Phoenix, Arizona, to discuss such matters as may be presented by members, staff of the Small Business Administration, or others present.

For further information, write or call Walter Fronstin, District Director, U.S. Small Business Administration, 3030 North Central Avenue, Suite 1201, Phoenix, Arizona 85012, telephone (602) 241-2206.

Dated: June 15, 1984.

Jean M. Nowak,

Director, Office of Advisory Councils.

[FR Doc. 84-16645 Filed 6-21-84; 8:45 am]

BILLING CODE 8025-01-M

VETERANS ADMINISTRATION

Agency Forms Under OMB Review

AGENCY: Veterans Administration.

ACTION: Notice.

The Veterans Administration has submitted to OMB for review the following proposals for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. Chapter 35). This document contains extensions and lists the following information: (1) The Department or Staff Office issuing the form; (2) The title of the form; (3) The agency form number, if applicable; (4) How often the form must be filled out; (5) Who will be required or asked to report; (6) An estimate of the number of responses; (7) An estimate of the total number of hours needed to fill out the form; and (8) An indication of whether section 3504(h) of Pub. L. 96-511 applies.

ADDRESSES: Copies of the forms and supporting documents may be obtained from Patricia Viers, Agency Clearance Officer (732), Veterans Administration, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 389-2146. Comments and questions about the items on this list should be directed to the VA's OMB Desk Officer, Dick Eisinger, Office of Management and Budget, 726 Jackson Place, NW, Washington, DC 20503, (202) 395-6880.

DATES: Comments on the information collections should be directed to the OMB Desk Officer within 60 days of this notice.

DATED: June 19, 1984.

By direction of the Administrator.

Dominick Onorato,

Associate Deputy Administrator for Information Resources Management.

Extensions

1. Department of Veterans Benefits.
2. VA Request for Determination of Reasonable Value/HUD Application for Property Appraisal and Commitment.
3. VA Form 26-1805/HUD 92800-1.
4. On occasion.
5. Individuals or households.
6. 448,000 responses.
7. 89,600 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Enrollment Certification (Under 38 U.S.C. 32, 34 or 35).
3. VA Forms 22-1999, 22-1999-1 and 22-1999-2.
4. On occasion, quarterly, semi-annually, or each school term.
5. Individuals or households, State or local governments, Farms, Businesses or other for-profit, Federal agencies or employees, Non-profit institutions, Small businesses or organizations.
6. 76,899 responses.
7. 286,667 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Notice of Lapse.
3. VA Forms 29-389 and 29-389-1.
4. On occasion.
5. Individuals or households.
6. 25,000 responses.
7. 4,166 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Request for Supplemental Information on Medical and Non-Medical Applications.
3. VA Form 29-615.
4. On occasion.
5. Individuals or households.
6. 15,000 responses.
7. 5,000 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Application for Ordinary Life Insurance (at age 65) and Information about Modified Life Insurance Reduction and Replacement Features (age 65).
3. VA Forms 29-8485 and 29-8700.
4. On occasion.
5. Individuals or households.
6. 6,818 responses.
8. 568 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Application for Ordinary Life Insurance (at age 70) and Information about Modified Life Insurance Reduction and Replacement Features (age 70).
3. VA Forms 29-8485a and 29-8701.
4. On occasion.
5. Individuals or households.
6. 6,818 responses.
7. 568 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Notice—Payment Not Applied.
3. VA Form 29-4499a.
4. On occasion.
5. Individuals or households.
6. 2,000 responses.
7. 500 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Application for Accrued Benefits by Veteran's Surviving Spouse, Child or Dependent Parent.
3. VA Form 21-551.
4. On occasion.
5. Individuals or households.
6. 1,000 responses.
7. 333 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Employment of Questionnaire.
3. VA Form 21-4140.
4. On occasion.
5. Individuals or housholds.
6. 45,480 responses.
7. 3,790 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Application for Accrued Amounts of Veteran's Benefits Payable to Widow, Widower, Child, or Dependent Parent.
3. VA Form 21-614.
4. On occasion.
5. Individuals or households.
6. 8,000 responses.
7. 4,000 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Obtaining Supplemental Information from Hospital or Doctor.
3. VA Form Letter 29-551b.
4. On occasion.
5. Individuals or households.
6. 250 responses.
7. 125 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Information from Remarried Widow/er.
3. VA Form 21-4103.
4. On occasion.
5. Individuals or households.
6. 22,000 responses.
7. 7,333 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Student Beneficiary Report—REPS.
3. VA Form 21-8938.
4. Annually.
5. Individuals or households.
6. 10,000 responses.
7. 3,333 hours.
8. Not applicable.

[FR Doc. 84-16310 Filed 6-21-84; 8:45 am]

BILLING CODE 8320-01-M

Sunshine Act Meetings

Federal Register
Vol. 49, No. 122
Friday, June 22, 1984

This section of the FEDERAL REGISTER contains notices of meetings published under the "Government in the Sunshine Act" (Pub. L. 94-409) 5 U.S.C. 552b(e)(3).

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1

FEDERAL TRADE COMMISSION

TIME AND DATE: 2:00 p.m., Wednesday, June 20, 1984.

PLACE: Room 532, (open); Room 540 (closed) Federal Trade Commission Building, 6th Street and Pennsylvania Avenue, NW., Washington, D.C. 20580.

STATUS: Parts of this meeting will be open to the public. The rest of the meeting will be closed to the public.

MATTERS TO BE CONSIDERED: Portions Open to Public:

(1) Oral Argument in Boise Cascade Corp., Docket No. 9133.

Portions closed to the Public:

(2) Executive Session to follow Oral Argument in Boise Cascade Corp., Docket No. 9133.

CONTACT PERSON FOR MORE INFORMATION: Susan B. Ticknor, Office of Public Affairs: (202) 523-1892; Recorded Message: (202) 523-3806.

Emily H. Rock,

Secretary.

[FR Doc. 84-16780 Filed 6-20-84; 9:31 am]

BILLING CODE 6750-01-M

2

UNITED STATES POSTAL SERVICE BOARD OF GOVERNORS

Meeting

The Board of Governors of the United States Postal Service, pursuant to its Bylaws (39 CFR 7.5) and the Government in the Sunshine Act (5 U.S.C. 552b), hereby gives notice that it intends to hold meetings at 1:00 p.m. on Monday, July 9, 1984, in Washington, D.C., and at 8:30 a.m. on Tuesday, July 10, in the Benjamin Franklin Room, U.S. Postal Service Headquarters, 475 L'Enfant Plaza, SW., Washington, D.C. As indicated in the following paragraph, the July 9 meeting is closed to public observation. The July 10 meeting is open to the public. The Board expects to discuss the matters stated in the agenda which is set forth below. Requests for information about the meetings should be addressed to the Secretary of the Board, David F. Harris, at (202) 245-3734.

At its meeting on June 5, 1984, the Board voted in accordance with the provisions of the Government in the Sunshine Act to close to public observation its meeting scheduled for July 9. (See 49 FR 24248, June 12, 1984.) The agenda item of the meeting to be closed concerns strategic planning in connection with collective bargaining negotiations involving parties to the 1981 National Agreements, between the Postal Service and four labor organizations representing certain postal employees, which are scheduled to expire in July 1984.

Agenda

Monday Session, July 9 (Closed)

1. Strategic Planning—Collective Bargaining.

Tuesday Session, July 10 (Open)

1. Minutes of the Previous Meeting, June 4-5, 1984.
2. Remarks of the Postmaster General. (In keeping with its consistent practice, the Board's agenda provides this opportunity for the Postmaster General to inform the Members of miscellaneous current developments concerning the Postal Service. Nothing that requires a decision by the Board is brought up under this item.)
3. Report on Operations Group Programs. (Mr. Jellison, Senior Assistant Postmaster General, Operations Group, will provide a report on Operations Group programs.)
4. Briefing on status of the Neighborhood Distribution and Collection Box Unit Program. (Mr. Hagburg, Assistant Postmaster General, Delivery Services Department, will brief the Board on the status of the "clusterbox" program.)
5. Review of Public and Employee Communications Programs. (Ms. Layton, Assistant Postmaster General, Public and Employee Communications Department, will report on communications and public affairs programs.)
6. Consideration of tentative agenda for the August 6-7, 1984, meeting of the Board in Cleveland, Ohio.

David F. Harris,

Secretary.

[FR Doc. 84-16828 Filed 6-20-84; 3:15 pm]

BILLING CODE 7710-12-M

3

TENNESSEE VALLEY AUTHORITY

[Meeting No. 1332]

TIME AND DATE: 6:00 p.m. (CDT), Tuesday, June 26, 1983.

PLACE: Jaycee Civic Center, 2701 Park Avenue, Paducah, Kentucky.

STATUS: Open.

AGENDA ITEMS: Approval of minutes of meeting held on June 11, 1984.

C—Power Items

C1. Amendment to power contract with Bowater Incorporated, Calhoun, Tennessee, providing for a 35.2-MW increase of firm power.

C2. Joint memorandum governing power supply to the Office of Agricultural and Chemical Development's water-pumping station.

C3. Supplement to Contract No. TV-34823A with Memphis Light, Gas and Water Division for natural gas at Allen Steam Plant.

C4. Marketing agreement with Southeastern Power Administration covering the marketing of Cumberland River Power and Energy.

C5. Operating agreement with Southeastern Power Administration and Army Corps of Engineers covering the operations of the Cumberland River Projects.

C6. Supplement to Contract No. TV-55782A with the Massachusetts Institute of Technology for Atmospheric Fluidized Bed Combustion Technology Studies.

D—Personnel Items

D1. Renewal of consulting contract with John M. Kellberg, Knoxville, Tennessee, for consultation on major hydro projects and engineering problems associated with thermal power plants, requested by the Division of Engineering Design.

D2. Supplement to personal services Contract No. TV-63924A with United Engineers & Constructors, Inc., Philadelphia, Pennsylvania, for services in connection with pipe support design for Watts Bar and Bellefonte Nuclear Plants, requested by the Division of Engineering Design.

D3. Supplement to personal services Contract No. TV-63923A with Gilbert Associates, Inc., Reading, Pennsylvania, for services in connection with pipe support design for Watts Bar and Bellefonte Nuclear Plants, requested by the Division of Engineering Design.

