above the odor threshold.

When inhaled, formaldehyde at massive concentrations has caused pulmonary edema [27,48] and death [27], while at concentrations of 1-11 ppm [43,47,51,52,54,98] it has caused upper respiratory tract irritation. Formaldehyde may be irritating or annoying to some individuals at airborne concentrations of 1-2 ppm. In addition, several investigators [52,54,58] have indicated that, despite the fact that the ability to perceive the odor of formaldehyde is blunted within 1-2 hours of exposure, this ability returns when the exposure is interrupted by lunch or upon returning to the workplace the next day.

Inhalation experiments with guinea pigs have shown transient alterations of airway resistance which vanished within 1 hour after exposure to formaldehyde at 11 ppm but persisted for over an hour after exposure at 49 ppm [113,114]. Immediately reversible airway resistance changes were noted following the exposure of guinea pigs to formaldehyde at as little as 0.31 ppm for 1 hour [113,114]. Such resistance changes were observed with 1-hour exposures to formaldehyde at as little as 0.11 ppm in the presence of an aerosal of NaCl solution acting as a carrier [126]. Considering the mass medium diameter of 0.04 μm and the particularly large proclivity of guinea pigs to undergo bronchioconstriction, the data are roughly in keeping with the correlation of airborne formaldehyde concentrations and reported upper respiratory tract irritation in humans. In cats, exposure to formaldehyde at as little as 0.8 ppm has caused slight microscopic alterations in lung tissue [93].

Inhalation of formaldehyde has caused allergic dermatitis in hypersensitive humans at concentrations of 10.5 ppm for a brief period, or when the skin contacted formaldehyde solutions as dilute as 1:5,000,000. Such findings demonstrate that it is undesirable for sensitized individuals to work in any area where formaldehyde is likely to be present. In addition to allergic dermatitis, primary irritation of the skin has been caused by solutions as dilute as 4% formaldehyde [65,66]. Based on reports of irritation, objectionable odor, and disturbed sleep for a few employees on exposure to formaldehyde at 0.3 ppm and of more general complaints at concentrations exceeding 1 ppm (Table III-1), a ceiling value of 1 ppm (1.2 mg/cu m) for formaldehyde (FM,FS) in air is proposed as the workplace environmental limit. Any other substance that readily decomposes to react as formaldehyde with chromotropic acid under the recommended conditions of sampling and analysis is also regarded as contributing to formaldehyde exposure. Individuals sensitized to formaldehyde should not be assigned to work in any area where formaldehyde, paraformaldehyde, or any other substance capable of releasing formaldehyde is likely to be present.

Many employees may be exposed to small amounts of formaldehyde or may work in situations where, regardless of the amount generated, there is only negligible exposure. In such situations, compliance with the provisions of this recommended standard which are intended to protect the health and provide for the safety of employees under more hazardous circumstances would not be necessary. However, to ensure that exposures remain at or below the ceiling limit, protective measures must be instituted when significant exposures begin to occur. Occupational exposure has been defined as exposure to formaldehyde at concentrations exceeding 0.6 mg/cu m (0.5 ppm), thereby delineating those exposure situations which require increased monitoring of the environment, medical surveillance of employees, and associated maintenance of records.

VI. WORK PRACTICES

The effectiveness of good work practices is entirely dependent on the knowledge and the cooperation of employers and employees. The employer must take all necessary steps to ensure that [6]:

(1) each employee receives adequate instruction and training in safe work procedures, the proper use of all operational equipment, the correct use of protective devices and practices, and all emergency procedures;

(2) each employee periodically receives refresher sessions and drills to maintain a high level of competence in safe work practices and emergency procedures;

(3) each employee is provided with proper tools, equipment, and personal protective clothing or devices; and

(4) each employee is given adequate, responsible supervision to assure that all safety requirements and practices are followed.

Only properly trained individuals should be permitted access to areas in which exposures to formaldehyde, paraformaldehyde, or formaldehyde-generating substances are likely. All such areas should be clearly identified by appropriate posted warnings (Chap I, Sect 3).

For the prevention of injuries from contact by formaldehyde solutions and/or formaldehyde-yielding substances with the eyes, skin or other sensitive tissues, good work practices include, but are not limited to, the wearing of personal protective garments and equipment as recommended or required in Chapter I, Section 4. Work practices, procedures, and protective equipment and devices should be developed and utilized so that the likelihood of employees suffering injurious contact with these chemicals is minimal. The wearing of personal protective garments and equipment is necessary for additional, positive protection in those activities and accidental situations where exposures are likely in spite of other precautions [6,49,97,198,200].

Each employee potentially exposed to gaseous formaldehyde or likely to come in contact with formaldehyde in solutions or solids must be provided with, and required to wear, adequate protective clothing and equipment for the tasks and area of work. Adequate supervision must be exercised to ensure that the protective clothing and equipment are regularly and properly worn. The garments and equipment must be inspected and maintained on a regular basis. Items damaged by wear or abuse to the extent that the effectiveness of protection is impaired or doubtful must be repaired or replaced. All personal protective devices must be washed thoroughly after each wearing and before being reused. If any such item becomes contaminated with formaldehyde during the work shift, it should be immediately flushed with large amounts of water; when such flushing makes the item unsuitable for continued wear, it must be removed and replaced by a clean one.

Eye protection is of particular importance because of the irritant effects of formaldehyde. Well-fitted chemical safety goggles must be worn as protection from irritating concentrations of formaldehyde gas or formaldehyde-yielding substances and as protection from mists, splashes, and spills of formaldehyde solution. Full-face respirators provide the necessary eye protection. Full-length, plastic face shields also should be worn to protect the face from splashes and spills, but the chemical safety goggles are still necessary to protect the eyes from vapor, mists, and splashes which may enter behind the edge of the shield [6].

In emergencies and in routine operational situations where engineering and administrative controls are not capable of reducing the amount of exposure at or below the recommended limit, the wearing of approved respiratory protection (see Chap I, Sect 4) is necessary. The use of cartridge or air-supplied half-mask respirators is limited to relatively low concentrations of formaldehyde [198], because such respirators do not afford eye protection and because the combination of half mask respirators with chemical goggles is neither well tolerated by employees nor as effective as a full face mask respirator.

Cartridge and canister respirators with full facepiece are rated to provide protection for limited periods in concentrations up to 20,000 ppm [211] and can be used for evacuation or escape purposes (Chap I, Sect 4, Table I-1).

At formaldehyde concentrations of 100 ppm or greater, breathing becomes very difficult or impossible [6,41]. A self-contained breathing apparatus with positive pressure in a full facepiece or a full facepiece supplied-air respirator of the pressure-demand type with auxiliary self-contained air supply is necessary, therefore, for working in such concentrations.

When employees are required to enter any room, equipment, or other confined space suspected of, or possibly subject to, contamination by formaldehyde, tests should be made to determine the safety of the atmosphere before entering. The irritant effects should provide adequate warning of dangerously high concentrations but not necessarily of the degree of respiratory protection required (Chap I, Sect 4).

