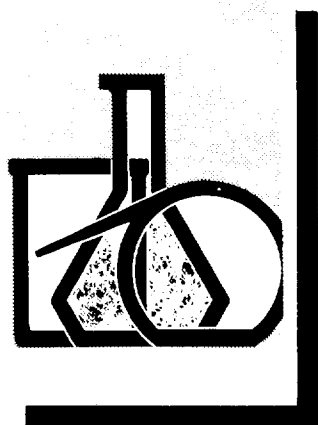
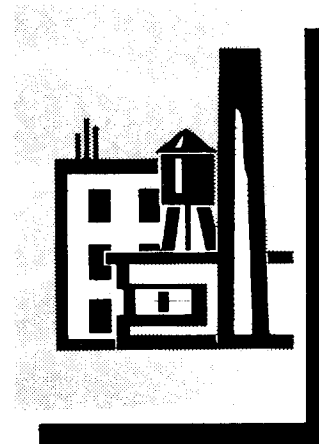


# **NIOSH**

## **SPECIAL OCCUPATIONAL HAZARD REVIEW with CONTROL RECOMMENDATIONS**



## **Use of Ethylene Oxide as a Sterilant in Medical Facilities**

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

SPECIAL OCCUPATIONAL HAZARD REVIEW  
WITH  
CONTROL RECOMMENDATIONS  
FOR THE  
USE OF ETHYLENE OXIDE AS A STERILANT IN MEDICAL FACILITIES

prepared by  
Zorach R. Glaser, Ph.D

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
Public Health Service  
Center for Disease Control  
National Institute for Occupational Safety and Health  
Division of Criteria Documentation and Standards Development  
Priorities and Research Analysis Branch  
Rockville, Maryland

August 1977

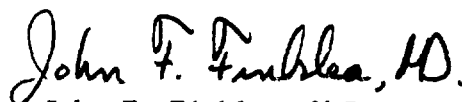
DISCLAIMER

Mention of company name or product does not constitute endorsement by the National Institute for Occupational Safety and Health.

**DHEW (NIOSH) Publication No.77-200**

## 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 in their workplace. Pursuant to the fulfillment of this need, the National Institute for Occupational Safety and Health (NIOSH) has developed a strategy of disseminating information about adverse effects of widely used chemical or physical agents intended to assist employers in providing protection for employees from exposure to substances considered to possess carcinogenic, mutagenic, or teratogenic potential. This strategy includes the development of Special Occupational Hazard Reviews which serve to support and complement the other major standards development or hazards documentation activities of the Institute. The purpose of Special Occupational Hazard Reviews is to analyze and document, from a health standpoint, the problems associated with a given industrial chemical, process, or physical agent, and to recommend the implementation of engineering controls and work practices to ameliorate these problems. While Special Occupational Hazard Reviews are not intended to supplant the more comprehensive NIOSH Criteria Documents, nor the brief NIOSH Current Intelligence Bulletins, they are nevertheless prepared in such a way as to assist in the formulation of regulations. Special Occupational Hazard Reviews are disseminated to the occupational health community at large, e.g., trade associations, industries, unions, and members of the scientific community.



John F. Finklea, M.D.  
Director, National Institute for  
Occupational Safety and Health

## ACKNOWLEDGEMENTS

Sincere appreciation is extended to Jerry LR Chandler, Ph.D., Norbert P. Page, D.V.M., Murray L. Cohen, M.P.H., and Jack L. Arthur, M. En., for assistance in the preparation of this report. Division reviewers consisted of Frank L. Mitchell, D.O. (chairman), J. Henry Wills, Ph.D., and Jon R. May, Ph.D. Valuable and constructive comments were also provided by Robert B. O'Connor, M.D., NIOSH consultant in occupational medicine.

The assistance of Masao Koketsu and Lynn Carssow, Industrial Hygienists with Stanford Research Institute (NIOSH contract No. 210-76-0162), was invaluable in conducting the field survey in medical facilities.

## SUMMARY AND CONCLUSIONS

Ethylene oxide (ETO) is used extensively within health care facilities for sterilization of equipment and supplies which are heat sensitive. It is unique for this purpose. Alternative chemicals or processes have, in themselves, serious limitations or health hazards. NIOSH recognizes, therefore, that the continued use of ETO as a gaseous sterilant is highly desirable in many situations. Recent results of tests for mutagenesis have increased the concern for potential health hazards associated with exposure to ETO. In order to assess the potential for exposure and associated hazards, NIOSH has undertaken this Special Occupational Hazard Review. An assessment is made of the evidence for toxic effects of ETO, especially with respect to mutagenic, teratogenic and carcinogenic potentials. Additionally, a limited field survey was conducted by NIOSH to document the use, problems, and potential for human exposure in medical facilities. The results of this survey were in agreement with data made available by the American Hospital Association, the U.S. Army, other Federal agencies, and industrial and professional organizations. Based on this review, measures for control of occupational exposure are recommended.

The acute toxic effects of ETO in man and animals include acute respiratory and eye irritation, skin sensitization, vomiting, and diarrhea. Known chronic effects consist of respiratory irritation and secondary respiratory infection, anemia, and altered behavior.