E—Real Property Transactions

E1. Grant of permanent easement to the city of Bristol, Virginia, for public recreation purposes, affecting approximately 41 acres of Beaver Creek Reservoir land located in Washington County, Virginia—Tract No. XTBBCR-2E.

E2. Grant of permanent easement to McMinn County, Tennessee, for the construction, operation, and maintenance of a road and appurtenances, affecting approximately 0.32 acre of Chickamauga Reservoir land located in McMinn County, Tennessee—Tract No. XTCR-173H.

E3. Grant of 20-year easement to Boy Scouts of America, Four Rivers Council, Inc., for group camp purposes, affecting approximately 354.8 acres of Kentucky Reservoir land located in Marshall County, Kentucky—Tract No. XGIR-906RE.

F—Unclassified

F1. Revised TVA Policy Code Relating to Budget, Plan.

F2. Revised TVA Policy Code Relating to Budget, Controls.

F3. TVA Policy Code Relating to Cooperative Agreements.

F4. Agreement No. TV-64012A with Tennessee State University and the State of Tennessee Board of Regents for construction, operation, and maintenance of Private Enterprise Incubation Center in Nashville, Tennesseee.

CONTACT PERSON FOR MORE INFORMATION: Craven H. Crowell, Jr., Director of Information, or a member of his staff can respond to requests for information about this meeting. Call (615) 632-8000, Knoxville, Tennessee. Information is also available at TVA's Washington Office (202) 245-0101.

Dated: June 19, 1984.

W. F. Willis,

General Manager.

[FR Doc. 84-16808 Filed 6-20-84; 1:37 pm]

BILLING CODE 8120-01-M

federal register

Friday
June 22, 1984

Part II

Department of Labor

Occupational Safety and Health Administration

29 CFR Part 1910

Occupational Exposure to Ethylene Oxide; Final Standard

DEPARTMENT OF LABOR

Occupational Safety and Health Administration

29 CFR Part 1910

Occupational Exposure to Ethylene Oxide

AGENCY: Occupational Safety and Health Administration (OSHA), Labor.

ACTION: Final Standard.

SUMMARY: In this Final Standard, the Occupational Safety and Health Administration (OSHA) establishes a permissible exposure limit for occupational exposure to ethylene oxide (EtO) of 1 part EtO per million parts of air (1 ppm) determined as an 8-hour time-weighted average concentration. The basis for this action is a determination by the Assistant Secretary, based on animal and human data, that exposure to EtO presents a carcinogenic, mutagenic, genotoxic, reproductive, neurologic and sensitization hazard to workers. The standard provides for, among other requirements, methods of exposure control, personal protective equipment, measurement of employee exposures, training, medical surveillance, signs and labels, regulated areas, emergency procedures and recordkeeping. An "action level" of 0.5 ppm as an 8-hour time-weighted average is established as the level above which employers must initiate certain compliance activities such as periodic employee exposure monitoring and medical surveillance. In instances where the employer can demonstrate that employee exposures are below the action level, the employer is not obligated to comply with most of the requirements set forth in this final rule. The 1 ppm 8-hour limit reduces significant risk from exposure to EtO and is considered by OSHA to be the lowest levels feasible.

EFFECTIVE DATE: This final standard shall become effective August 21, 1984, except the following paragraphs which contain information collection requirements which are under review at OMB: § 1910.1047 (a)(2), (d), (e), (f)(2), (g)(3), (h), (i), (j)(1), (j)(2), and (j)(3).

FOR FURTHER INFORMATION CONTACT: Mr. James F. Foster, OSHA, U.S. Department of Labor, Office of Public Affairs, Rm. N-3641, 200 Constitution Avenue, N.W., Washington, D.C. 20210, Telephone (202) 523-8151.

For additional copies of this regulation, contact: OSHA, Office of Publications, U.S. Department of Labor, Room N-4101, Washington, D.C. 20210, telephone 202-523-9667.

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I. Physical Properties, Manufacture and Uses of Ethylene Oxide

Ethylene oxide (EtO), also known as 1,2-epoxyethane, oxirane, and dimethylene oxide, is a colorless gas with a characteristic ether-like odor. Its chemical formula is C_2H_4O, molecular weight is 44.06 and CAS Registry Number is 75-21-8. Although several processes exist for the production of EtO, all United States producers currently manufacture EtO through the catalytic oxidation of ethylene in the presence of a silver catalyst. EtO is completely miscible with water, alcohol, acetone, benzene, ether, carbon tetrachloride and most organic solvents. It is also highly reactive and potentially explosive when heated or when in the presence of alkali metal hydroxides and highly active catalytic surfaces. EtO is relatively stable in aqueous solutions or when diluted with carbon dioxide (CO_2) or halocarbons. In order to reduce explosion hazards when EtO is used as a fumigant or sterilant, it is often used in gaseous mixtures (such as 10% EtO and 90% CO_2, or 12% EtO and 88% halocarbon).

Since its first domestic production in 1925, EtO has become a major industrial chemical and is presently one of the 25 chemicals of highest production volume in the United States. During the period from 1967 to 1978, for example, the average rate of growth in the EtO industry was 6.7 percent. In 1980, over 5.2 billion pounds of EtO were produced domestically. Current production capacity is about 6.7 billion pounds per year [Ex. 2-14].

The primary use of EtO is as an intermediate in the manufacture of other products. Over 99% of total EtO production is used in the manufacture of other products, and almost 90% is consumed by the EtO manufacturers themselves. On a volume basis, the largest use of EtO is as an intermediate in the production of ethylene glycol, a major component of automotive and other anti-freeze products. Approximately 70% of all domestically produced EtO goes into the manufacture of ethylene glycol.

EtO is also widely employed in the production of non-ionic surface-active agents which are used in household detergents and as industrial sufactants. Other products manufactured from EtO include: (1) ethanolamines, used in sweetening natural gas and in the production of specialty chemicals, detergents and cosmetics; (2) glycol ethers, utilized as a jet fuel additive and in the formulation of coatings, cleaners,

automotive brake fluids and inks; (3) diethylene and triethylene glycol, used in drying natural gas and in the manufacture of polyester resins, emulsifiers, lubricants and plasticizers; (4) tetraethylene glycol, utilized to extract aromatic hydrocarbons from nonaromatic hydrocarbons; (5) polyethylene glycols, from which cosmetics, plasticizers, lubricants and dispersants are produced; (6) polyethylene glycols, used for water-soluble packaging and for warp sizing, and (7) crown ethers, used for extraction of liquids.

A small fraction of EtO production (less than 0.5 percent) is consumed by sterilant or fumigant users. EtO is utilized as a sterilizing agent by various facets of the health care industry for the sterilization of delicate instruments and heat or moisture sensitive devices, and is employed as a fumigant for a number of miscellaneous items, such as spices, black walnut meats, books, furniture, textiles, empty bin equipment, empty cargo holds, cosmetics and dairy packaging.

As used in the U.S. for gas sterilization, EtO is generally sold in gas cylinders. The cylinder contains various mixtures of EtO with either chlorofluorocarbons or carbon dioxide. EtO is also available in glass ampules. The concentration and duration of exposure to EtO plus the temperature, atmospheric pressure, and relative humidity determine the effectiveness of sterilization. The sterilant gas is held in the chamber, generally under high pressure, long enough to thoroughly penetrate all articles. In determining exposure time, the types of articles and wrappings are important considerations. Some porous articles require longer exposures, as do articles sealed in polyethylene bags. Moreover, some bacteria are expecially resistant and, thus, take longer to destroy. The concentration of EtO is important, but even with the highest concentration it is still necessary to properly humidify articles to be sterilized, and to allow sufficient time for the sterilant gas to diffuse into small pores and crevices. After a sufficient exposure time, the sterilant gas is evacuated from the chamber. When high ethylene oxide concentrations are used, extended aeration time (5 to 45 minutes) may be required to thoroughly purge the chamber of EtO vapor. After sterilization, all plastic and rubber articles must be aerated to allow residual ethylene oxide to diffuse from the article. This phase of the sterilization procedure is particularly critical for any articles that are used to administer materials to the human body. Examples of such articles are catheters, face masks, and tubing used in heart-lung machines and artificial kidneys.

II. Pertinent Legal Authority

The primary purpose of the Occupational Safety and Health Act (29 U.S.C. 655 *et seq.*) (the Act) is to assure, so far as possible, safe and healthful working conditions for every American worker over the period of his or her working lifetime. One means prescribed by the Congress to achieve this goal is the mandate given to, and the concomitant authority vested in, the Secretary of Labor to set mandatory safety and health standards. The Congress specifically directed that:

> The Secretary, in promulgating standards dealing with toxic materials or harmful physical agents under this subsection, shall set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life. Development of standards under this subsection shall be based upon research, demonstrations, experiments, and such other information as may be appropriate. In addition to the attainment of the highest degree of health and safety protection for the employee, other considerations shall be the latest available scientific data in the field, the feasibility of standards, and experience gained under this and other health and safety laws. [Section 6(b)(5).]

Where appropriate, the standards are required to include provisions for labels or other appropriate forms of warning to apprise employees of hazards, suitable protective equipment, exposure control procedures, monitoring and measuring of employee exposure, employee access to the results of monitoring, appropriate medical examinations, and training and education. Moreover, where a standard prescribes medical examinations or other tests, they must be available at no cost to employees [section 6(b)(7)]. Standards may also prescribe recordkeeping requirements where necessary or appropriate for enforcement of the Act or for the development of information regarding occupational accidents and illnesses [section 8(c)].