The hazards of contact with formaldehyde solutions and gas or with formaldehyde-yielding substances are best controlled (when enclosure is not possible or practical) by a combination of good work practices to eliminate or minimize splashes, spills, and other causes of contact (Chap I, Sect 6) and the wearing of proper protective garments and equipment (Chap I, Sect 4). The use of automated and remote control methods can reduce the number of situations presenting the hazard of possible contact.

Formaldehyde gas is a flammable vapor having explosive limits of 7.0-73% by volume [6]. Paraformaldehyde solid is combustible and airborne dust of paraformaldehyde is explosive at concentrations of or in excess of, 32 mg/liter with more than 8.6% oxygen (v/v) [198]. At elevated temperatures, paraformaldehyde (PF) will yield the more flammable formaldehyde gas (FM). In storage areas and in any process or handling system, appropriate measures are necessary to ensure that concentrations do not exceed the lower flammable limit, that electrical and mechanical systems are well grounded and explosion-proof, and that fire and explosion safety systems and equipment are provided. [6,198,199]

Respiratory protective devices approved for escape or evacuation from areas of excessive exposure to formaldehyde should be provided for each employee in any area of potential emergency or should be readily available at prominently and clearly identified locations throughout the area. The equipment should be available in numbers sufficient for use by all employees likely to be present in the area.

The program for respiratory protective equipment shall meet the requirements and standards as provided in 28 CFR 1910:134 and ANSI Z88.2-1969 Standard Practice for Respiratory Protection [211]. This program provides for the routine regular cleaning, inspection, servicing, and maintenance of respirators for effective and safe usage.

Each plant must establish an emergency plan and program to meet any emergency which can reasonably be anticipated. The employees and emergency teams must be thoroughly informed and trained in their responsibilities and actions for emergencies. Stations equipped with first-aid supplies and equipment, approved respiratory protective devices, protective garments, and other special equipment as needed should be established and maintained in readiness at easily accessible locations adjacent to areas of likely emergencies.

Eye-flushing stations and safety showers should be available in plant areas where splashes or spills of formaldehyde solutions are possible. Immediately on any contact with formaldehyde, the individual should flush the eye or skin areas with a copious flow of water [198,199].

To prevent and limit contact dermatitis from formaldehyde the employees should practice good personal hygiene. Showers, washing facilities, lockers, and change rooms should be provided. Facilities for flushing the eyes and skin with large amounts of water should be provided and readily available from areas where splashes or other contact hazards are likely to occur. These facilities should be clearly marked as to location and should have emergency and first-aid instruction posted nearby.

Employees should exercise care not to transfer formaldehyde from contaminated gloves or other protective garments to unprotected eye or skin surfaces. Such contact with formaldehyde has been a reported cause of some eye injuries and dermatitis [49].

Administrative control through selective assignment of employees may be necessary to protect hypersensitive or sensitized individuals [79].

Sensitive individuals may experience adverse reactions to low formaldehyde concentrations tolerated by most other employees.

The following work practices and procedures should be observed by all employees:

(1) Enclosed process machinery and containers of formaldehyde solutions should be kept closed or covered, except when operations require otherwise.

(2) Respirators and protective clothing and equipment should be worn in accordance with recommendations and requirements (Chap I, Sect 4).

(3) Containers of formaldehyde should be securely closed during transport of such containers.

(4) Large containers (carboys, drums, etc) should be moved and handled by mechanical equipment of design applicable to the procedure.

(5) Carboys or other breakable containers should be handled with care. Specially designed inclinators should be used for pouring from carboys.

(6) Transfer of formaldehyde solutions from a container should be done with care to minimize any splashing and to prevent spills. Transfer by pumping through hermetically sealed systems or lines is preferred.

(7) Transfer of formaldehyde solutions from tank cars or tank trucks must be done only by specially trained employees under responsible supervision.

(8) Tanks, machines, pumps, valves, and lines must be drained and flushed thoroughly with water before doing maintenance or repair work on them. Care must be exercised to avoid contact with the drained or flushed fluids.

(9) No individual may enter any tank or equipment until it has been flushed free of formaldehyde, the atmosphere therein has been determined to be safe, and a permit has been issued by a responsible supervisor.

(10) No individual may enter any tank or confined space whose entrance is not large enough to admit an individual fitted with safety harness, lifeline, and an emergency respiratory protective device.

(11) An individual may work in a tank or confined space only with another person outside in constant contact and having rescue equipment and assistance available.

(12) Pipelines and hoses, if any, shall be blanked off or disconnected to prevent inadvertent entry of formaldehyde into a confined space wherein an individual is working.

(13) Containers and lines shall be purged of formaldehyde before doing any external welding, grinding, or other operation which might offer a source of ignition for flammable vapors.

(14) Spills and leaks of formaldehyde solution shall be immediately flushed away with an abundant flow of water. Employees shall wear respiratory protection and protective garments during the clean-up of spills.

(15) Eyes and skin surfaces coming into contact with formaldehyde shall be immediately flushed with large amounts of water. In the case of contact with the eyes, a physician should be consulted as soon as possible.

(16) Employees shall properly utilize ventilation, enclosures, remote controls, and other engineering or administrative controls provided.

(17) Employees must wear protective clothing and respiratory protection during such operations.

VII. OCCUPATIONAL RESEARCH PRIORITIES FOR FORMALDEHYDE

(1) Effects of Repeated Exposures in Man

More information is needed on effects produced by prolonged repeated exposures to low airborne concentrations of formaldehyde. Information on effects produced at the recommended environmental ceiling limit of 1.2 mg/cu m based on a 30-minute sampling period would be particularly useful. Research on the development of hypersensitivity produced by formaldehyde reaction with skin proteins could provide an understanding of possible immune mechanisms involved and allow identification of individuals at higher risk of exposure. Epidemiologic investigations of various occupational groups exposed to formaldehyde with data on airborne concentrations associated with clinical findings, if any, would allow refinement of the recommended standard.

(2) Formaldehyde Chemistry

The chemistry of formaldehyde is complex, and reactions of formaldehyde in air or solutions, including polymerization, degradation, and combinations with other substances, require continued investigation. Numerous substances may act as sources of FM or FS, producing adverse effects. Development of an analytical and sampling technique suitable for personal monitoring and rapid analysis in the field would be particularly useful. Such a technique should allow specific identification and quantitative determination of formaldehyde and substances acting as sources of formaldehyde. The reaction of monomeric formaldehyde in either gas or liquid phase with Lewis acids in the presence of halogens requires additional study. Monitoring of occupational environments for chloroethers would be appropriate.

(3) Metabolism

Additional information on the metabolic fate of formaldehyde could provide an understanding of the underlying toxic effects, leading to a more definitive medical treatment for intoxication and prevention of adverse physiologic effects, both acute and chronic.