The observations of (a) heritable alterations in at least 13 different lower biological species following exposure to ETO, (b) alterations in the structure of the genetic material in somatic cells of the rat, and (c) covalent chemical bonding between ETO and DNA support the conclusion that continuous occupational exposure to significant concentrations of ETO may induce an increase in the frequency of mutations in human populations. At present, however, a substantive basis for quantitative evaluation of the genetic risk to exposed human populations does not exist.

No definitive epidemiological studies, and no standard long-term carcinogenesis assays, are available on which to assess carcinogenic potential. Limited tests by skin application or subcutaneous injections in mice did not reveal carcinogenicity. However, the alkylating and mutagenic properties of ETO are sufficient bases for concern about its potential carcinogenicity. Neither animal nor human data are available on which to assess the potential teratogenicity of ETO.

NIOSH recommends that ETO be considered as mutagenic and potentially carcinogenic to humans, and that occupational exposure to it be minimized by eliminating all unnecessary and improper uses of ETO in medical facilities. Whenever alternative sterilization processes are available which do not present similar or more serious hazards to the employee, they should be substituted for ETO sterilization processes whenever possible. Although this review is limited to ETO, concern is also expressed for hazards from such hydration and reaction products of ETO as ethylene glycol and ethylene chlorohydrin, the latter a teratogen to some lower biological species.

This report includes a summary of the airborne ETO concentrations measured within health care facilities as part of the field survey. NIOSH estimates that there are in excess of 10 thousand ETO sterilizers in use in U.S. health care facilities, and that approximately 75 thousand workers are potentially exposed to ETO in those facilities. Reasons for the unnecessary exposure of personnel were found to include: improper or inadequate ventilation of sterilizers, aerators, and working spaces; improper handling and/or storage of sterilized items; untrained workers operating some sterilization equipment; improper operating techniques leading to mishandling of some ETO sterilizing equipment; poor design of the sterilization facility; and, design limitations of the sterilization equipment.

NIOSH recommends, based on the recent results of tests for mutagenesis, that exposure to ETO be controlled so that workers are not exposed to a concentration greater than 135 mg/cu m (75 ppm) determined during a 15-minute sampling period, as a ceiling occupational exposure limit and in addition, with the provision that the time-weighted average (TWA) concentration limit of 90 mg/cu m (50 ppm) for a workday not be exceeded. As additional information on the toxic effects of ETO becomes available, this recommended level for exposures of short duration may be altered. The adequacy of the current U.S. ETO standard, which was based on the data available at the time of promulgation, has not been addressed in this report. Further assessment of other ETO exposure situations, and of the adequacy of the ETO occupational exposure standard will be undertaken during the FY 80 development of a NIOSH criteria document for occupational exposure to epoxides. In the interim, NIOSH strongly recommends that control strategies, such as those described in this document, or others considered to be more applicable to particular local situations, be implemented to assure maximum protection of the health of employees. Good work practices will help to assure their safety.

Where the use of ETO is to be continued, improved techniques of exhausting the gas from the sterilizer, the aerator, and the sterilized items need to be implemented. Gas sterilization should be supervised and the areas into which ETO may escape should be monitored to prevent all unnecessary exposure of personnel. When proper control measures are instituted, the escape of ETO into the environment will be greatly reduced. Under such control, the use of ETO as a gaseous sterilizant in medical facilities can be continued with considerably less risk to the health of occupationally-exposed employees.

## CONTENTS

	<u>Page</u>
PREFACE	iii
SUMMARY AND CONCLUSIONS	v
CONTENTS	vii
INTRODUCTION	1
I. PROPERTIES	3
A. Identification	3
B. Physical/Chemical Properties of ETO	3
II. USES AND OCCURRENCE IN MEDICAL FACILITIES	4
A. Characterization of Occupational Exposure During ETO Sterilization Procedures	4
B. ETO Residues in Sterilized Medical Equipment	5
C. Alternatives to the Use of ETO Sterilization	7
III. SUMMARY OF RESULTS OF FIELD STUDIES CONDUCTED IN MEDICAL FACILITIES	8
A. ETO Sterilizer Use, and Number of Workers Potentially Exposed to ETO	8
B. Potential Exposure Situations Encountered in the Field Study	9
C. Measurement of Ambient Levels of ETO	11
D. Conclusions	12
IV. BIOLOGIC EFFECTS OF EXPOSURE TO ETO	14
A. Effects in Animals and Lower Biological Systems	14
1. Acute Toxicity	15
2. Sub-Chronic Toxicity	15
3. Chronic Toxicity	16
4. Carcinogenic, Mutagenic, Reproductive, Teratogenic, and Metabolic Studies	16
B. Effects in Humans	21
1. Acute Toxicity	21
2. Chronic Effects	23
3. Sensitization Response	26
4. Hemolytic Effects	26
C. Tabulation of Biologic Effects of ETO	26
V. OCCUPATIONAL EXPOSURE LIMITS	38
Table of Occupational Exposure Limits for ETO and Some Hydration and Reaction Products	39



CONTENTS (Continued)