In vacating OSHA's revision to its benzene standard, the Supreme Court required in *Industrial Union Department, AFL–CIO* v. *American Petroleum Institute*, 448 U.S. 601, 65 L. Ed. 2d 1010, 100 S. Ct. 2844 (1980), that before the issuance of a new or revised standard pursuant to section 6(b)(5) of the Act, OSHA must make two threshold findings. These are that a significant risk exists under the current standard and that the issuance of a revised standard would reduce or eliminate that risk. The Court stated:

> We agree * * * that § 3(8) requires the Secretary to find, as a threshold matter, that the toxic substance in question poses a significant health risk in the workplace and that a new, lower standard is therefore "reasonably necessary or appropriate to provide safe and healthful employment and places of employment." (448 U.S. 607 at 614–15; 65 L. Ed. 2d 1010 at 1018–19)

The Court also stated:

> * * * before he can promulgate any permanent health or safety standard, the Secretary [of Labor] is required to make a threshold finding that a place of employment is unsafe—in the sense that significant risks are present and can be eliminated or lessened by a change in practices * * * (448 U.S. at 642, 65 L. Ed. 2d at 1035)

The decision, although it recognized the uncertainties involved, indicated that the determination of "significant risk" should, if at all possible, be established on the basis of an analysis of the best available evidence through such means as quantitative risk assessments. However, in making that determination, the Supreme Court in its general guidance for the future, noted that:

> * * * the requirement that a "significant" risk be identified is not a mathematical straitjacket. It is the Agency's responsibility to determine, in the first instance, what it considers to be a "significant risk". (448 U.S. at 655, 65 L. Ed. 2d at 1043)

It pointed out that while OSHA:

> * * * must support its finding that a certain level of risk exists by substantial evidence, we recognize that its determination that a particular level of risk is "significant" will be based largely on policy considerations. (448 U.S. at 656, n. 62, 65 L. Ed. 2d at 1043, n. 62)

Finally, the Court pointed out that:

> * * * OSHA is not required to support its finding that a significant risk exists with anything approaching scientific certainty. Although the Agency's findings must be supported by substantial evidence * * * OSHA [has] some leeway where its findings must be made on the frontiers of scientific knowledge. (448 U.S. at 656, 65 L. Ed. 2d at 1043)

In the only concrete example of "significance of risk," the Court stated:

> Some risks are plainly acceptable and others are plainly unacceptable. If, for example, the odds are one in a billion that a person will die from cancer by taking a drink of chlorinated water, the risk clearly could not be considered significant. On the other hand, if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2% benzene will be fatal, a reasonable person might well consider the risk significant and

take appropriate steps to decrease or eliminate it. (*Id.* at 655, 656 L. Ed. 2d at 1043)

After OSHA has determined that a significant risk exists and that such risk can be reduced or eliminated by the revised standard, it must set the standard "which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health * * *." [section 6(b)(5) of the Act] The Supreme Court has interpreted this section to mean that OSHA must enact the most protective standard possible to eliminate a significant risk of material health impairment, subject only to the constraints of technological and economic feasibility. (*American Textile Manufacturers Institute, Inc.* v. *Donovan*, 452 U.S. 490 (1981)). The Court held that "cost-benefit analysis is not required by the statute because feasibility analysis is." (*Id.* at 509.)

In addition to section 6(b), authority to issue this standard is also found in section 8(c) of the Act. In general, this section empowers the Secretary to require employers to make, keep, and preserve records regarding activities related to the Act. In particular, section 8(c)(3) gives the Secretary authority to require employers to "maintain accurate records of employee exposures to potentially toxic materials or harmful physical agents which are required to be monitored or measured under section 6." Provisions of OSHA standards which require the making and maintenance of records of medical examinations, exposure monitoring, and the like are issued pursuant to section 8(c) of the Act.

The Secretary's authority to issue this final standard is further supported by the general rulemaking authority granted in section 8(g)(2) of the Act. This section empowers the Secretary "to prescribe such rules and regulations as he may deem necessary to carry out (his) responsibilities under the Act"—in this case as part of, or ancillary to, a section 6(b) standard. The Secretary's responsibilities under the Act are defined largely by its enumerated purposes which include:

Encourage employers and employees in their efforts to reduce the number of occupational safety and health hazards at their places of employment, and to stimulate employers and employees to institute new and to perfect existing programs for providing safe and healthful working conditions (29 U.S.C. 651(b)(1));

Authorizing the Secretary of Labor to set mandatory occupational safety and health standards applicable to business affecting interstate commerce, and by creating an Occupational Safety and Health Review Commission for carrying out adjudicatory functions under the Act (29 U.S.C. 651(b)(3));

Building upon advances already made through employee and employer initiative for providing safe and healthful working conditions (29 U.S.C. 651(b)(4));

By providing for the development and promulgation of occupational safety and health standards; providing for appropriate reporting procedures with respect to occupational safety and health, which procedures will help achieve the objective of this Act and accurately describe the nature of the occupational safety and health problem; exploring ways to discover latent diseases, establishing causal connections between diseases and work in environmental conditions * * * (29 U.S.C. 651(b)(6));

Encouraging joint labor-management efforts to reduce injuries and diseases arising out of employment (29 U.S.C. 651 (b)(13));

And developing innovative methods, techniques, and approaches for dealing with occupational safety and health problems (29 U.S.C. 651(b)(5)).

Because the EtO standard is reasonably related to these statutory goals, the Secretary finds that this standard is necessary to carry out his responsibilities under the Act. In addition to its status as a section 6(b) standard, therefore, it also falls within the broader class of section 8 regulations.

In addition, section 4(b)(2) of the Act provides for OSHA standards to apply to construction and other workplaces where the Secretary determines these standards to be more effective than existing standards which would otherwise apply to these workplaces. The Secretary so finds, and this standard will therefore apply to all workplaces where the Secretary has authority to regulate.

Section 4(b)(1) of the Act restricts application of the Act so that it does not apply to working conditions with respect to which other Federal Agencies exercise statutory authority to prescribe or enforce standards or regulations affecting occupational safety and health. On April 18, 1984, the Environmental Protection Agency published a notice under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), 7 U.S.C. 136 *et seq.*, containing labeling changes for EtO pesticide products, and designed to limit ethylene oxide exposures resulting from the application of EtO as a sterilant or fumigant (49 FR 15268). The relevance of the FIFRA rule to OSHA jurisdiction is discussed below.

III. History of the Regulation

The OSHA standard for EtO that is being revised by this rule (29 CFR 1910.1000, Table Z-1) required employers to ensure that the level of employee exposure to EtO did not exceed 50 parts of EtO per million parts of air (50 ppm), determined as an 8-hour time-weighted average (TWA). That standard was adopted in 1971 from an existing Walsh-Healey Federal standard. The source of the Walsh-Healey standard was the Threshold Limit Value (TLV) recommend in 1968 by the American Conference of Governmental Industrial Hygienists (ACGIH) [Ex. 2-2].

The documentation for the exposure level recommended by the ACGIH in 1968 consisted of limited data from six month animal inhalation studies in which no adverse effects were observed at levels below 50 ppm and a study of employees exposed for 10 years or more to EtO at levels of 5 to 10 ppm with no reported adverse effects [EX 2-3]. No indications of the potential carcinogenicity of EtO were available at that time. Since 1968, however, a substantial number of new studies have become available that have added significantly to the body of knowledge regarding potential adverse health effects related to EtO exposure.

In 1977, the National Institute for Occupational Safety and Health (NIOSH) issued a "Special Occupational Hazard Review" [Ex. 2-5] on EtO, in which it recommended adoption of a ceiling limit of 75 ppm (based on a 15-minute sampling period) for EtO in addition to the 50 ppm TWA. Based upon observation of changes in the genetic material of cells in at least 13 biological species following EtO exposure and covalent chemical bonding between EtO and DNA, NIOSH also concluded that occupational exposure to EtO might increase the frequency of mutations in exposed populations. Although these observations raised concern regarding the potential carcinogenicity of EtO, no epidemiologic studies or long-term bioassays were available to assess its carcinogenic potential for humans.

In 1979, ACGIH published a Notice of Intended Change for EtO to lower its TLV to 10 ppm [Ex. 2-6]. ACGIH based its recommendation on a number of short-term, *in vitro* studies which demonstrated positive mutagenic responses for EtO and on a 1979 case report by Hogstedt et al. [Ex. 2-8] regarding the occurrence of 3 cases of leukemia in a group of 230 workers (more fully discussed in the Health Effect section). The ACGIH adopted this change in 1981 [Ex. 2-7].

The 1981 ACGIH publication [Ex. 2-7] also designated EtO as a substance suspected of having carcinogenic potential in humans and proposed to further lower the TLV for EtO to 5 ppm, based on the positive results from a two

year inhalation study in rats conducted at the Bushy Run Research [Ex. 2–9], which is discussed in the Health Effects section. On June 10, 1982, ACGIH adopted a proposal to lower the TLV to 1 ppm, such change to be effective in 1984.

On May 22, 1981, NIOSH issued a "Current Intelligence Bulletin" [Ex. 2–10] to inform employees and employers about the potential carcinogenic hazard of exposure to EtO. NIOSH recommended that EtO be regarded as a potential occupational carcinogen and that the current OSHA standard be reexamined in light of the information which has become available subsequent to the original adoption of that standard.

On January 26, 1982, OSHA published an ANPR (47 FR 3566) announcing its intention to conduct a reevaluation of the EtO standard. Interested parties were invited to submit data, views and comments with respect to the development of a revised standard for EtO and particularly with respect to a number of specified questions.

In August 1981, prior to publication of the ANPR, Public Citizen Health Research Group (Public Citizen) petitioned OSHA to issue an Emergency Temporary Standard (ETS) reducing the permissible exposure limit for EtO to an eight-hour time-weighted average of 1 ppm [Ex. 2–11]. OSHA denied Public Citizen's petition in September 1981 on the grounds that the available evidence did not indicate that an emergency situation existed to trigger the issuance of an ETS in accordance with section 6(c) of the Act [Ex. 2–12]. Prior to the denial of the petition, Public Citizen brought suit in U.S. District Court for the District of Columbia to obtain an order requiring the Agency to issue an ETS (*Public Citizen Health Research Group et al.* v. *Auchter*, 554 F. Supp. 242). On January 5, 1983, the District Court Judge ruled that OSHA's determination not to issue an ETS represented a "clear error of judgment," and ordered the Agency to promulgate an ETS within 20 days of the Court's decision [Ex. 6–1]. OSHA then sought and obtained a temporary stay of the District Court order pending review on the merits by the U.S. Court of Appeals for the District of Columbia Circuit.