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IX. APPENDIX I
SAMPLING OF FORMALDEHYDE IN AIR

Sampling

Air samples are collected to represent the breathing zone of employees by drawing air through two all-glass midget impingers in series, each containing 20 ml of distilled water. (If other aldehydes are present, use 20 ml of 1% sodium bisulfite solution.) Under certain conditions, it may be possible to attach the impingers to employees clothing. A personal sampling pump may also be worn by the employee. In other instances, employee movements may make sampling in this manner impractical, but samples should be collected as close to the breathing zone as possible. A prefilter assembly should be used when dusty or smoky conditions prevail and should be connected to the impinger using a minimum amount of tubing. The air being sampled should not pass through any other tubing or equipment before entering the impinger. Sampling is performed for at least 30 minutes at a rate of 1 liter/minute. The flow rate, with the impingers on line, should be checked as a minimum precaution before and after the sample is taken.

Two impingers must be used in series, because under conditions of sampling the collection efficiency of only one impinger is approximately 80% [179]. With two impingers in series, the total collection efficiency is 95% [179]. The contents of each impinger may be analyzed separately if relatively high concentrations are suspected, or may be combined and analyzed as a single sample. If each impinger is analyzed separately and the second impinger is found to contain more than about 30% of the amount collected in the first impinger, appreciable loss of sample has most likely occurred, and resampling is required to obtain an adquate value.

After sampling, the impinger stems can be removed and cleaned, first tapping the stem gently against the inside wall of the impinger bottle to recover as much of the sampling solution as possible, then washing with a small amount (1-2 ml) of distilled water and adding the wash to the impinger flask. The impinger flask is then sealed tightly with a hard, nonreactive stopper, preferably Teflon, but never with rubber. If shipping the impinger flasks with the stems in, is preferred, the outlets of the stem should be sealed with Parafilm or equivalent nonrubber covers, and the ground glass joints sealed, usually by means of plastic tape. Care should be taken to minimize spillage or loss by evaporation at all times. If analysis cannot be done within a day, samples should be refrigerated to prevent sample loss due to polymerization. Whenever possible, hand delivery of the samples is recommended, or special impinger shipping cases should be used to ship the samples. A blank impinger should be handled in exactly the same manner as the other samples (fill, seal, and transport) except that no air is sampled through this impinger.

Calibration

Since the accuracy of an analysis can be no greater than the accuracy of the volume of air which is measured, the accurate calibration of a sampling device is essential. The frequency of calibration required depends on the use, care, and handling to which the pump is subjected. Pumps should be calibrated if they have been subjected to abuse or if they have just been repaired or received from a manufacturer. Under certain conditions of heavy usage, more frequent calibration may be necessary.

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, a 1-liter buret or wet-test meter is recommended, although other standard calibrating instruments such as spirometer, Marriot bottle, or drygas meter can be used. The actual set-up should be the same for any of the instruments mentioned above. The calibration instrument should be connected in sequence to the sampling train which will be followed by the sampler pump. In this way, the calibration instrument will be at atmospheric pressure. If the personal sampler pump is used, each pump must be calibrated separately. If the buret is used, it should be set up so that the flow is toward the narrow end of the unit.

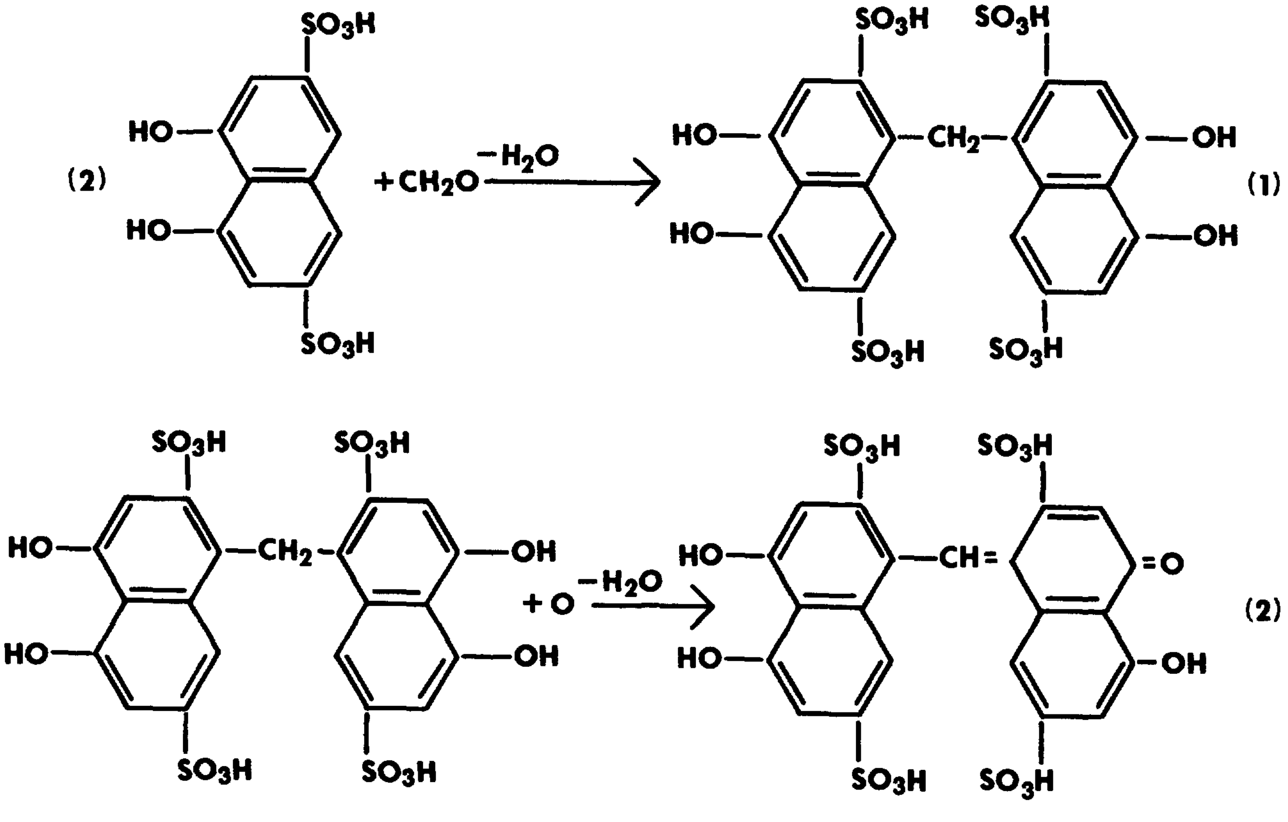
Care must be exercised in the assembly to ensure that seals at the joints are airtight and that the length of connecting tubing is kept at a minimum. Calibration should be performed under essentially the same conditions of pressure and temperature under which it is anticipated the sampling will be performed. The calibrated pump rotameter should be used to set the flow rate in the field.

X. APPENDIX II

ANALYTICAL METHOD FOR FORMALDEHYDE IN AIR

Principle of the Method

Formaldehyde reacts with chromotropic acid-sulfuric acid solution to form a purple monocationic chromogen. The absorbance of the colored solution is read in a spectrophotometer at 580 nanometers (nm) and is proportional to the amount of formaldehyde in the solution. The chemistry of this color reaction is uncertain. Fiegel [212] proposed that the chromogen is formed as follows:



Range and Sensitivity

From 0.1 μg/ml to 2.0 μg/ml of formaldehyde can be measured in the 10-ml final volume of solution.