	<u>Page</u>
VI. HAZARDS, CONTROL MEASURES, MEDICAL SURVEILLANCE, AND RECORD KEEPING	40
A. Hazards and Precautions, Prevention, and Emergency Procedures	40
1. Fire, Explosion, and Reactivity Data	40
2. Spill, Leak, and Disposal Procedures	40
3. Sanitation Practices	41
B. Recommendations for Control of Hazardous Exposure Situations	41
1. Posting of Signs	41
2. Protective Clothing and Respirators	41
3. Engineering and Other Control Technology	42
4. Training in Proper Operational Procedures	43
C. Medical Surveillance, Record Keeping, and Informing Employees of the Hazard	43
1. Medical Surveillance	43
2. Record Keeping and Availability of Records	44
3. Informing Employees of the Hazard	44
VII. SAMPLING AND ANALYTICAL METHODS	46
A. Airborne-ETO Monitoring Techniques and Equipment	46
B. Principle of the NIOSH Standard Method	46
C. Range of Sensitivity of the Method	47
D. Interference	47
E. Precision and Accuracy	47
APPENDIX	48
VIII. REFERENCES	49

## INTRODUCTION

Ethylene oxide (ETO) is a high volume chemical used primarily as an intermediate in the production of ethylene glycol (27% of total consumption), polyethylene terephthalate polyester fiber and film (23%), non-ionic surface-active agents (13%), ethanolamines (9%), with production of di- and tri-ethylene glycol, choline and choline chloride, and other organic chemicals consuming most of the remaining ETO. Although it is estimated that only about 0.02% of the total amount of ETO produced in the U.S. in 1976 was used for sterilization in medical facilities, this amounted to approximately 500,000 kg.

ETO is registered with the U.S. Environmental Protection Agency as a fungicide for fumigation of books, dental, pharmaceutical, medical and scientific equipment and supplies (glass, metals, plastics, rubber or textiles), drugs, leather, motor oil, paper, soil, bedding for experimental animals, clothing, furs, furniture, and transportation vehicles, such as jet aircraft, buses, and railroad passenger cars.

It has been used also to sterilize foodstuffs such as spices, cocoa, flour, dried egg powder, desiccated coconut, dried fruits and dehydrated vegetables (Wesley et al, 1965), and to accelerate the "maturing" of tobacco leaves (Fishbein, 1969). At one time (Stehle et al, 1924), ETO was used briefly as a possible anesthetic agent, but was discarded due to toxic effects.

This Hazard Review Document pertains only to the use of ETO in sterilization of medical supplies and equipment within medical and related facilities. The term "medical facilities" will be used to include hospitals, nursing and "total care" homes, medical, dental and veterinary clinics or facilities, and certain research laboratories affiliated with medical centers.

ETO is manufactured by the catalytic oxidation of ethylene with air (or oxygen) in the presence of a silver catalyst. Since 1972, this has been the only method used in the U.S. Wurtz, in 1859, prepared ETO from ethylene chlorohydrin and potassium hydroxide. Until 1957, the chlorohydrin process was the principal method of manufacturing ETO in the U.S.

In March 1973, the 13 companies which produced ETO in the U.S. and Puerto Rico had a total production of 1,892 million kg. In 1976, the annual U.S. production of ETO had grown to approximately 2,100 million kg, giving to this chemical a position within the top twenty-five chemicals (by volume) produced in the U.S. It is used extensively worldwide, with total production in Japan in 1974 of 415 million kg. European production in 1972 has been estimated at 865 million kg.

The current U.S. standard (OSHA) for occupational exposure to ETO is 50 parts per million (ppm) parts of air, as a time weighted average (TWA) concentration for an 8-hour exposure (CFR 1910.1000), which corresponds approximately to 90 milligrams per cubic meter of air (mg/cu m). The USSR has a standard of 0.5 ppm, (1 mg/cu m), which was adopted in 1966 [Winell, 1975]. Standards of 50 ppm and 20 ppm (36 mg/cu m) are in effect in the Federal Republic of Germany and Sweden, respectively.

While this review includes all known biohazards of ethylene oxide, special emphasis was devoted to its potentials for exerting carcinogenic,

mutagenic, and teratogenic effects. Recent reports of the mutagenic potential of ETO [Embree and Hine, 1975; Ehrenberg et al, 1974], coupled with the "Report of the Secretary's Commission on Pesticides and their Relationship to Environmental Health" [Mrak, DHEW Report, 1969], have prompted a reassessment of the adequacy of the current U.S. occupational exposure standard, as well as a critical appraisal regarding re-registration of the compound by the Environmental Protection Agency (as required under the Federal Insecticide, Fungicide, and Rodenticide Act, FIFRA). This latter action has resulted in a reappraisal by the Department of Health, Education, and Welfare of the use of ETO for sterilization purposes within health care facilities.

During the preparation of this review, a limited field survey of ETO use in medical facilities was conducted by NIOSH in order to better assess the actual occupational exposure situation. A summary of the results of the field survey is presented, and serves as a basis for the recommended control measures. Extensive use was made of information provided by other federal agencies, and from industrial, trade, and professional organizations. In addition, the "Draft Technical Standard and Supporting Documentation for Ethylene Oxide," prepared under the joint NIOSH/OSHA Standards Completion Program, assisted in the preparation of the engineering and control sections of this review. NIOSH was represented on the Ethylene Oxide Subcommittee of the Committee to Coordinate Toxicology and Related Programs (CCTRP), U.S. Department of Health, Education, and Welfare. The Subcommittee met during the period January 30 - March 30, 1977. Certain sections of this NIOSH Special Hazard Review were provided to the CCTRP Subcommittee for inclusion in its Risk/Benefit Analysis of public health uses of ETO (HEW, 1977).