On March 15, 1983, the Court of Appeals rendered its decision on the merits in *Public Citizen Health Research Group et al.* v. *Auchter et al.*, 702 F. 2d 1150 [Ex. 6–2]. In that decision, the Court ruled that the District Court had "impermissibly substituted its evaluation for that of OSHA" in ordering an ETS to be issued, 702 F. 2d at 1153. However, the Court then determined that, because, in the Court's terms, a "significant risk of grave danger" exists with regard to EtO exposures, the failure of the Agency to publish a proposed standard of EtO for 18 months after the Advance Notice of Proposed Rulemaking constituted rulemaking action "unreasonably delayed," under section 6(g) of the OSHA Act (29 U.S.C. 655(g)), and sections 555(b) and 706(1) of the Administrative Procedure Act (5 U.S.C. 555(b), 706(1)). Therefore, the Court ordered the Agency to expedite its development of a proposed rule on EtO, and to issue its proposal within 30 days of the Court decision.

In its January 5 decision, the District Court considered OSHA's arguments that the Environmental Protection Agency (EPA) had exercised its statutory authority over working conditions involving the application and use of EtO as a sterilant and fumigant under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136 *et seq.*, and that this exercise served to preempt OSHA regulation of these same working conditions pursuant to section 4(b)(1) of the OSH Act. The District Court determined, and the Court of Appeals subsequently agreed, that OSHA coverage of EtO was not preempted in "areas—such as the health care industry—where EPA has apparently exercised *minimal if any regulatory authority in an overlapping manner*" (emphasis added).

Pursuant to the Court decision, OSHA's proposed rule on Ethylene Oxide was published April 21, 1983 (48 FR 17284) and included within its scope EtO exposures resulting from the application of EtO as a sterilant or fumigant, including hospital and health care uses, as well as exposure to employees involved in the production and ethoxylation of EtO.

The proposal limited EtO exposure to 1 ppm (8-hour TWA) and contained additional provisions which OSHA believed appropriate. In the preamble to the proposal, OSHA requested public comments, information, and evidence on all issues raised.

The informal rulemaking hearing was convened by Administrative Law Judge Rhea Burrow on July 19, 1983 pursuant to notice and section 6(b) of the Act (29 U.S.C. 655(b)(3)). The hearing lasted through July 28, 1983. Post-hearing submissions of data requested by parties at the hearing were received through August 29, 1983; post-hearing comments and briefs were received through September 19, 1983.

The entire record, including over 300 exhibits and approximately 1600 transcript pages and errata, was certified by Judge Burrow on November 7, 1983, in accordance with 29 CFR 1911.17. Copies of materials contained in the record may be obtained from the OSHA Docket Office, Room S6212, U.S. Department of Labor, 200 Constitution Avenue N.W., Washington, D.C. 20210. The final standard on occupational exposure to Ethylene Oxide is based on full consideration of the entire record of this proceeding, including materials discussed or relied upon in the proposal, the record of the informal hearing, and all written comments and exhibits received.

In the *Public Citizen* case discussed above, OSHA argued that the labeling requirements which are mandated under FIFRA, and which are enforceable against users of EtO pesticides, constituted an exercise by EPA of that agency's statutory authority over working conditions involving EtO. Because of section 4(b)(1) of the OSH Act, OSHA contended that EPA's exercise of authority under FIFRA was sufficient to preempt OSHA's exercise of authority over the same working conditioins.

The Court in *Public Citizen* determined that EPA's exercise of authority under FIFRA was not sufficient to oust OSHA of jurisdiction, and directed OSHA to proceed with its rulemaking over all uses of EtO, including its use in pesticides and sterilants. Although OSHA maintains its previous views on the preemption issue, the Agency has complied with the Court decision, and has included hospital, health care, and other sterilant uses of EtO within the scope of both its proposed and final rules.

EPA has since published a notice in the **Federal Register** (April 18, 1984, 49 FR 15268), as modified in today's **Register**, providing guidance to manufacturers of certain EtO sterilants used in hospitals and health care facilities control methods and work practices to reduce EtO exposures.

OSHA has reviewed the EPA notice and has determined that the recommendations are not inconsistent with OSHA's final standard. As noted earlier, OSHA maintains the views on preemption that it argued unsuccessfully in *Public Citizen*. Nonetheless, based on the Court decision, OSHA is proceeding to regulate employee exposure to EtO in hospitals, health care facilities, and other workplaces where EtO is used as a sterilant or fumigant.

IV. Health Effects

OSHA has found that EtO can cause several serious adverse health effects. Studies in experimental animals supported by epidemiological studies of

working populations indicate that EtO is a potential occupational carcinogen. The evidence suggests that EtO may cause cancers of the blood (leukemia), as well as other organs in humans. In addition, EtO exposure causes mutations, increases the rate of chromosomal aberration and sister chromatid exchange, and causes other undesirable changes in the DNA of mammalian cells. These effects support OSHA's conclusion regarding the carcinogenicity of EtO. EtO exposure has also been associated with an increased risk of spontaneous abortion among pregnant women and is capable of causing other adverse reproductive effects in both men and women. Exposure to high concentrations of EtO causes central nervous system depression and other neurological effects which are thought to be reversible with cessation of exposure. In addition, exposure to EtO gas causes sensitization and irritation of human tissues, including the eyes and respiratory tract.

Three epidemiological studies indicate an association between worker exposure to EtO and a significant increase in the risk of death from cancer. Hogstedt et al. [Ex. 2–8] found an increased risk of death from leukemia among employees exposed to EtO when used as a sterilant. In a second study, these investigators confirmed an increased leukemia risk and also observed a significant excess of stomach cancer deaths and total cancer deaths among production workers [Ex. 2–22]. Morgan et al. [Ex. 6–5] found an increased risk of mortality from Hodgkin's disease and pancreatic cancer among EtO production workers.

Studies in experimental animals have provided definitive evidence that EtO is carcinogenic in multiple species and by several routes of administration. Leukemia, brain cancer and mesothelioma have been induced in animals exposed to EtO by inhalation. Cancers of the forestomach have been induced as a result of EtO administration by oral gavage. Injection site sarcomas and skin cancers have been observed in animals exposed to EtO by injection.

The studies in experimental animals in conjunction with the epidemiological studies indicate that EtO has the potential to cause cancers of the lymphohematopoietic system and other organs in humans. In addition, evidence derived from short-term tests clearly demonstrates DNA damage, mutations and chromosomal change in non-mammalian cells, mammalian cells, intact experimental animals or in occupationally exposed workers. These data provide supportive evidence that EtO is carcinogenic to humans.

EtO has been shown to induce cancer in laboratory animals at concentrations that are well below the current PEL of 50 ppm. Further, the available data on the effects of human exposure are consistent with the results of the animal studies. The health effects of EtO have been comprehensively and strikingly established. OSHA considers EtO to be a potential occupational carcinogen.

Based on the Hemminki et al. study (Ex. 6–7) of increased spontaneous abortions among hospital workers exposed to EtO and numerous studies in experimental animals supporting these findings, OSHA also concludes that exposure to EtO constitutes an occupational reproductive hazard. Adverse reproductive consequences of exposure to EtO have been manifested most frequently in animal studies by embryonic or fetal loss related to exposure of the female parent during critical periods of gestational development or exposure of the male parent prior to conception.

There is also substantial evidence that EtO is a direct-acting mutagen capable of causing mutations in the tissues of exposed humans. Inhaled EtO reacts with mammalian gonadal DNA as demonstrated by the induction of heritable translocations in male offspring and unscheduled DNA synthesis and dominant-lethal mutations in germinal cells. EtO that reaches the DNA of human germ cells is presumed to induce heritable mutations affecting future generations.

Exposure to high airborne concentrations of EtO causes respiratory tract irritation and central nervous system depression. Excessive exposures have produced convulsive movements, neuropathy, pulmonary edema and bronchitis in humans; headache, nausea, vomiting and diarrhea also are common systemic effects of EtO exposure. Evidence from human case reports also indicates that neurological effects (sensory motor neuropathy, seizures, headache) may result from intermittent high exposures. Hematologic effects (reduced hemoglobin and elevated lymphocytes) have been observed in production plant workers chronically exposed to EtO.

Following accidental or experimental exposure of human skin, liquid EtO has caused edema and erythema with progression to blister formation in 6–12 hours. The degree of skin injury is related to concentration and duration of exposure. These effects are reversible. As concentrated EtO evaporates, a freezing effect occurs, which may cause frostbite. Dilute solutions may penetrate the skin, producing a chemical burn. Skin burns have also been caused by the residual EtO in leather goods, belts and footwear. Skin sensitization has been associated with repeated dermal exposure.

High concentrations of EtO are irritating to the eyes of humans and animals. Direct ocular contact with liquid EtO can produce corneal injury. Repeated exposure to high airborne concentrations of EtO may result in the formation of cataracts.

Adverse effects of acute exposures also have been observed in experimental animals. Paralysis and periodic convulsions frequently have preceded death due to lung edema or secondary infection. Signs of poisoning from subchronic exposure by different routes of administration in various species of experimental animals include hindquarter neuropathy indicating neurotoxicity, and congestive and degenerative changes in the lungs, liver, spleen and kidneys. In addition, adverse testicular changes (tubular degeneration) and hematologic changes (anemia) have been produced.

Detailed information on the effects of exposure to EtO and deliberations on these data during the rulemaking are discussed in this section.

A. Carcinogenicity

Epidemiologic Studies

Three epidemiologic studies investigating the relationship between occupational EtO exposure and cancer have appeared in the scientific literature: Morgan et al. (Ex. 6–5); Hogstedt et al. (Hogstedt I, Ex. 2–8); and Hogstedt et al. (Hogstedt II, Ex. 2–22).