A concentration as low as 0.16 ppm of formaldehyde can be determined in a 25-liter air sample based on an aliquot of 4 ml from 20 ml of absorbing solution and a difference of 0.05 absorbance unit from the blank.

Interferences

The chromotropic acid procedure has very few interferences [179] from other aldehydes. Saturated aldehydes give less than 0.01% positive interference [179], and the unsaturated aldehyde acrolein results in a few percent positive interference [179]. Ethanol and higher molecular weight alcohols and olefins in mixtures with formaldehyde are negative interferences [179]. However, concentrations of alcohols in air are usually much lower than formaldehyde concentrations and, therefore, do not usually cause a serious interference with the estimation of formaldehyde [179].

Phenols result in a 10-20% negative interference [179] when present at an 8:1 excess over formaldehyde. They are, however, ordinarily present in the atmosphere at lesser concentrations [179] than formaldehyde and, therefore, usually do not cause serious interference with the method.

Ethylene and propylene in a 10:1 excess over formaldehyde result in a 5-10% negative interference, and 2-methyl-1,3-butadiene in a 15:1 excess over formaldehyde showed a 15% negative interference [179]. Aromatic hydrocarbons may produce a negative interference [188]. It has recently been found that cyclohexanone causes a bleaching of the final color [179].

Precision and Accuracy

The method was checked for reproducibility by having three different analysts in three different laboratories analyze standard formaldehyde samples. [179,180] The results listed in Table X-1 agreed within ±5%.

TABLE X-1

COMPARISON OF FORMALDEHYDE RESULTS FROM THREE LABORATORIES

Formaldehyde	Absorbance		
Micrograms	Lab. 1	Lab. 2	Lab. 3
1	0.057	0.063	0.061
3	0.183	0.175	0.189
5	0.269	0.279	0.262
7	0.398	0.381	0.392
10	0.566	0.547	0.537
20	1.02	0.980	1.07

Apparatus

(a) Sampling Equipment

The sampling unit for the impinger collection method consists of the following components:

(1) Two graduated midget impingers containing distilled water.

(2) A pump capable of delivering a flow rate of 1 liter/minute. The sampling pump is protected from splashover or water condensation by an absorption tube loosely packed with a plug of glass wool and inserted between the exit arm of the impinger and the pump.

(3) An integrating volume meter such as a dry-gas or wet-test meter, or a calibrated rotameter.

(4) Thermometer.

(5) Manometer.

(6) Stopwatch.

(b) Spectrophotometer

An instrument capable of measuring the absorbance of a colored solution at 580 nm.

(c) Associated laboratory glassware for use with a spectrophotometer.

Reagents

(a) Chromotropic acid reagent

Dissolve 0.10 g of 4,5-dihydroxy-2,7-naphthalenedisulfonic acid disodium salt in water and dilute to 10 ml. Filter if necessary and store in a brown bottle. Make up solution weekly, but discard if solution turns yellow or brown.

(b) Concentrated sulfuric acid

(c) Formaldehyde standard solution "A" (1 mg/ml)

Dilute 3.0 ml of 37% formalin solution to 1 liter with distilled water. This solution must be standardized as described below. The solution is stable for at least a 3-month period. Alternatively, sodium formaldehyde bisulfite can be used as a primary standard. Dissolve 4.4703 g in distilled water and dilute to 1 liter.

(d) Formaldehyde Standard Solution "B" (10μg/ml)

Dilute 1 ml of standard solution "A" to 100 ml with distilled water. Make up solution daily.

(e) Iodine, 0.1 N (approximate)

Dissolve 25 g of potassium iodide in about 25 ml of water, add 12.7 g of iodine and dilute to 1 liter.

(f) Iodine, 0.01 N

Dilute 100 ml of the 0.1 N iodine solution to 1 liter. Standardize using either sodium thiosulfate or arsenic trioxide.

(g) Starch solution, 1%

Make a paste of 1 g of soluble starch and 2 ml of water and slowly add the paste to 100 milliliters of boiling water. Cool, add several milliliters of chloroform as a preservative, and store in a stoppered bottle. Discard if a mold growth is noticeable.

(h) Sodium carbonate buffer solution

Dissolve 80 g of anhydrous sodium carbonate in about 500 ml of water. Slowly add 20 ml of glacial acetic acid to give a final pH of 9.6, and dilute to 1 liter.

(i) Sodium bisulfite, 1%

Dissolve 1 g of sodium bisulfite in 100 ml of water. It is best to prepare a fresh solution weekly.

Procedure

(a) Cleaning of equipment

Care must be exercised to ensure the absence of probable contaminants like organic materials that can be charred by concentrated sulfuric acid. After normal cleaning with detergent solution, glassware should be soaked for 1 hour in a 1:1 mixture of nitric and sulfuric acids, followed by thorough rinsing with doubly deionized water to remove all possible organic contaminants.

(b) Collection and shipping of samples

Pour 20 ml of the absorbing solution (distilled water) into each graduated midget impinger and collect formaldehyde from air and prepare samples as described in Appendix I.

(c) Analysis of samples

(1) Transfer the sample from each impinger to either a 25-ml or 50-ml graduate. Note the volume of each impinger solution.

(2) Pipet a 4-ml aliquot from each of the sampling solutions into glass stoppered test tubes. A blank containing 4 ml of distilled water must also be run. If the formaldehyde content of the aliquot exceeds the limit of the method, use a smaller aliquot diluted to 4 ml with distilled water. Alternatively, aliquots from each impinger can be combined for a single analysis

(3) Add 0.1 ml of 1% chromotropic acid reagent to the solution and mix.

(4) Into the solution from step 3, pipet slowly and cautiously 6 ml of concentrated sulfuric acid. The heat produced by the addition of the sulfuric acid is required to promote the reaction, but the acid should be added sufficiently slowly to prevent loss of sample because of boiling and spattering.

(5) Allow to cool for 20 minutes. Read absorbance at 580 nm in a suitable spectrophotometer using a 1-cm cell. Determine the formaldehyde content of the sampling solution from a curve previously prepared from standard formaldehyde solutions.

(6) During the analysis, it is good practice to group together the two impingers from each sampling series and label them as "A" and "B". The formaldehyde content calculated in "A" is added to that calculated in "B" to give the total amount of formaldehyde collected by the impingers in series.

Calibration and Standards

(a) Standardization of formaldehyde solution

(1) Pipet 1 ml of formaldehyde standard solution "A" into an iodine flask. Into another flask, pipet 1 ml of distilled water. This second flask serves as the blank.

(2) To each flask, add 10 ml of 1% sodium bisulfite and 1 ml of 1% starch solution.

(3) Titrate with 0.1 N iodine to a dark blue color.

(4) Destroy the excess iodine with 0.05 N sodium thiosulfate.

(5) Add 0.01 N iodine until a faint blue end point is reached.

(6) The excess inorganic bisulfite is now completely oxidized to sulfate, and the solution is ready for the assay of the formaldehyde bisulfite addition product.