The information and recommendations that follow should aid the U.S. Department of Labor, industrial hygienists, physicians, employers, and architects or other designers of health care facilities in protecting the worker from the hazards of ETO exposure. Furthermore, it will aid the worker in recognizing the hazard.

## I. PROPERTIES

This information has been compiled primarily from the Chemical Safety Data Sheet of the Manufacturing Chemists Association, for Ethylene Oxide, (No. SD-38), 1971, with supplementation from other sources.

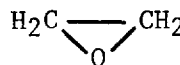
### A. Identification

1. synonyms: 1,2-epoxyethane, oxirane, oxiran, dimethylene oxide, ETO, EO, oxane, dihydrooxirene, oxacyclopropane, oxidoethane, and anprolene

2. CAS number: 75-21-8

3. formula: C<sub>2</sub>H<sub>4</sub>O,

4. molecular weight: 44.05



### B. Physical/Chemical Properties of ETO

1. appearance and odor: colorless gas or volatile liquid with a characteristic ether-like odor (irritating in high concentrations).

2. boiling point: 10.4 C (50.7 F) at 760 mm Hg

3. melting point: -112.6 C (-170.7 F)

4. specific gravity: 0.8711 (apparent) (20/20 C), (68 F):  
0.897 (0/4 C)

5. vapor density: 1.5 (air = 1)

6. vapor pressure at 20 C: 1095 mm Hg

7. solubility: completely miscible with water, alcohol, acetone, benzene, ether, carbon tetrachloride, and most organic solvents. Powerful solvent for fats, oils, greases, waxes, and some rubber formulations.

8. reactivity: (gas and liquid). Highly exothermic and potentially explosive with alkali metal hydroxides, or highly active catalytic surfaces (such as anhydrous chlorides of Fe, Sn and Al, and oxides of Fe and Al), or when heated. Relatively non-corrosive to materials other than certain rubbers. Relatively stable in aqueous solution, and when diluted with CO<sub>2</sub> or gaseous halocarbons. An alkylating agent which reacts directly (and virtually irreversibly) with -COOH, -NH<sub>2</sub>, -SH, and -OH groups. Reacts with the ring nitrogen of purine and pyrimidine bases, and the amino groups of amino acids and proteins.

9. explosive limits: 3 to 100 (% by vol in air).

10. flashpoint: -6C (20 F), (Tag. open cup).

## II. USES AND OCCURRENCE IN MEDICAL FACILITIES

The routine use of ETO in medical and related health care facilities is to sterilize heat-sensitive surgical instruments, equipment, and other objects (or fluids) that come in contact with biological tissue (particularly the vascular system), or extracorporeal equipment through which blood may flow. The absence of all microbiological life forms such as viruses, bacteria, yeast, fungi, and especially persistent spore forms is essential in order to prevent infectious diseases in patients and animals.

Complete sterilization by either heat or gaseous agents is essential for many purposes, although varying degrees of disinfection with chemical germicides (which may sharply reduce the populations of many vegetative forms) may be sufficient for some applications.

Heat sterilization is normally the preferred method; however, this method can not always be employed because of the heat-sensitive nature of some items. In addition, ETO gas sterilization is more economical for some applications, such as the industrial sterilization of inexpensive disposable, i.e., single-use, items such as syringes and needles.

### A. Characterization of Occupational Exposure During ETO Sterilization Procedures

There is current large-scale industrial use of ETO gas for sterilization of medical supplies and equipment because such use is effective and economical. In addition, alternate methods often are impractical, hazardous, undependable, or uneconomical. Gaseous ETO is generally used industrially for sterilization processing of disposable sterile kits containing items such as disposable syringes and needles, disposable microbiological laboratory supplies, and life-support items such as electronic cardiac "pacemakers," blood oxygenators, and dialysers. An estimated 80% of all such items are processed by ETO gas sterilization in the U.S. [CDC, 1977]; many could not be processed, regardless of cost, by any other currently available method [CDC, 1977]. The majority of industrial ETO gas sterilization is performed in less than 50 large (greater than 1,000 cu ft) sterilizers and in approximately the same number of smaller industrial units [HIMA, 1976]. It has been reported that such ETO sterilizers are operated in accord with manufacturers' recommendations, industry safety regulations, state and local fire codes, and provisions of insurance underwriters [HIMA, 1977]. While this review contains information applicable to the few large industrial users of ETO for sterilization, it was primarily intended for medical facility applications (as defined in the Introduction).

There are approximately 8,100 hospitals in the U.S., of which about 7,200 are members of the American Hospital Association (AHA). The AHA estimates that 5,500 to 6,500 of its member hospitals have ETO gas sterilizers [AHA, 1976]. Whereas the majority of these sterilizers are small table top units, it is estimated that 1,000-2,000 large sterilizers (permanent installations with chamber volumes greater than 4 cu ft) are also in use [HIMA, 1977]. Most hospitals have more than one ETO sterilizer. In addition to hospitals, ETO sterilizers are also used in

smaller medical, dental, or veterinary clinics or facilities. While the exact number of sterilizers is not known, NIOSH estimates that it exceeds 10,000 units.