The Morgan et al. study (Ex. 6–5) reported the mortality experience of 767 potentially exposed (based on work history records) male workers who had been employed at an ethylene oxide-producing chemical plant for at least 5 years between 1955 and 1977. Industrial hygiene measurements taken at typical leak sources in the facility's operating units in July 1977 revealed no detectable EtO levels in most of the production areas. A leak in the tube used to gauge the level of EtO in tank cars during loading operations resulted in an isolated measurement of 6,000 ppm. At the sources of EtO (pump, valve, pipe flanges, spigots, and gauges), levels of less than 10 ppm were recorded. All other measurements were below 50 ppm. Fewer deaths were observed in the study population than expected from all causes and from all malignancies, based on U.S. mortality statistics; the

standardized mortality ratios (SMR's) for these causes were 58 and 79, respectively. No deaths from leukemia were observed, compared to 0.70 expected. A significant excess of deaths was demonstrated for pancreatic cancer (3 observed versus 0.8 expected, P less than 0.5) and for Hodgkin's disease (2 observed versus 0.35 expected, P less than 0.05) among workers at this plant.

Hogstedt and coworkers (Hogstedt I, Ex. 2–8) reported that three cases of leukemia had occurred between 1972 and 1977 among workers in a Swedish factory where a mixture of 50 percent ethylene oxide and 50 percent methyl formate had been used since 1968 to sterilize hospital equipment. Based on age and sex-specific Swedish national rates for 1972, 0.2 leukemia cases would have been expected between 1968 and 1977 among the 230 workers potentially exposed in this facility during this period. In 1977, the 8-hour TWA exposure concentration in the areas where two women who died from leukemia had worked was estimated to be 20±10 ppm; the levels of previous exposure for these women were not known. These two individuals had had no known occupational exposure to suspect leukemia-inducing agents other than EtO; the third individual who died from leukemia (a male manager exposed to EtO approximately 3 hours per week) had had occasional contact with benzene in laboratory work. The leukemias were classified as chronic myeloid leukemia and acute myelogenetic leukemia in the women and as primary macroglobulinemia in the man.

Hogstedt et al. (Hogstedt II, Ex. 2–22) reported the results of an historical prospective mortality study of 241 workers employed for more than one year in a Swedish EtO production facility. The study included three subcohorts, comprised of 89 full-time exposed men, 86 intermittently exposed men (maintenance workers), and 66 men who had no known exposure to EtO. The follow-up period started in January 1961 and continued until the end of December 1977. Exposure to EtO in the production areas was estimated to average below 14 ppm with peaks to 728 ppm in the 1940's, 6 to 28 ppm during the 1950's and 1960's with peaks above the odor threshold (approximately 700 ppm), and 0.6 to 6 ppm in the 1970's with occasional higher values. Among the 89 full-time workers in the EtO production areas, a significant excess in total mortality was observed (23 deaths observed, 13.5 expected based on Swedish national statistics, $p < 0.05$). Significant excesses in total cancer mortality (9 observed, 3.4 expected, $p < 0.01$) and in deaths from diseases of the circulatory system (12 observed, 6.3 expected, $p < 0.05$) were also reported in this group. Site-specific excess cancer mortality was noted for leukemia (2 observed, 0.14 expected, $p < 0.01$) and stomach cancer (3 observed, 0.4 expected, $p < 0.01$) for the full-time exposed workers. No statistically significant excess mortality was noted among the 86 intermittently exposed maintenance workers from the same facility or among the 66 workers who had never been exposed to EtO, although one leukemia death was noted among the group of maintenance workers (0.13 expected). The production and maintenance workers who were exposed to EtO were also exposed to ethylene, ethylene dichloride, ethylene chlorohydrin, and bis(2-chloroethyl) ether. Because of these multiple exposures, the authors were unable to attribute the excess cancer incidence to a specific chemical, although they speculated that EtO and ethylene dichloride were the most likely causative agents.

Several commenters (Exs. 66, 110, Tr. 632, 1529) pointed to weaknesses in these epidemiological studies. For example, Robert W. Morgan of Environmental Health Associates, who had been asked by the Ethylene Oxide Industry Council (EOIC) of the Chemical Manufacturers Association to evaluate the epidemiologic data on ethylene oxide, testified (Tr. 636) that the results of his study (the Morgan et al. study, Ex. 6–5) failed to support a causal link between EtO exposure and leukemia, and that his study should therefore be considered a negative study. However, OSHA notes that the study demonstrates a significant excess of deaths from pancreatic cancer and Hodgkin's disease among workers in EtO production.

Sidney Wolfe of the Public Citizen Health Research Group noted (Tr. 792) that the Morgan et al. study (Ex. 6–5) contained little information on the exposures of the 767 workers in the study, and thus the true size of the cohort exposed to EtO was not known. The inclusion in the Morgan et al. study of individuals with little or no exposure to EtO would bias the results toward an underestimation of any risk associated with EtO exposure.

Philip Landrigan, Director of NIOSH's Division of Surveillance, Hazard Evaluation and Field Studies, suggested that the findings of the Morgan study should be considered inconclusive rather than negative for leukemia because of the study's limited statistical power (Tr. 341). OSHA believes that Landrigan's characterization of the Morgan et al. study is an accurate one, because, as the study's authors themselves report, only "an excess of leukemia deaths as small as 10.5-fold could be detected at the 95 percent confidence level" (Ex. 6–5). As noted by Jeanne M. Stellman of the Women's Occupational Health Resource Center, Columbia University, "* * * a 10.5-fold (increase in) risk is well beyond the risk observed for most environmental agents, including cigarette smoking" (Ex. 4–59). Stellman, supporting the conclusion reached by Landrigan regarding the Morgan et al. study, commented:

> Had * * * (Morgan et al.) subsumed Hodgkin's disease under hematologic and hematopoietic cancer sites, this organ system would have shown an elevated SMR of 191.
>
> Therefore, instead of contradicting previous studies * * * (the two Hogstedt studies), this paper confirms an increased risk of hematologic and hematopoietic malignancy due to EtO exposure * * * Rather than being viewed as a negative study, Morgan et al. * * *. (Ex. 6–5) should be considered as a strong piece of evidence indicating that even in very small cohorts, with exposures well below the current OSHA standard, excess cancer risk (sic) was detected (Ex. 4–59).

Morgan criticized the first Hogstedt et al. paper (Ex. 2–8) reporting three leukemia deaths as being "anecdotal," and noted further that the numbers in this study were "simply too small," (Ex. 66). In testimony (Tr. 634), Morgan stated that the first Hogstedt study (Ex. 2–8) was "a description of a cluster * * * rather than an epidemiologic study."

The first Hogstedt study (Ex. 2–8) was also criticized by several commenters (Exs. 11–74, 47, 126) because workers in the cohort were exposed to a mixture of EtO and methyl formate. For example, Saul Kaye, independent consultant to hospitals and industry on sterilization practices, stressed that exposure to a mixture of EtO and methyl formate might be more hazardous to humans than exposure to EtO alone (Exs. 11–74, 126, Tr. 841). However, at the hearing, Kaye acknowledged the fact that there is no evidence in the reported literature that would indicate that methyl formate itself is carcinogenic (Tr. 845).

Several commenters (Exs. 11–74, 47, 126) also noted that the second Hogstedt study (Ex. 2–22) cohort had been exposed to several other chemicals (including ethylene dichloride, ethylene, ethylene chlorohydrin, bis (2-chloroethyl)ether).

NIOSH reviewed the two Hogstedt studies (Exs. 2–8, 2–22) in its Current

Intelligence Bulletin on EtO and concluded:

> These epidemiological investigations cannot be cited as definitive evidence of an excess risk of cancer resulting from EtO exposure, but they should be considered evidence that excess risk of cancer may exist for the EtO workers studied. (Ex. 2-10)

Despite these methodological shortcomings, only two commenters (Exs. 66, 110) concluded that the epidemiologic evidence failed to demonstrate that EtO exposure posed an increased risk of cancer. In comments prepared for the EOIC, Morgan concluded that, " * * * the ethylene oxide mortality studies fail to demonstrate any appreciable or significant risk of malignancy" (Ex. 66). However, Morgan went on to state " * * * because of the limited number of subjects involved in these studies, they may not provide as much reassurance (that EtO is not a carcinogen) as some would like" (Ex 66).

Although OSHA believes that none of the available epidemiologic studies are, in and of themselves, definitive evidence of EtO's carcinogenicity, the Agency agrees with Philip Landrigan of NIOSH that the two Hogstedt studies "provide evidence of a possible association between occupational exposure to ethylene oxide and death from leukemia" (Tr. 341). As Leon Golberg, Professor of Community and Occupational Medicine at Duke University and consultant to the EOIC observed, although "one cannot say that * * * (the human data) are positive, it is * * * impossible to say that they are entirely negative" (Tr. 520).

The increasing number of reports of EtO-induced mutagenic changes, manifested by alterations in the genetic material of peripheral blood cells in humans, as well as EtO's established genotoxic effects in other species, and the evidence for the induction of leukemia and solid tumors in experimental animals, such as brain tumors, lend credence to the observations of excess risk from leukemia and other cancers (including brain tumors) observed in the epidemiologic studies of workers exposed to EtO. The Hogstedt et al. and Morgan et al. studies are limited by the constraints that accompany any attempt in humans to characterize rare events in small populations that have been exposed to unspecified levels of contaminants. Nonetheless, OSHA finds that the epidemiologic evidence, although not by itself conclusive, is supportive of EtO's potential carcinogenic, and particularly leukemogenic, effects. OSHA thus agrees with NIOSH's assessment that EtO should be regarded as a potential human carcinogen (Tr. 303).

Experimental Studies

The experimental evidence most applicable to the question of EtO's occupational carcinogenicity is that provided by two studies involving inhalation as the route of EtO exposure: The Snellings et al. study performed at Bushy Run Research Center (BRRC Study, Bushy Run study) (Ex. 2-9) and the Lynch et al. study at NIOSH (NIOSH study) (Exs. 6-6, 6-16).

The Bushy Run Study. Snellings and colleagues conducted a two-year chronic inhalation study in which three groups of male and female Fischer 344 rats (120 rats per sex per group) were exposed to EtO at concentrations of 100, 33, or 10 ppm for 6 hours per day, 5 days per week. Two groups of rats served as concurrent controls and were exposed to air only.