(7) Chill the flask in an ice bath and add 25 ml of chilled sodium carbonate buffer. Titrate the liberated sulfite with 0.01 N iodine, using a microburet, to a faint blue end point. The amount of iodine added in this step must be accurately measured and recorded.

(8) One milliliter of 0.00100 N iodine is equivalent to 0.15 mg of formaldehyde. Therefore, since 1 milliliter of formaldehyde standard solution was titrated, the milliliter of 0.01 N iodine used in the final titration multiplied by the factor, 0.15, gives the formaldehyde concentration of the standard solution in mg/ml.

(9) The factor 0.15 must be adjusted or determined in accord with the exact normality of the iodine solution.

(b) Preparation of Standard Curve

(1) Pipet 0, 0.1, 0.3, 0.5, 0.7, 1.0, and 2.0 ml of standard solution "B" into glass stoppered test tubes.

(2) Dilute each standard to 4 ml with distilled water.

(3) Develop the color as described in the analysis procedure under Section (C).

(4) Plot absorbance against micrograms of formaldehyde in the color developed solution. Note that the microgram concentration of the

formaldehyde is determined based on the standardization value obtained for solution A.

Calculations

(a) Convert the volume of air sampled (V) to the volume of air at standard conditions (Vs) of 760 mm of mercury and 25 degrees C, using the correction formula:

$$Vs = \frac{V \times P \times 298}{760(T + 723)}$$

where:

Vs = volume of air in liters at standard conditions
V = volume of air sampled in liters
P = barometric pressure in mm of mercury
T = temperature of sample air, C

(b) Determine the total concentration (Ct) of formaldehyde present in the two sample impingers in series, A and B.

$$Ct = Ca \times Fa + Cb \times Fb$$

where:

Ct = total μg of formaldehyde in the sample
Ca and Cb = respective formaldehyde concentration in μg of the sample aliquots taken from impingers A and B as determined from the calibration curve
Fa and Fb = respective aliquot factor; $\frac{\text{sampling soln. vol. in ml}}{\text{ml aliquot used}}$

(c) The concentration of formaldehyde in the sampled atmosphere may be calculated by using the following equation, assuming standard conditions are taken as 760 mm of mercury and 25 degrees C:

$$\text{ppm (volume)} = \frac{Ct \times 24.47}{Vs \times M.W.}$$

where:

Vs = liters of air sampled at standard conditions

M.W. = molecular weight of formaldehyde (30.03)

24.47 = μl of formaldehyde gas in one micromole at 760 mm Hg and 25 degrees C.

XI. 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 name need not be listed.

(b) Section II. Hazardous Ingredients

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

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

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

Toxic hazard data shall be stated in terms of concentration, mode of exposure or test, and animal used, eg, "100 ppm LC50-rat," "25mg/kg LD50-skin-rabbit," "75 ppm LC man," 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. Flammability or reactivity data could be flashpoint, 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 flashpoint and autoignition temperature in degrees Fahrenheit (Celsius in parentheses); flammable limits, in percent by volume in air; suitable extinguishing media or materials; special firefighting procedures; and unusual fire and explosion hazard information. If the product presents no fire hazard, insert "NO FIRE HAZARD" on the line labeled "Extinguishing Media."

(e) Section V. Health Hazard Information

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

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

> Skin Contact--single short contact, no adverse effects likely; prolonged or repeated contact, mild irritation and possibly some blistering.
>
> 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," "Suitable for dusts not more toxic than lead," etc. Protective equipment must be specified as to type and materials of construction.

(i) Section IX. Special Precautions

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

(j) Signature and Filing

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

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

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IX SPECIAL PRECAUTIONS

PRECAUTIONARY STATEMENTS	
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XII. TABLES AND FIGURES

TABLE XII-1

PROPERTIES AND CHARACTERISTICS OF FORMALDEHYDE (FM)

Formula	HCHO
Molecular weight	30.03
Physical state	Gas
Melting point	-92 C
Boiling point	-21 C
Specific gravity	0.815
Relative vapor density	1.075 (air = 1)
Solubility	Soluble in water, alcohol, and ether
Color	Colorless
Odor	Pungent and irritating
Explosive limits:	
Gas	7.0-73% by volume in air
Aqueous solution	Vapor may be flammable
Flashpoint (closed cup) of aqueous solution	50 C (122 F)
Autoignition temperature	430 C (806 F)

1 mg/cu m = 0.81 ppm
1 ppm = 1.23 mg/cu m

Derived from references 6,213

TABLE XII-2

USE OF FORMALDEHYDE IN THE UNITED STATES

Supply capacity - 1972	7,530 million pounds*
Demand - 1972	5,000 million pounds*
Demand - 1976 (estimated)	6,300 million pounds*
Growth (1961-1971)	7.9%/year
Growth through 1976 (estimated)	7.5%/year

*expressed as 37% solution

From reference 137 (1972)

TABLE XII-3

FORMS OF FORMALDEHYDE POLYMERS

Substance	Type Formula	Range of Polymerization, n	CH2O Content, Wt %	Melting Range, C	Acetone	Water	Dilute Alkali	Dilute Acid
1. Linear polymers (On vaporization these depolymerize to monomeric formaldehyde gas.)								
Lower polyoxymethylene glycols	HO(CH2O)nH	2-8	77-93	80-120	s-i	vs	vs	vs
Paraformaldehyde	HO(CH2O)nH	8-100	91-99	120-170	s-i	ds	s	s
alpha-Polyoxymethylene	HO(CH2O)nH	100-300	99.0-99.9	170-180	i	vds	s	s
beta-Polyoxymethylene	HO(CH2O)nH +H2SO4 (trace)	100-300	98-99	165-170	i	vds	ds	ds
Polyoxymethylene glycol derivatives*** polyoxymethylene diacetates	CH3COO(CH2O)nCOCH3	2-200	37-93	up to ca 165	i for n >10	i	ds	ds
Lower polyoxymethylene dimethyl ethers	CH3O(CH2O)nCH3	2-200	72-93	up to ca 175		i for n >15	i for n >15	ds
gamma-Polyoxymethylene (higher polyoxymethylene dimethyl ethers)	CH3O(CH2O)nCH3	200-500	93-99	160 to ca 180	i	i	i	ds
delta-Polyoxymethylene	CH3O(CH2O)n CH2CH(OH)OCH3	g100	96-97	150-170	i	i	i	ds
epsilon-Polyoxymethylene	(CH2O)n	probably g100	99.7-99.9	195-200	i	i		
high-molecular-weight polyoxymethylenes****	HO(CH2O)nH	500-5000	99.9-100	170-185	i	i	vds	vds
2. Cyclic polymers (On vaporization these do not depolymerize.)								
Trioxane (alpha-trioxymethylene)	(CH2O)3	3	100	61-62	s	s	s	s
Tetraoxymethylene	(CH2O)4	4	100	112	s	s	s	s

From Walker [2]