Of the almost 2.1 billion kg of ETO currently produced annually in the U.S. [Chemical & Engineering News, 1976], it is estimated that 500,000 kg (0.02% of the total produced) are used for sterilization within medical facilities [NIOSH, 1977]. This use is increasing.

NIOSH (1977) estimates that approximately 75,000 health care workers employed in sterilizer areas are potentially directly exposed to ETO. In addition, an estimated 25,000 others are "casually" exposed due to improper (or inadequate) venting of sterilizers and aerators, storage (or use) of improperly/incompletely aerated ETO-sterilized items, the physical arrangement of the sterilization facility or workroom (which necessitates passage in close proximity to a gas sterilizer or aerator), and mishandling or failure of the equipment (such as, leaking sterilizer door seals). Thus, the total number of exposed workers in medical and related facilities is estimated to exceed 100,000.

The principal items processed in such hospital "gas" sterilizers are air-powered surgical instruments, anesthesia supplies and equipment, cardiac catheters, endoscopes and other equipment containing lenses intended to be introduced into the human body, humidifiers and nebulizers, implantable body parts, electronic "pacemakers," ophthalmic instruments, x-ray supplies and related equipment, respiratory therapy supplies and equipment, some medications, reusable supplies, thermometers, and equipment contaminated by use in "isolation rooms" (i.e., containing patients with infections). Note some significant differences between the items sterilized by the "user" and the items sterilized by the "vendor".

ETO is used in sterilizers produced by at least six different manufacturers. In certain small sterilizers it is used full strength, or diluted to a composition of 84% ETO with inert ingredients. In larger sterilizers a non-explosive sterilant mixture is commercially available, either 10% ETO/90% CO<sub>2</sub>, tradenamed Carboxide (TM), or 12% ETO/88% halocarbon. Halocarbon products, such as Refrigerant-12 (or -11), sold under tradenames such as Freon (TM) or U-con (TM), are used. The Federal standard for occupational exposure to dichlorodifluoromethane (Refrigerant-12) is 1,000 ppm (4,550 mg/cu m) as an 8-hour TWA concentration. No federal exposure limit exists for trichloromonofluoromethane (Refrigerant-11). The impact of the possible removal (for environmental considerations) of certain halocarbon-containing products from general use has not been considered in this report.

#### B. ETO Residues in Sterilized Medical Equipment

Residues (or byproducts) are produced mainly by two reactions of ETO: (a) from its slow chemical combination with water to form glycols, or (b) from its combination with chloride ion in the presence of water to form the chlorohydrin. Since even dry materials contain some moisture, it is apparent that glycol formation is unavoidable. Moreover, without the presence of some moisture, ETO sterilization cannot be effected. However, traces of glycols have been generally regarded as relatively harmless and permissible for human exposure.

The formation of persistent, toxic ethylene chlorohydrin in foodstuffs fumigated with ETO has been described (Wesley et al, 1965). Chlorohydrins are relatively non-volatile, and are considered highly toxic substances. The Federal standard (CFR 1910.1000) for occupational exposure to ethylene chlorohydrin is 5 ppm parts of air as an 8-hour TWA concentration. Attempts have been made to determine the conditions necessary for elimination of chlorohydrin residues from foods by volatilization and decomposition at elevated temperatures. In general, these attempts have not been successful. Nor would they be applicable for most sterilized medical products, particularly those which are heat sensitive.

While no reference to the formation and levels of ethylene chlorohydrin in medical facilities was found, the possibility that it will be present cannot be ignored.

The use of ETO for sterilization of medical devices and equipment raises a number of significant questions regarding (a) the possible entrapment of ETO in a plastic item that may then exert a toxic effect when placed in contact with living tissue, and (b) the effect of (sorbed) ETO on the physical and chemical properties of the rubber and plastic items. Plastic tubing that has been sterilized with ETO has caused significant hemolysis when placed in contact with human blood (Rose et al, 1953; Clarke et al, 1966; Bain and Lowenstein, 1967). For example, Bain and Lowenstein (1967) reported that when mixed leukocyte cultures were incubated in disposable plastic tubes sterilized with ETO, survival of the cells was severely affected by a toxic residue left on the plastic. The residue was dissipated only after 4 or 5 months' storage at room temperature, whereupon the survival of cells cultured in such stored tubes returned to values similar to those obtained with ultraviolet-sterilized (control) tubes.

O'Leary and Guess (1968), in their study of the toxic properties of medical plastics sterilized with gaseous ETO, presented data demonstrating the ability of ETO to remain entrapped in non-closed systems, such as, surgical tubing, gas washing bottles, plastic syringes, or plastic bottles, at various temperatures above the ETO boiling point. The hemolyzing ability of known amounts of ETO was determined. Freshly gas-sterilized plastic pharmaceutical products were shown quantitatively to produce blood cell hemolysis in proportion to the amount of ETO remaining in the plastic. Additionally, the effects of plasticizers of the ester type upon the sorption of ETO into polyvinyl chloride (PVC) products was also described. The residual ETO could present a hazard in the sterilization of such devices as plastic syringes. For example the residual ETO gas might have toxic effects due to some of its oxidation products.