Based on histopathological evaluation, the Bushy Run researchers concluded that the incidence of mononuclear cell leukemia and of peritoneal mesothelioma was significantly increased as a result of exposure to EtO. The incidence of mononuclear cell leukemia in female rats was dose-related, increasing with exposure concentration. A statistically significant increase in mononuclear cell leukemia was observed in the group of female rats exposed at 100 ppm. For female rats exposed to 33 ppm, the cumulative percentage of animals developing leukemia was significantly higher than that for one control group and for both control groups combined, but was not higher than the incidence for the second control group alone. The regression analysis of leukemia incidence versus exposure concentration was significant, with a correlation coefficient of +0.99, indicating that the induction of the leukemia was highly correlated to exposure at each concentration.

An increase in mortality from peritoneal mesothelioma was reported in the male rats exposed to 33 and 100 ppm. Among the males exposed at 100 ppm, the cumulative percentage developing a tumor of this type was reported to be statistically significantly higher than that of the controls, beginning with the 21st month of exposure, whereas the incidence of these tumors in males exposed at 33 ppm was not appreciably higher than that in the controls until the final month (the 24th) of the study. These peritoneal tumors originated in the testicular mesothelium and were confined to the abdominal cavity.

In addition, the Bushy Run investigators reported that EtO exposure was associated with a higher frequency and/or earlier onset of mononuclear cell leukemia in male rats. The researchers also reported that a mortality-adjusted trend analysis indicated that the onset of normally occurring pituitary adenomas in male and female rats was significantly accelerated by exposure to EtO.

Finally, the authors concluded that there was a dose-related increase in the number of rats with one or more primary neoplasms. Specifically, female EtO-exposed rats had an increase in the mean number of neoplasms per neoplasm-bearing rat, and the incidence of multiple neoplasms in females at all three exposure levels was significantly greater than that in the combined controls. The authors further pointed out: "* * * biologically significant adverse effects were observed at all concentrations tested" (Ex. 2-9).

The BRRC investigators also have reported, based on further evaluation of their slides, that there was a dose-related increase of gliomas (brain cancers) in the experimental animals (Ex. 15). The incidence of these tumors is given in Table 1. As can be seen from Table 1, there was a statistically significant increase in the incidence of gliomas in the male rats exposed at 100 ppm. The incidence of gliomas in the female rats exposed at 100 ppm was not statistically significant when a Bonferroni correction was applied to the test. (A Bonferroni correction adjusts p-values to account for multiple comparisons). However, the results of the test for linear trend were significant at the 5% level for both males and females, which corroborates that there is a dose-effect relationship between exposure to ethylene oxide and the incidence of these rare brain tumors.

TABLE 1.—FREQUENCY OF PRIMARY BRAIN NEOPLASMS IN RATS IN TWO-YEAR INHALATION STUDIES

Study	Sex	O C(I)	O C(II)	10 ppm	33 ppm	50 ppm	100 ppm
BRCC [1]	Male	[2] 1/98	0/98	1/99	5/98		7/99
	p-values [3]	0.0003			0.017		0.0024
	Female	1/98	0.96	1/95	3/99		4/99
	p-values	0.014			0.11		0.046

TABLE 1.—FREQUENCY OF PRIMARY BRAIN NEOPLASMS IN RATS IN TWO-YEAR INHALATION STUDIES—Continued

Study	Sex	O C(I)	O C(II)	10 ppm	33 ppm	50 ppm	100 ppm
NIOSH [4]	Male		0/76			2/77	5/79
	p-values [5]		0.011			0.2516	0.0323

[1] Ex. 15, Data for 18 and 24 months sacrifices, dead/euthanized.
[2] Numerator equals the number of brains with neoplasms. Denominator equals total number of animals whose brain tissues were examined microscopically.
[3] First p-value in row is for one-sided Cochran-Armitage test for a dose-response trend. Remaining p-values are for Fisher's exact test (one-sided) comparing responses in combined controls to those in the respective treatment groups (Ex. 34).
[4] Ex. 40.
[5] First p-value in row is for one-sided Cochran-Armitage test for a dose-response trend. Remaining p-values are for Fisher's exact test (one-sided) comparing responses in combined controls to those in the respective treatment groups.

Several commenters (Exs. 11–74, 47, 110, 126, 144, 152) submitted specific criticisms of the Bushy Run study to the record. Despite these criticisms, however, both the EOIC (Ex. 152) and the Health Industry Manufacturers Association (HIMA) (Ex. 153) concluded that the Bushy Run study presents evidence that EtO is carcinogenic. Several issues related to the Bushy Run study that were raised by commenters are discussed below.

First, two commenters (Exs. 11–74, 47) questioned the validity of the study results because they believe that the occurrence of the sialodacryoadenitis (SDA) viral infection among the rats in the study during the fifteenth month may have confounded the results. The EOIC (Ex. 47) speculated about the effects such a viral infection might have had on the immune status of the rats, and HIMA (Ex. 11–74) suggested that the SDA infection might have had an impact on the rat's long-term pulmonary absorption of EtO.

Clinically, SDA infections usually occur as acute epizootics that are manifested as cervical swellings, enlarged submaxillary salivary glands, red-brown-colored ocular and nasal discharges, sneezing, photophobia, and ophthalmic lesions. Histopathological lesions in rats infected with SDA virus have been characterized and described; the lesions involve the submaxillary salivary glands, Harderian gland, and parotid salivary glands. SDA viral epizootics vary in duration from 12 to 32 days.

The development of SDA viral infections among study animals would in general have an insignificant impact on the outcome of most toxicological studies. The possible occurrence of secondary infection could compromise respiratory ventilation and result in the appearance of acute clinical symptoms. Such an occurrence may compromise the results of an inhalation toxicology study in terms of high mortality from infectious diseases, altered pulmonary absorption of the test substance and, consequently, altered pulmonary morphology.

William Snellings, director of the Bushy Run study, testified (Tr. 525) with regard to the potential effects of the viral infection and the possibility of flaws in the study as follows:

> The thing that we did was to look not only at our two control groups very carefully, but control groups in our laboratory, the historical controls and also controls that have been published in (the) literature and results from controls published in (the) literature. In particular, in the tumors that were found * * * we found no difference * * * between the two controls * * * in the group * * * in the same study or the controls in our lab (or) historical controls or (controls) within (the) literature.
>
> So we made a statement that at least in the control groups we had no adverse affect (sic) that would contribute to an increase or a decrease in the normal spontaneous rate of tumor production in the Fisher (sic) rat.

J.M. Ward of the National Cancer Institute (NCI), a pathologist active in NCI's bioassay program, testified on behalf of OSHA (Tr. 1113) that:

> * * * There's been no evidence for any types of studies that show that (the) presence or absence of a virus or a bacterial infection or pneumonia will actually make a chemical become a carcinogen or not become a carcinogen * * *. I would * * * not consider any infections in these rat bioassays as being significantly important for deciding whether the chemical may or may not be a carcinogen * * *. There are many bioassays performed all throughout the world where most animals will have some type of infectious disease even when they're maintained in a very clean environment (Tr. 1114).

Since the tissues giving rise to tumors in the Bushy Run experiment are not those traditionally affected by the SDA virus (salivary glands, Harderian gland), and since in the Bushy Run controls the SDA infection did not have any effect that might conceivably influence the rate or occurrence of tumors, and in light of Ward's testimony, OSHA concludes that the outbreak of this infection among the animals used in this study did not have a substantial impact on the validity of the results of the study.

Other commenters (Exs. 47, 126) noted that the mononuclear cell leukemia (MCL) observed in the rats of the Bushy Run study did not occur in other strains of rats and mice and had no human counterpart. However, Jerrold M. Ward of NCI, testifying on behalf of OSHA, noted that:

> The leukemia in the Fisher (sic) rats in the Bushy Run study that was increased in incidence has been recently described as a specific type of leukemia not only in rats but also in humans as well * * * Recent reports of specific kinds of lymphocytic leukemia in humans have demonstrated that there are some, if not many, types of lymphocytic leukemias which have a similar or identical characteristics as * * * (those) of the Fisher (sic) rat mononuclear cell leukemia (Tr. 1107).

OSHA agrees with Ward that these recent findings demonstrate similarities between certain types of human and rat leukemias, a finding which increases the relevance of the BRRC results to humans.

The EOIC (Ex. 47) also criticized the findings of the Bushy Run study because, they contended, the only types of tumors that occurred among the treated animals were those that occur spontaneously in this strain of rat.

In this regard, the EOIC stated that:

> The tumors which have been observed have all been late-occurring neoplasms with a spontaneous incidence in the Fischer 344 rat. No unique tumors were produced by EO exposure, suggesting the possibility that EO is active through a mechanism which does not involve initiation but rather promotion or another form of modulation of the spontaneous tendency to tumor development (Ex. 47).

However, when questioned about the likelihood that EtO is a promoter rather than a frank carcinogen, Ward responded as follows:

> * * * The increase[d] incidence of spontaneous tumors (in the Bushy Run study) has been used by many people to say that the chemical is not a true carcinogen but * * * may be a promoter or a potentiator or a modifier * * *.
>
> But there are many potent carcinogens that most people will agree * * * also increase the incidence or apparently increase the incidence of spontaneous tumors and you can almost say that every type of induced tumor * * * seen in rats has also been seen in control animals at least once.
>
> * * * I think the fact that ethylene oxide causes an increased incidence of leukemias and also squamous cell carcinomas may be indicative of the fact that the chemical may act on different types of tissues * * * which may increase the incidence or actually cause the type of leukemia that's found (Tr. 1119–1120).

When asked about whether there might be a promotional effect by EtO and

what the significance of such an effect might be, Ward responded:

> * * * Promotion is a fairly broad term * * *. [W]e can almost say that * * * most carcinogens are promoters because they would promote * * * rare tumors. So I don't like to use that term unless we really know more about the chemical (Tr. 1120).
>
> * * * Up until now, many papers and scientists have said that promoters may be less dangerous than carcinogens * * *. In the last two years * * * we have evidence that tumor promotion may also occur after * * * not only long-term exposure but after short-term exposure to low doses. So the tumor promoters may in fact be just as dangerous for causing or increasing the risk of cancer as * * * potent carcinogens * * * in my opinion, promoters may be as dangerous * * * as chemicals that are not thought of * * * [as] promoters. (Tr. 1121).