TABLE XII-4

USES OF FORMALDEHYDE

Phenolic resins	25 %
Urea-formaldehyde resins	25
Polyacetal resins	8
Melamine	8
Pentaerythritol	7
Hexamethylenetetramine	6
Fertilizers	5
Acetylenics	2
Export and miscellaneous	14
Total	100 %

From reference 137

TABLE XII-5

POTENTIAL OCCUPATIONAL EXPOSURES TO FORMALDEHYDE

Occupation	Reference
Anatomists	214
Agricultural workers	215,216,217
Bakers	214
Beauticians	65,71,72,73
Biologists	214
Bookbinders	214
Botanists	214
Crease-resistant textile finishers	214
Deodorant makers	214
Disinfectant makers	68,74,217
Disinfectors	214,217,218
Dress goods store personnel	214
Dressmakers	214
Drugmakers	214
Dyemakers	1,215.217
Electrical insulation makers	88
Embalmers	214,215,217
Embalming fluid makers	214,215,217
Ethylene glycol makers	214
Fertilizer makers	2,215
Fireproofers	1
Formaldehyde resin makers	214,217,218
Formaldehyde employees	214,215
Foundry employees	219
Fumigators	217
Fungicide workers	214,215,217
Furniture dippers and sprayers	214
Fur processors	214
Glass etchers	214
Glue and adhesive makers	92,70
Hexamethylenetetramine makers	214
Hide preservers	214
Histology technicians	214
Ink makers	214
Lacquerers and lacquer makers	214
Medical personnel	215,217,220
Mirror workers	1
Oil well workers	214
Paper makers	76,77,89,214,217

TABLE XII-5 (CONTINUED)

POTENTIAL OCCUPATIONAL EXPOSURES TO FORMALDEHYDE

Pentaerythritol makers	214
Photographic film makers	1,214,215,218
Plastic workers	1,218
Resin makers	214,217,218
Rubber makers	214,217
Soil sterilizers and greenhouse workers	216
Surgeons	220
Tannery workers	1,215,217,218
Taxidermists	215,221
Textile mordanters and printers	214,215
Textile waterproofers	214,215
Varnish workers	88,65
Wood preservers	214

TABLE XII-6

DOSE-RESPONSE RELATIONSHIPS IN ANIMALS EXPOSED TO FORMALDEHYDE

Species	No.	Route	Dose	Response	Ref.
Cat	3	Inhal	1,630-7,830 ppm for 4.7 hr	Death occurred after 20 min, 4.7 hr, and 4 days	108
"	2	"	667 ppm for 8-8.7 hr	Deaths occurred on days 4 and 6, after salivation, acute dyspnea, vomiting, and cramps	108
"	2	"	211-667 ppm for 3.5-4 hr	Irritation of mucous membranes, slight dyspnea, recovery in 2 days	108
Dog	2	"	3.7 ppm, 24 hr/d/90d	Interstitial inflammation of lungs	121
Guinea pig	6	"	6,000 ppm for 1 hr	Increased airway resistance, decreased respiration rate, increased tidal volume, decreased minute volume, no change in compliance	119
Guinea pig (tracheotomized)	6	"	"	No changes in any of above parameters	119
Guinea pig	6	"	1,000 ppm for 1 hr	Increased airway resistance, decreased respiration rate, increased tidal volume, decreased minute volume, no change in compliance	119
Guinea pig (tracheotomized)	6	"	"	No changes in any of above parameters	119
Guinea pig	6	"	50 ppm for 1 hr	Increased airway resistance, decreased respiration rate, increased tidal volume, decreased minute volume, no change in compliance	119
Guinea pig (tracheotomized)	6	"	"	No changes in any of above parameters	119
Guinea pig	3	"	50 ppm for 4 hr	Increased flow resistance for 1 hr then drop off, decreased compliance	113
"	11	"	49 ppm for 1 hr	Increased, airway resistance, decreased compliance, increased tidal volume, decreased breathing frequency, decreased minute volume, increased elastic work, increased resistive work, increased total work	114
"	8	"	47 ppm + 10 mg NaCl/cu m for 1 hr	Increased airway resistance	112

TABLE XII-6 (CONTINUED)
DOSE RESPONSE RELATIONSHIPS IN ANIMALS EXPOSED TO FORMALDEHYDE

Species	No.	Route	Dose	Response	Ref.
Guinea pig	12	Inhal	27 ppm + 12.1 mg NaCl/cu m for 1 hr	Increased resistance	114
"	20	"	16.3 ppm for 10 hr (aerosol)	Initial increase in activity, animals blinked, closed eyes, rubbed faces with paws, settled down, slow deep res-	112
"	20	"	15.4 ppm for 10 hr (gas)		
"	10	"	11.0 ppm for 1 hr	Increase in airway resistance, decreased compliance, decrease in breath frequency, decrease in minute volume	114
"	8	"	10.8 ppm + 10.7 mg NaCl/cu m for 1 hr	Increased resistance	114
"	7	"	9.6 ppm + 30 mg NaCl/cu m for 1 hr	"	114
"	5	"	4.8 ppm + 4.1 mg NaCl/cu m for 1 hr	"	114
"	9	"	3.9 ppm for 1 hr	69% increase in slow airway resistance, 29% increase in tidal volume, 27% decrease in respiratory rate	118
"	15 M 15 F	"	3.7 ppm, 24 hr/d/90 d	Interstitial inflammation of lungs, focal chronic inflammatory changes in heart and kidney, no clinical illness	121
"	10	"	3.6 ppm for 1 hr	Increased airway resistance, decreased compliance, increased resistive work, increased total work	114
"	10	"	3.5 ppm for 1 hr	Increase in flow resistance, decrease in compliance	113
"	15	"	3.5 ppm + 26 mg NaCl/cu m for 1 hr	Increased airway resistance	114
"	8	"	2.6 ppm + 8.7 mg NaCl/cu m for 1 hr	"	114
"	4	"	1.22 ppm for 1 hr	Increased airway resistance, increased elastic work, increased resistive work, increased total work	114
"	6	"	1.2 ppm + 3.5 mg NaCl/cu m for 1 hr	Increased airway resistance	114

TABLE XII-6 (CONTINUED)
DOSE RESPONSE RELATIONSHIPS IN ANIMALS EXPOSED TO FORMALDEHYDE

Species	No,	Route	Dose	Response	Ref.
Guinea pig	7	Inhal	1.01 ppm + 22 mg NaCl/cu m for 1 hr	Increased resistance	114
"	8	"	0.76 ppm + 12.8 NaCl/cu m for 1 hr	"	114
"	23	"	0.58 ppm for 1 hr	Increased resistance, decreased compliance	114
"	7	"	0.58 ppm + 3.0 mg NaCl/cu m for 1 hr	Increased resistance	114
"	8	"	0.34 ppm + 35 mg NaCl/cu m for 1 hr	"	114
"	8	"	0.32 ppm + 11.3 mg NaCl/cu m for 1 hr	"	114
"	13	"	0.31 ppm for 1 hr	Increased resistance, decreased compliance	114
"	10	"	0.24 ppm + 4.3 mg NaCl/cu m for 1 hr	Increased resistance	114
"	13	"	0.11 ppm + 3.9 mg NaCl/cu m for 1 hr	"	114
"	4	"	0.07 ppm + 7.5 mg NaCl/cu m for 1 hr	No resistance change	114
"	13	"	0.06 ppm + 3.5 mg NaCl/cu m for 1 hr	"	114
"	18	"	0.05 ppm for 1 hr	No change	114
Monkey	3	"	3.7 ppm, 24 hr/d/90 d	Interstitial inflammation of lungs, no clinical signs of illness	121