ETO, if not removed, may be released at a later time (i.e., while under use) and cause hemolysis, erythema, and edema of the tissues. (Clarke et al, 1966; Bain and Lowenstein, 1967; O'Leary and Guess, 1968; Kulkarni et al, 1968; and Sykes, 1964). Other studies relating to the general problem of interaction of ETO with constituents of rubber and plastic have been reported. Downey (1950) demonstrated that the mercaptobenzothiazole vulcanization accelerators found in rubber reacted rapidly with ETO to produce (hydroxyethyl-mercapto)-thioazole, despite the fact that residual ETO concentration in the rubber tubing had been reported to have been dissipated after 5 hours' aeration. Little is known about the

parenteral toxicities of these compounds, or other possible reaction products in ETO-sterilized rubber.

Cunliffe and Wesley (1967) have shown that ethylene chlorohydrin was given off from PVC tubing 6 days after ETO sterilization. Gunther (1965) also demonstrated that high concentrations of ETO can be taken up by polyethylene, gum rubber, and plasticized polyvinylchloride. This re-emphasizes the general problem of entrapment of ETO within sterilized plastics. Reports of local skin irritation from contact with ETO-sterilized plastic items have appeared [ ]. This irritation can become severe if sensitization occurs. Items sterilized with ETO must be properly aerated before application to the human body in order to prevent such adverse reactions.

### C. Alternatives to the Use of ETO Sterilization

The reported alternatives to ETO sterilization include: steam, dry heat, steam-formaldehyde, steam at sub-atmospheric pressure, wet pasteurization, radiation (including gamma-ray, X-ray, ultraviolet radiation, and electron beam exposure), liquid glutaraldehyde, liquid or gaseous formaldehyde, propylene oxide, liquid (or gaseous) beta-propiolactone, epichlorohydrin, ethylene imine, glycidaldehyde (i.e., 2,3-epoxy-1-propanal), hypochlorite, peracetic acid, methyl bromide, chloropicrin, and ozone. As a completely different strategy, single use, unsterilized disposable supplies have been considered by some. Although the safety of such items has been questioned, microbial contamination capable of causing disease is rarely present [HEW Rept., 1977].

A number of other chemicals or processes have been used (or considered) for sterilization of medically related items. For various reasons their general use is limited.



### III. SUMMARY OF RESULTS OF FIELD STUDIES CONDUCTED IN MEDICAL FACILITIES

In February 1977, NIOSH conducted a limited field survey of hospitals to gain some perspective on situations related to the use of ETO sterilizers that might result in exposure of hospital staff and patients to ETO. The survey involved four hospitals in a metropolitan area, selected to represent both large and small health care facilities. Although a survey limited to only four medical facilities obviously can not be used with confidence as a basis for describing the conditions of the actual wide-spread use of ETO, it nevertheless does present a general impression of the usage of this compound, and some of the potential problems related to its use. The brief summary of the results of the survey presented below is from a more detailed report [Glaser, 1977].

In addition to the data from the NIOSH field survey, information was obtained from other government agencies including EPA, FDA, CDC, and NIH, and from the U.S. Army and U.S. Navy. Information was also made available by the Health Industry Manufacturers Association (HIMA), the American Hospital Association (AHA) and their member group, the American Society for Hospital Central Service Personnel, the Manufacturing Chemists Association (MCA), the Association for the Advancement of Medical Instrumentation (AAMI), the American National Standards Institute (ANSI), the American Society of Hospital Engineers (ASHE), ETO sterilizer and aerator manufacturers, and ETO "gas" manufacturers. From the NIOSH field survey and the above sources, the following account of the use of ETO in medical facilities, and the problems incident to such use, was developed. The results obtained in the NIOSH survey are in agreement with a similar study conducted by the U.S. Army in three of its hospitals (Army, 1977), and with data obtained by a study recently conducted by the American Hospital Association (Runnells, 1977).

#### A. ETO Sterilizer Use, and Number of Workers Potentially Exposed to ETO

The number of gas sterilizers per hospital observed in the survey ranged from 1 to 9 (average of 4), with each hospital having at least one large sterilizer in the Central Supply (CS) area. Smaller sterilizers were installed in one or more of the following locations: Operating Room (OR), Surgery, Cardiac Catheterization Laboratory (Cath Lab), Anesthesiology Department, Ear-Nose-Throat (ENT) Clinic, Dental Clinic, Intensive Care Unit (ICU), Urology Department, and Inhalation Therapy Clinic. Additionally, some hospital-related research facilities have gas sterilizers, used in connection with the banking and transplantation of human tissue and organs (i.e., Tissue Bank), and in veterinary facilities which maintain germ-free (i.e., gnotobiotic) animal colonies. The size of the hospitals in the NIOSH survey varied from 115 beds to 750 (immediately expandable to 1135), with the size of the average hospital being between 460 and 500 beds. Nationally, the number of gas sterilizers per "average" size (i.e., 200-300 beds) hospital appears to be 2. [Runnells, 1977]

The frequency of operation of the large sterilizers (i.e., Central Supply) varies from 3-4 cycles in 24 hours to approximately one cycle every

other day. Sterilizers in other areas generally were operated 2-5 times per week. These frequencies agree with data from other sources.