Although the EOIC argued (Ex. 47) that interpretation of the results of this study may be "complicated by the absence of a unique early-occurring tumor," this uncertainty was put to rest by the observation of gliomas in the Bushy Run slides. Gliomas, malignant tumors of the central nervous system, were generally characterized by Legator as "very rare" tumors (Tr. 104), and, as was pointed out by Lemen of NIOSH: "Gliomas had a low spontaneous instance (sic, incidence) in these two studies (BRRC, NIOSH): Goodman reported incidence rates of 1 to 2 per thousand in untreated Fischer 344 rats used as controls in several carcinogenicity tests" (Tr. 312).

Another study (Ex. 93) submitted by Ward confirmed the historically low spontaneous incidence of gliomas in the Fischer 344 rat; the spontaneous incidence of gliomas among almost 52,000 Fischer 344 rats used in the NCI bioassay program was reported to be 6.6 per thousand in male rats and 5.4 per thousand in female rats. Ward also testified that the incidence of brain tumors in EtO-treated rats might have been higher than the incidence found in the Bushy Run study if the rats had been exposed to EtO in utero or postnatally:

> * * * (The presence of) brain tumors suggest[s] that * * * these animals may, if exposed to this chemical * * * (in utero or postnatally) develop a higher incidence of tumors * * *.
>
> The brain tumors (found) * * * are also very disturbing because there are very few chemicals that cause brain tumors * * * (in animals exposed) after four weeks of age * * *.
>
> So I would have to say that potentially this chemical poses a * * * significant hazard based on the results of [the Bushy Run] bioassay * * * (Tr. 1128–1129).

The Health Industry Manufacturers Association (HIMA) questioned (Ex. 11–74) whether the large number of statistical analyses performed on Bushy Run data "may have produced some misleading results identified as significant" (Ex. 11–47, Appendix H). The Bushy Run researchers applied a statistical correction to their results, based on the Boneferroni inequality, to prevent just this type of problem. However, HIMA (Ex. 11–74, Appendix H) argued that had the BRRC study protocol been designed originally to include life-table analysis and the performance of statistical tests only at 12, 18, and 24 months, rather than at monthly intervals, the study's conclusions would have been more valid. HIMA pointed out that conducting so many statistical tests increases the likelihood of obtaining a significant number of false positives.

To test whether the number of statistical tests conducted had influenced the BRRC results, OSHA used an alternative approach to the Bonferroni inequality correction. The alternate approach bases calculations of significance on the assumption that the individual tests are independent. This would represent the "worst case," since any relation among tests decreases the probability of detecting false positives. After removing the Bonferroni corrections made by the BRRC researchers and applying the assumption that tests for survival rate are independent, OSHA determined that the probability of finding 15 tests with $p < 0.01$, or of finding five tests with $p < 0.001$ among the 260 tests is much less than 0.05. Therefore, OSHA finds that the statistical tests employed in treating the BRRC data are valid and that the Agency can be confident in its conclusion that the survival of male rats in the Bushy Run study was significantly diminished by exposure to ethylene oxide. If a similar probability approach is used on the survival test results for the female rats, the null hypothesis—that there was no mortality increase with exposure—is rejected even more decisively

If similar probability calculations are made for the results of the life table analysis, significant exposure-related effects are demonstrated for mononulcear cell leukemia among the female rats and for peritoneal mesothelioma among the male rats. To indicate a significant ($p < 0.05$) tumorigenic effect among the more than 250 tests conducted, at least 20 tests must be significant at $p < 0.05$, or 6 tests must be significant at $p < 0.01$, or 2 tests must be significant at $p < 0.001$. In the tests for female mononuclear cell leukemia, the results of at least 10 tests are significant at $p < 0.001$. In the tests for male peritoneal mesothelioma the results of at least 15 tests were significant at $p < 0.01$, and at least 7 tests are significant at $p < 0.001$. A significant overall tumorigenic effect is confirmed by the fact that the number of tests that are significant at the lower values of P exceeds the minimum number of tests that would have to be significant to demonstrate a significant overall tumorigenic effect.

The most important statistical argument for a dose effect is the identification of a progressive relationship between dose group and response. The BRRC used time-adjusted trend test analyses that were sensitive to differences in both tumor frequency and time-to-tumor, and consistently found significant positive trends in each of the five tests conducted to examine dose-effect. Further, the tests demonstated significant effects when dose groups were compared to controls, and additionally found significantly increased tumor incidences when high-dose groups were compared to low-dose groups. Because the BRRC study clearly identified these relationships, OSHA concludes that exposure to EtO significantly increased both mortality and tumorigenicity among the BRRC rats.

The NIOSH Study. The other animal evidence that relates most strongly to the question of carcinogenicity from occupaitonal exposure to EtO is provided by a two-year, NIOSH-conducted chronic inhalation study of male rats and male monkeys. The preliminary results of this study were reported in a 1982 memorandum from NIOSH (Ex. 6–16). In that study, two groups each of 80 male Fischer 344 rats and 12 male Cynomolgus monkeys were exposed to EtO at 50 ppm and 100 ppm, respectively. Two groups, one of 80 rats and one of 12 monkeys, were used as controls and exposed to conditioned ambient air. Durign the study, all of the rat groups became infected with *Mycoplasma pulmonis* which, begining with the sixteenth month, caused the death of a large portion of the rat population (Lynch et al. 1982, as cited in Ex. 47). Exposure was discontinued for two weeks to permit animals to recover from the infection.

Preliminary results of histopathological evaluations of the spleens from the EtO-exposed rats indicate an exposure-related increase of mononuclear cell leukemia in the rats exposed at 50 ppm but not in those exposed at 100 ppm. NIOSH has acknowledged (Ex. 6–16) that these preliminary results must be interpreted in light of the known spontaneous incidence of leukemia in Fischer 344

rats. It should be noted, however, that excess mortality occurred in the 100 ppm group (19 percent survived as compared to 49 percent of the controls). At the terminal kill a significantly higher frequency of leukemia was found only in the group exposed to EtO at 100 ppm.

Of equal or greater importance, however, is the study's dose response relationship between exposure and the development of gliomas, a rare tumor in Fischer 344 rats, as noted earlier (Ex. 15). Gliomas were found in 5 of 79 rats exposed at 100 ppm and 2 of 77 rats exposed at 50 ppm of EtO. There were no gliomas found in the 76 control rats (see Table 1). A significant association between exposure to EtO and the occurrence of peritoneal mesothelioma was also found in rats exposed to 100 ppm EtO, but not in those exposed at 50 ppm EtO. The findings of gliomas, peritoneal mesothelioma, and leukemia in the study parallel the findings made in the Bushy Run study.

None of the monkeys in the NIOSH study (Ex. 6–16) demonstrated any evidence of leukemia. Two of the monkeys in each exposure group were sacrificed for neuropathological evaluation. The only significant findings were the presence of axonal dystrophy in the nucleus gracilis (a specialized component of the central nervous system) and demyelination of portions of the gracilis tract in one monkey from the low and one from the high dose groups (Sprinz et al., 1982, as cited in Ex. 47). Based on this limited evidence, the researchers were not able to reach any conclusions as to the cause or significance of these findings, but they remain noteworthy in view of the findings of gliomas in the rats in this study, and confirm that EtO affects the central nervous system.

The overwhelming majority of comments on the NIOSH study agreed with OSHA's conclusions that these preliminary results provide additional evidence of EtO's carcinogenicity in experimental animals. Leon Golberg, consultant to the EOIC, testified that the Bushy Run and NIOSH studies "yield mutually confirming information, a dose response relationship is apparent for certain endpoint effects, and the exposure conditions were well controlled and monitored" (Tr. 491). In light of the finding of gliomas in the Bushy Run and NIOSH studies, Jerrold Ward (NCI) stated (Tr. 1129) that these "consistent results are also very disturbing because there are very few chemicals that cause brain tumors postnatally."

Other studies. Additional evidence supporting EtO's carcinogenicity has been obtained from animal studies using routes of exposure other than inhalation. Dunkelberg (Ex. 2–18) and Walpole (Ex. 2–20) administered EtO by subcutaneous injection; Van Duuren et al. (Ex. 2–21) observed the effects of dermal exposure, and Reyniers et al. (Ex. 2–19) observed the effects in rats accidentally exposed to EtO-treated bedding, while another study by Dunkelberg (Ex. 19) investigated the effects of intragastric administration of EtO. Several of these studies were discussed in the preamble to the proposal; a short review of each will be presented here.

In 1979, Dunkelberg (Ex. 2–18) reported preliminary results of a long-term carcinogenicity bioassay in which 100 female NMRI mice were given subcutaneous injections of EtO in 0.1 ml tricaprylin in weekly dosages of 0.1, 0.3, or 1.0 mg EtO per animal. Two control groups, 100 untreated and 100 tricaprylin-treated mice, were used. After 91 weeks of treatment, Dunkelberg reported that the number of sarcomas at the injection site increased with dosage, while no injection-site tumors had occurred in the control mice. The first tumor appeared in the fiftieth week of treatment. The number of tumors at sites distant from the injection sites was not significantly greater in the treated groups than in the controls.

HIMA's submission to the docket stated that, "the Dunkelberg study is of limited value because it lacked suitable controls and because irritants are known to cause oncogenic effects at the site of injection" (Ex. 11–74, Appendix G). However, OSHA agrees with Ward of the National Cancer Institute, who stated that, "inductions [sic] of tumors at the injection site means generally that when the chemical is given at other sites, it will cause tumors as well at other sites, either at the site of application or systemically" (Tr. 1124).

The further importance of the Dunkelberg study (Ex. 2–18) was brought to light when OSHA reviewed the results of that study, which were tabulated by the EOIC in its "Hazard Assessment" (Ex. 47). This tabulation shows that, regardless of the control population used, EtO treatment at the middle dose only once weekly induced a 100% increase in tumors as compared to treatment at the low dose.

Walpole (Ex. 2–20) subjected 12 "stock" rats to repeated subcutaneous injections of a dose of 1 g/kg EtO in Archis oil for 94 days. The small sample of animals was observed over their lifetimes. No sarcomas were observed at the injection site.