TABLE XII-6 (CONTINUED)
DOSE RESPONSE RELATIONSHIPS IN ANIMALS EXPOSED TO FORMALDEHYDE

Species	No.	Route	Dose	Response	Ref
Mouse	?	Inhal	731 ppm for 2 hr	Death from massive pulmonary hemorrhage and edema	122
"	42	"	162 ppm, 1 hr/d, 3 d/wk, 11 total exposures	4 tracheobronchial basal cell hyperplasias, 8 tracheobronchial stratifications, 16 squamous cell metaplasias, 5 atypical metaplasias, no tumors, 12 deaths	122
"	60	"	81 ppm, 1 hr/d, 3 d/wk, 35 wk, 105 exposures	10 tracheobronchial basal cell hyperplasias, 14 tracheobronchial stratifications, 6 squamous cell metaplasias, no tumors in 64 weeks. Subsequent exposure of the mice at 300 mg/cu m coal tar indicated no predisposition to cancer from the HCHO exposure	122
"	60	"	41 ppm, 1 hr/d, 3 days/wk, 35 wk, 105 exposures	6 tracheobronchial basal cell hyperplasias, 9 tracheobronchial stratifications, no metaplasia, no tumors. Subsequent exposure at 150 mg/cu m from the 35th to the 70th week failed to produce any tumors in 37 of the animals so exposed	122
"	?	"	33 ppm, 2 hr/d/4 d	no "Substantial" distress or weight loss	122
"	50	"	16.3 ppm aerosol for 10 hr	Initial increase in activity, blinked, closed eyes, rubbed faces with paws, settled down, slow deep respiration, convulsion, death in 48 animals	112
"	50	"	15.4 ppm for 10 hr	Same as above but death in 17 animals	112
Rabbit	5	"	16.3 ppm aerosol for 10 hr	Same as above but death in 1 animal	112
"	5	"	15.4 ppm for 10 hr	Same as above but death in 3 animals	112
"	3	"	3.7 ppm, 24 hr/d/90 d	Interstitial inflammation of lungs, no clinical signs of illness, however	121

TABLE XII-6 (CONTINUED)
DOSE RESPONSE RELATIONSHIPS IN ANIMALS EXPOSED TO FORMALDEHYDE

Species	No.	Route	Dose	Response	Ref
Rat	72	"	490-1400 ppm	LC50 = 81 ppm	108
"	8	"	35 ppm for 18 hr	Increased liver alkaline phosphatase activities; dyspnea and nasal irritation	110
"	15	"	3.7 ppm, 24 hr/d/90 d	Interstitial inflammation of lungs, 1 death, focal chronic inflammatory changes in heart and kidney	121
"	25	Inhal	2.5 ppm/3 mo	Lymphohistologic elements in interalveolar walls, peribronchial and perivascular spaces, moderate hyperemia, mild histologic changes in cells of respiratory tract, liver, kidney, and cerebral cortex	93
"	25	"	0.8 ppm/3 mo	"	93
"	25	"	0.03 ppm/3 mo	No histologic changes	93
"	25	"	0.01 ppm/3 mo	"	93
Rat (pregnant)	12	"	0.01 ppm 16-21 d 24 hr/d	Increased litter size, increased mean duration of pregnancy, increased weight of fetal adrenals and mean duration of pregnancy, infetal lungs and liver	125
Rat (pregnant)	12	"	0.8 ppm for 24 hr/d for 16-21 d	Increased litter size, and mean duration of pregnancy, mean duration of pregnancy, dedecreased weight of fetal lung and liver, increased adrenals, kidney, and total body weight	125
Mouse	72	Sc	0.15-0.46 g/kg	LD50=0.30 g/kg (Deaths within 20 min) Survivors recovered in 2-3 d	107
Rat	64	"	0.30-0.64 g/kg	LD50=0.42 g/kg (Deaths within 68 hrs) Survivors recovered 2-3 d	122

TABLE XII-7

FORMALDEHYDE STANDARDS IN EFFECT

Country	Standard mg/cu m	Standard ppm	Standard Type	References
USA 1) Federal Standard	--	3	TWA	FR 39 (125):23540-43, 1974
	--	5	Ceiling	"
	--	10	30 min Ceiling	"
2) ACGIH TLV	2.5	2	Ceiling	222
3) ANSI Z-37	--	3	TWA	204
	--	5	Ceiling	204
	--	10	30 min Ceiling	204
Bulgaria	5	4	Ceiling	210
Czechoslovakia	2	--	"	208
	5	--	Peak	208
Finland	6	5	Ceiling	210
Federal Republic Germany	6	5	"	210
German Democratic Repub.	5	--	"	208
Great Britain	12	10	"	208
Hungary	1	--	"	210
Italy	5	--	"	210
Japan	6	5	"	210
Poland	5	--	"	210
Rumania	3	--	"	210
UAR	--	20	"	210

TABLE XII-7 (CONTINUED)
FORMALDEHYDE STANDARDS IN FORCE

Country	Standard mg/cu m	ppm	Type	References
USSR	0.5	0.4	Ceiling	210
Yugoslavia	6	5	"	210
USA - Florida	--	5	"	210
- Hawaii	--	10	"	210
- Massachusetts	--	3	"	210
- Mississippi	--	5	"	210
- Pennsylvania	--	5	TWA	210
"	--	5	5 min Ceiling	210
- South Carolina	--	5	Ceiling	210

TABLE XII-8

CONCENTRATION EFFECT RELATIONSHIPS COMPILED BY CZECHOSLOVAK COMMITTEE OF MAC

Author	Year	mg/cu m	Symptoms
Lazareff	1959	0.2	Odor
Morill	1961	0.2	Odor
Bourne	1959	1.2-2.5	Strong subjective neurasthenic complaints
Chifman acc. to Lazareff		1.0-9.5	Light irritation of conjunctivas and mucosa of upper respiratory tract
Smyth	1956	6	Slight irritation of eyes, nose, respiratory tract
Elkins	1950	±6-7	Irritation of conjunctivas in unaccustomed persons
		6-7	Irritattion at inspiration
Smyth	1956	12	Odor
Fairhall	1949	24	"Such low" concentration irritates mucosa strongly
Lazareff	1959	25	Severe irritation of mucosa
Smyth	1956	60	Significant irritation of eyes, nose, and resp. tract danger of lung damage
Patty	1949	250	In cats after 3.5-hour exposure, rapid recovery without damage
		800	After 8 hour-exposure, edema and hemorrhage in lungs, later inflammation of lungs, and usually death