The number of personnel directly involved in the sterilization process varied widely. Some facilities reported that only a few (3-5) workers actually operate (i.e., load/unload) the sterilizers and aerators, and then generally only one person at a time. Such a situation occurred mostly in the CS and specific research-related areas (such as the Tissue Bank). The Cath Lab or OR technical staff appear to operate the sterilizers on a rotating, random or assigned, basis with a somewhat larger number of people (3-15) directly involved.

While the number of personnel who may be exposed during operation of the sterilizing equipment may be small, many more persons were potentially exposed for a variety of reasons. In one case, access to a main lavatory required that personnel walk directly in front of two large gas sterilizers and a large aerator. In other cases, persons passing between the workroom and stock room had to walk within 2 feet of the fronts of sterilizers located in a small room or area between the CS workroom and the CS stock/storage area. Another sterilizer was located in a small appendage (vestibule) to the OR workroom, adjacent to a doorway to a heavily trafficked hallway. Within a period of less than 15 minutes, more than 30 people were observed passing within 4 feet of the sterilizer and aerator. The aerator vented directly into the workroom, providing additional ETO exposure to workers in that area.

In some facilities, staff from various departments withdrawing sterile supplies from the Central Supply walk directly into the sterilizer or stock areas. ETO can enter stock areas from improper ventilation of aeration areas, or by the placing in stock of incompletely aerated items, resulting in diffusion of ETO into the ambient air.

While the number of potentially exposed persons may be large, depending on the actual physical arrangements, the number most likely to be exposed was estimated to be between 6 and 60 in each of the hospitals included in this study. This range agrees with an estimate obtained from a nation-wide survey of hospital central service/central sterile supply personnel conducted by the American Society for Hospital Central Service Personnel, of the American Hospital Association, in 1977.

#### B. Potential Exposure Situations Encountered in the Field Study

In addition to the potential for accidental exposures due to the physical arrangements, in a few cases problems were observed in installation, maintenance, and operation that could increase the unnecessary and/or inadvertent exposure of sterilizer operators to ETO. These are:

##### 1. Improper or Inadequate Venting of Sterilizers:

a. Exhaust vent passed through a window and ended within 1 foot of the intake air duct of an air conditioner. While probably very little of the ETO is actually drawn back into the room by the air conditioner intake, it does illustrate a potential source of exposure.

b. An exhaust pipe from a sterilizer discharged into an open floor drain and gave off a cloud of vapors, including ETO, steam, Freon, and possibly other components (such as ethylene chlorohydrin) from the sterilizer into the machinery-room. A local ETO concentration of approximately 8,000 ppm was measured 1 foot above such a drain during a sterilization cycle. High local concentrations of ETO could be significantly reduced by minor modifications of the physical facility. In general, these situations do not result in elevated concentrations of ETO in the operator's breathing zone (BZ), but may contribute to the low background concentration of ETO in the sterilizing area.

c. Incomplete sterilizer flushing prior to opening its door allowed very high concentrations of ETO to enter the room immediately upon opening the door of the sterilizer. This could create a hazardous situation for the operator attending the door. Approximately 1,200 ppm was recorded at one installation immediately upon opening the chamber door.

d. An operator was able to open one sterilizer during use, to add or remove items, even though its chamber contained ETO. This represents, potentially, a very hazardous situation for the equipment operator.

e. Effluent gas from sterilizers and aerators is not treated to destroy all unreacted ETO as well as hazardous byproducts such as ethylene chlorohydrin, so as to render the resulting effluent innocuous. The development of an apparatus (such as a catalytic converter or combustion device) designed to ensure the complete destruction of unreacted ETO at the end of the sterilization procedure should be given high priority to ensure worker safety, as well as to prevent environmental pollution by ETO.

## 2. Improper Aeration of Sterilized Equipment:

a. With only one notable exception, all aerator cabinets in the medical facilities visited were vented directly into the room in which they were installed, or into the machinery space behind the cabinet. Airborne ETO concentrations of 300 to 500 ppm were not unusual above and behind some aerator cabinets.

b. Aeration was permitted on open shelves in the CS or OR workroom or stock room areas in one facility. Values of 25-50 ppm were measured 1 foot above stored items which had been sterilized more than 24 hours earlier.

c. Sterilized items were stored (following aeration?) in glass cabinets with tightly fitting doors in two facilities visited; an odor of ETO was obvious upon opening one of the cabinets, indicating improper aeration before storage, and lack of venting of the cabinet.

d. Exposure to ETO sterilizer gaseous products is of obvious concern, as some technicians reported skin irritation from contact with recently sterilized items, while others reported that their eyes "watered" while removing items from the sterilizer.

### 3. Inadequate Room Ventilation:

Ineffective or non-existent room ventilation was noted in some facilities, which allowed the buildup of ETO to a high level within the room. A 10 x 10 x 12 foot unventilated room housed a small sterilizer which was found to have a leaking door gasket. ETO concentration at the BZ near the sterilizer was greater than 1,000 ppm.

### 4. Malfunctioning or Leaking Equipment:

a. A leaking door seal (gasket) on a sterilizer caused an extremely high value of airborne ETO in a small, non-ventilated and closed room. Results are cited above.

b. ETO leaks were observed at some gas tank valves, threaded fittings, and near some chamber fittings and piping. This could be very serious for personnel entering poorly ventilated machinery spaces. Leaks producing instrument readings ranging from 400 to 3,000 ppm were located.