From reference 208

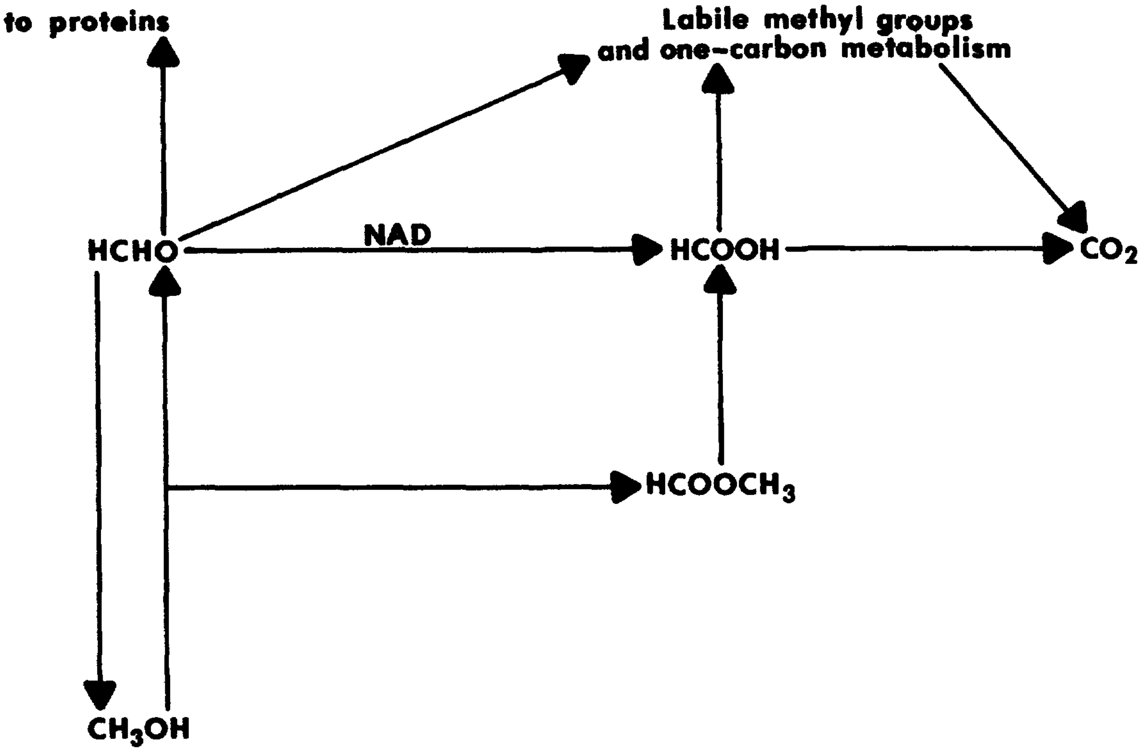

FIGURE XII-1
PROPOSED METABOLIC FATE OF FORMALDEHYDE

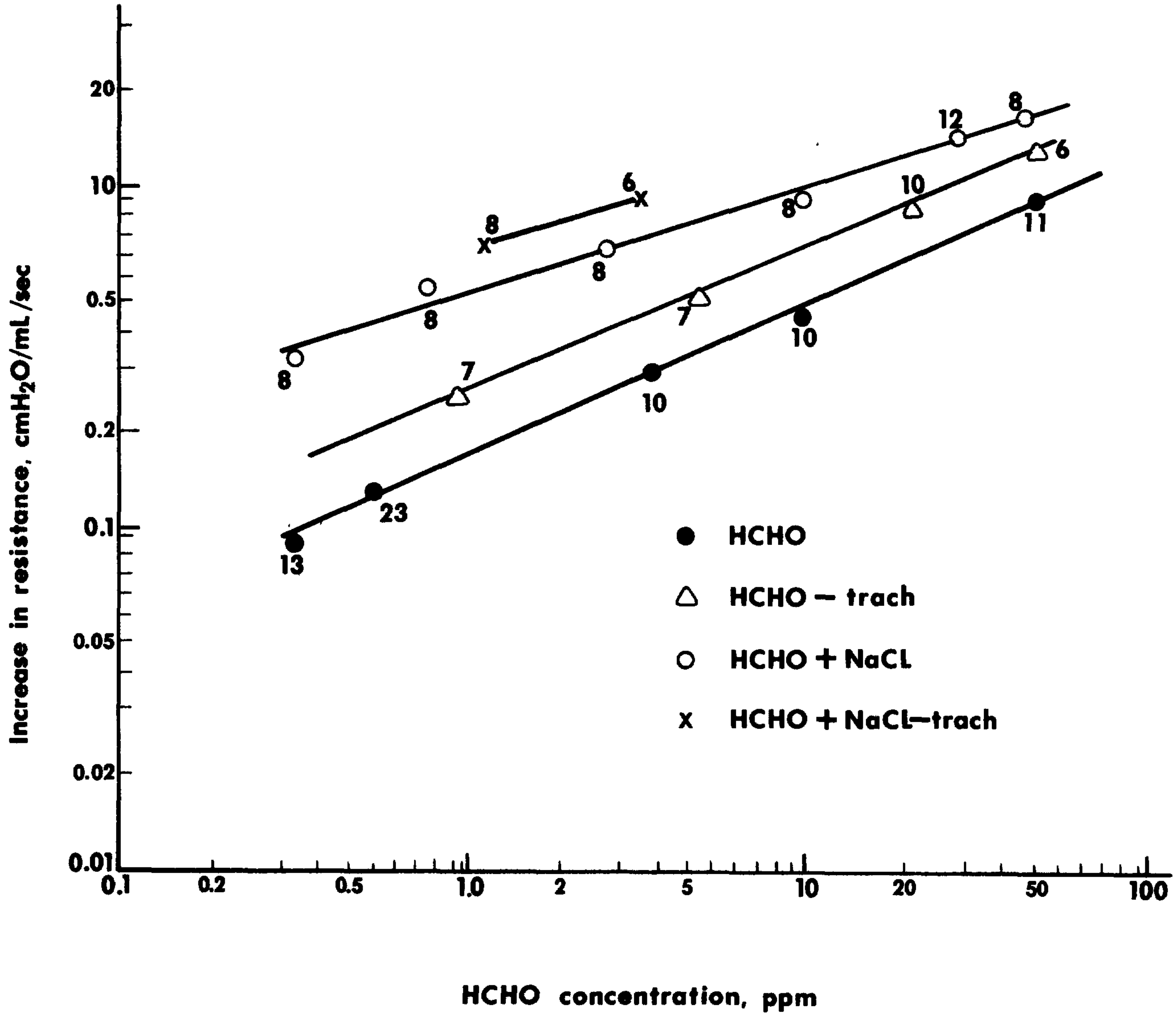

FIGURE XII-2
DOSE RESPONSE RELATIONSHIPS FOR TRACHEOTOMIZED AND UNTRACHEOTOMIZED GUINEA PIGS EXPOSED TO HCHO AND HCHO IN THE PRESENCE OF AN AEROSOL OF 1% AQUEOUS SOLUTION OF SODIUM CHLORIDE AT 10 MG NaCL/CU M

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