### 5. Improper Operating Procedures:

Sterilized items were removed from the sterilizer and transported on carts through a heavily congested hallway to the aerator or storage area. High rates of off-gassing, 200-300 ppm 1 foot above the cart, were noted during the movement of the sterilized items.

### C. Measurement of Ambient Levels of ETO

The method used for the sampling and analysis of airborne ETO consisted of the absorption of ETO on charcoal, and gas chromatographic determination following desorption of the ETO with carbon disulfide [NIOSH Standard Completion Set T, 1976].

A series of measurements were obtained at various locations in rooms containing sterilizers and/or aerators, before, during, and after periods of operation of the equipment. Sampling was also conducted in other places of potential exposure, such as hallways, and vent exhaust areas.

In general, the concentrations of ETO in the employee's breathing zone (BZ) were below the current federal (OSHA) standard (CFR 1910.1000) of 50 parts per million (ppm) parts of air as a time weighted average (TWA) over an 8-hour day. General area air samples collected during a 5.5 hour period in front of a bank of two ETO sterilizers and an aerator contained only 1-2 ppm of ETO. However, many values were recorded which were at, or above, the ACGIH tentative Threshold Limit Value (TLV) for short term exposure (i.e. short-term exposure limit, STEL, of 75 ppm for short-time periods of less than 15 minutes). In fact, some very high short-term BZ values were observed, including a peak of 460 ppm within the first minute after opening the sterilizer door, lasting for about 1 minute. Even higher concentrations, for shorter periods, were noted on occasion. Although there is no absolute maximum or "ceiling" value for ETO, one should regard the recommended STEL as a level not to be exceeded.

#### D. Conclusions

1. The survey revealed a number of conditions which resulted in unnecessary, preventable exposure of hospital staff, and possibly patients, to ETO.

2. Many of the conditons were due to faulty equipment or improper operating procedures. These can be corrected by minor modifications, e.g., venting floor waste drains, replacing leaking sterilizer door seals or pipe joints, and improved work practices, including techniques for removing items from the sterilizer and aerator. In addition, the operator should avoid contact with both ETO gas and liquid which may remain in the flexible connecting lines when changing sterilizer gas cylinders. Protective gloves and goggles are available, and should be worn by personnel changing gas cylinders or cleaning up following an accidental spill. Gas cylinders should be changed in such a manner as not to expose the technician to ETO. Transfer carts should be used to remove sterilized items from large sterilizers, and gloves and forceps should be used whenever possible to remove items from small sterilizers. This will minimize the inhalation of ETO by the operator, and the possibility of dermal contact with ETO.

3. Other conditions resulted from improper installation and ventilation of sterilizers, aerators, or rooms in which such equipment was installed. This may require more extensive modifications such as additional venting ducts, high velocity vacuum pick-up ducts at the sterilizer door, improved room ventilation, and measures to exhaust decontaminated effluent in such a way as to prevent exposure within the hospital. An absolute minimum of 10 air changes per hour should be provided to all rooms containing gas sterilizers, aerators, or stored ETO-sterilized items. Air should not be recirculated in these spaces. Devices which completely destroy all unreacted ETO need to be developed.

4. Modification or engineering re-design of some sterilizer chambers may be necessary to assure effective displacement of the ETO gas following sterilization. It is desirable to have repeated air flushing of the sterilizer before it is opened. A power-operated door-opening device exists on some large sterilizers. It allows the operator to push a button, then walk away, while the sterilizer door slowly opens. If, after a suitable period of time to permit the chamber to "air out," a buzzer could call the operator back to unload the chamber, safer sterilizer operations would result. In lieu of the power door, an alternative might be for the operator, upon completion of the sterilization cycle, to open the chamber door approximately 6 inches and wait 5-15 minutes before removing a load from the sterilizer.

Aerators (which are forced-draft, warm air cabinets) should not vent directly into the room; rather, they should be connected to exhaust ducts to carry effluent out of the work area. Aeration performed under ambient conditions (i.e., in the open, at room temperature and atmospheric pressure) is not generally used, due to the lengthy time required to eliminate ETO "residues" from the sterilized material. In the absence of aerators, removal of ETO from sterilized items should be permitted only in dedicated, well-ventilated areas, such as in hoods.

5. Many items are being sterilized with ETO when they could be processed by other methods, e.g., steam or ultraviolet radiation.

6. Most (but not all) hospitals provide a "standard operating procedures" manual, containing ETO sterilization techniques, and conduct thorough on-the-job training programs including the sterilization procedures with ETO.

7. Medical and Health records of personnel employed in areas in which ETO is used were not maintained in all cases. The keeping of employee medical and health records, as well as occupational exposure records needs to be improved in some medical facilities.

8. Within the past few years, sterilizer and aerator equipment manufacturers appear to be making stronger recommendations in the instruction manuals, and in training aids, courses, seminars, and in advertising as to the proper ventilation, location, use, etc., of sterilizers and aerators. Some early equipment manuals did not contain such recommendations. It is necessary that architects and designers of health care facilities, supervisors of the equipment operators, facility safety staff, industrial hygienists, etc., rigorously follow the recommendations and instructions stated by the equipment manufacturers, to protect the worker from the hazards of ETO exposure.