Van Duuren et al. (Ex. 2–21) applied 100 mg of a 10 percent EtO solution in acetone to the dorsal skin of 30 female Swiss Millerton mice three times per week for life. No tumors were observed. However, as Jeanne M. Stellman suggested, either the minimal dose of EtO administered or the route of dermal application may have accounted for the negative results seen in this study (Ex. 4–59).

Reyniers et al. (Ex. 2–19) accidentally exposed a colony of inbred albino mice to EtO-treated bedding for 150 days and then moved the survivors to untreated bedding for the remainder of their lifespans. The tumor incidence in the 73 surviving females, ranging in age from 300 to 900 days, was 86.3 percent. The most common tumors were ovarian, leukemic (malignant lymphomas), and pulmonary. In contrast, there were no grossly detectable tumors in 86 females, 100 to 600 days of age, in the mouseline from which the accidentally exposed colony was started. HIMA criticized the validity of this study on the grounds that any residual EtO would have been desorbed before the mice contacted the EtO-treated bedding (Ex. 11–74). Since the bedding was not analyzed for EtO content, the validity of HIMA's assertion cannot be tested. However, the authors of this study concluded that the incidence of tumors in the surviving mice could only be explained by their contact with the EtO-impregnated bedding.

Dunkelberg (Ex. 19) reported the results of a study in which 50 female Sprague-Dawley rats were intragastrically given EtO in 1 ml of salad oil twice weekly in doses of 7.5 or 30 mg/kg body weight for 150 weeks. Two control groups, 50 untreated rats and 50 salad-oil-treated animals, were used. Although no local tumors were induced in either of the control groups, 16 percent and 62 percent of the EtO-treated groups, respectively, incurred local tumors, mainly squamous cell carcinomas of the forestomach. The first tumor occurred in the 79th week. No tumors were induced at sites distant from the point of administration.

Conclusions

This comprehensive review of the scientific evidence in the rulemaking record has convinced OSHA that EtO is carcinogenic in laboratory animals and that a significant cancer risk exists for workers exposed to EtO. The Agency's conclusion is based on information from many investigations in several species of experimental animals involving different routes of administration, as well as positive results from several human studies.

The epidemiological study conducted by Morgan and coworkers (Ex. 6–5) showed that a significant increase in

pancreatic cancer and Hodgkins disease occurred among 767 workers generally exposed to EtO levels of 50 ppm or less. Another study (Ex. 2–8) described three cases of leukemia (vs. 0.2 expected) during the period 1972–1977 among Swedish factory workers exposed to an EtO-methyl formate mixture. Two of these workers with leukemia were exposed to an estimated EtO level of approximately 20 ppm (plus or minus 10 ppm). In a third human study (Ex. 2–22) significant excesses of mortality from leukemia and mortality from stomach cancer occurred among 89 full-time workers exposed to EtO. Although each of these studies report small numbers of cancer cases and is limited by the methodological constraints that usually accompany any attempt to describe rare events in small populations exposed to hazardous substances, both Stellman (Ex. 4–59) and representatives of NIOSH (Ex. 2–10) commented that these studies should be considered as evidence that EtO may produce an excess cancer risk for exposed workers. The Agency also agrees with the opinions of Landrigan (Tr. 341) and Golberg (Tr. 520) that, although these studies do not provide definitive evidence of carcinogenicity, they are suggestive of an association between occupational exposure to EtO and cancer (leukemia) mortality.

Among the animal studies examined in the record, the BRRC study (Ex. 2–9) provided the strongest evidence that EtO is carcinogenic. Following lifetime exposure to 33 ppm or 100 ppm EtO, there was a significant increase in the incidence of mononuclear cell leukemia in female Fischer 344 rats and of peritoneal mesothelioma in male rats of the same species, and both of these effects were shown to be dose-related. In addition, there was a significant dose-related increase in the incidence of gliomas, which are characterized as rare tumors, in both male and female rats. A study performed by NIOSH (Ex. 6–6, 6–16), in Fischer 344 rats showed results similar to those of the Bushy Run study. In the NIOSH study, there were significant increases in mononuclear cell leukemia, peritoneal mesothelioma, and gliomas among rats exposed to 50 or 100 ppm. Although not as well documented as the BRRC study, other studies have demonstrated the carcinogenicity of EtO in animals exposed by injection (Ex. 2–18) or oral (Ex. 19) routes.

OSHA agrees with NCI's Ward, who testified that these studies "provide significant evidence for the carcinogenicity of ethylene oxide" (Tr. 1106).

OSHA also concludes that the findings of gliomas among exposed rats in both the Bushy Run and NIOSH studies and findings described by Ward of similarities between the Fischer 344 rat leukemia model and some human leukemias, dramatically increase the importance and relevance of these studies in assessing the carcinogenic risk to EtO-exposed employees. In addition, since significant increases in tumor incidence occurred among rats exposed to EtO at 50 ppm (in the NIOSH study) or less (in the BRRC study), OSHA is confident that EtO's carcinogenic response is manifested at levels at and below those of OSHA's current PEL of 50 ppm, thus establishing that an excess significant cancer risk exists at the 50 ppm PEL.

B. Mutagenic and Cytogenetic Effects

In the preamble to the proposed rule on EtO, OSHA presented evidence that EtO is mutagenic in both experimental animals and in humans. As stated by NIOSH in its Current Intelligence Bulletin on EtO:

> The ability of a chemical to serve as an alkylating agent and to cause mutations in a variety of biological test systems is widely accepted as an indicator that the chemical may have carcinogenic potential. Both alkylation and mutagenicity have been demonstrated for EtO. Further, effects of a chemical on basic genetic material within the cells of living mammals are relevant for assessing mutagenic and carcinogenic hazards for humans. Evidence of this nature is available for EtO (Ex. 2–10).

The mutagenicity of EtO has been observed in a wide range of biological systems, including several microbial and plant systems, Drosophila, mice and rats. The submammalian studies have been reviewed extensively elsewhere (Ex. 2–10) and serve to further demonstrate the mutagenicity of EtO. Virtually every mutagenicity test system applied to EtO has shown the chemical to be mutagenic. Considerable scientific evidence also demonstrates the ability of EtO to induce chromosomal aberrations (structural changes in chromosomes that are mutational events) and sister chromatid exchanges (SCE) (the exchange of segments between the two chromatids of a chromosome) in several mammalian species, including humans.

Experimental Studies

Embree and coworkers (Ex. 2–35) have shown that EtO causes mutations in rat germinal cells using the dominant-lethal assay. Male Long-Evans rats were exposed to a single inhalation exposure of 1,000 ppm EtO for 4 hours. Each male rat was then mated to two females each week for 10 weeks. Significant increases in post-implantation fetal deaths were observed in the EtO test group when compared with the control group.

Dominant-lethal mutations and heritable translocations (a rearrangement between chromosomes which results in reduced fertility and has been passed from one generation to the next) were induced by EtO in two experiments conducted by Generoso and colleagues (Ex. 2–36). In the first experiment, male mice were injected intraperitoneally with 150 mg/kg EtO (the maximum tolerated dose) and caged with female mice for 22 days after treatment. In the second experiment, male mice were given intraperitoneal EtO injections of either 60 or 30 mg/kg for 5 days per week for 5 weeks. Immediately after the last injection, males were each caged with 3 females for one week. In addition to observed dominant-lethal effects, a dose-related increased frequency of heritable translocations was reported in male offspring of mice exposed to EtO. These findings demonstrated that EtO is highly effective in inducing genetic damage that is transmittable to subsequent generations.

Cumming et al. (Ex. 2–37) found that unscheduled DNA synthesis (a measure of repair of DNA damage) in the germ cells increased with increasing dose after male (101 x C3H) F1 hybrid mice were exposed to 300 or 500 ppm of EtO for 8 hours per day, 5 days per week for one week. Furthermore, EtO at doses of 600 and 800 ppm was found to inhibit the repair of DNA damage, as measured by a reduction in unscheduled DNA synthesis occurring after the first 4 hours of exposure. Following several exposure periods in a work-week type of exposure regimen, the capacity of germ cells to repair DNA damage decreased. Thus, EtO was found both to induce and to inhibit DNA repair, depending on dose and exposure schedule.

A study conducted by NIOSH (Exs. 4–60; 6–6; 6–16) was designed to explore the cytogenetic effects of EtO exposure in monkeys. Groups of 12 Cynomolgus monkeys were exposed by inhalation for 7 hours per day, 5 days per week for 24 months, to 0, 50, or 100 ppm EtO. Cytogenetic and spermatogenic evaluations of the monkeys were performed after 24 months of exposure. Peripheral lymphocytes were cultured and examined for chromosomal aberrations and sister chromatid exchanges (SCE); bone marrow was examined for the presence of micronucleated erythrocytes. NIOSH reported that exposure to EtO significantly increased the frequency of chromosomal aberrations in peripheral lymphocytes of monkeys in both

exposed groups; lymphocytes from animals exposed at 50 or 100 ppm showed approximately a 3-fold or 5.6-fold increase, respectively, in abnormal cells compared to the rate of aberrations found in unexposed animals. The aberrations observed by NIOSH included triradials and quadriradials. NIOSH noted that the presence of triradial and quadriradial aberrations in lymphocytes was also observed by Abrahams among EtO-exposed workers (Ex. 2–39), and the NIOSH results lend strong support to his findings. The mean number of SCE per cell was also significantly increased in EtO-exposed monkeys. The mean number of SCE per cell was 5.7 in the unexposed group, 10.2 in the group exposed at 50 ppm, and 16.8 in the group exposed at 100 ppm. There was also an increase in the number of micronuclei in polychromatic erythrocytes from the bone marrow of EtO-exposed monkeys (5 per 1,000 cells) as compared to controls (1 to 2 per 1,000 cells). NIOSH concluded that these results support the cytogenetic toxicity of EtO. The total sperm count and the percentage of motile sperm were reduced in monkeys exposed to either 50 or 100 ppm EtO when compared with controls, indicating an adverse effect on testicular function and thus on fertility.

Yager and Benz (Ex. 22) exposed groups of four male New Zealand white rabbits to 0, 10, 50, or 250 ppm of EtO by inhalation for 6 hours per day, 5 days per week for 12 weeks. Peripheral blood samples were taken before the start of exposure, at intervals during exposure, and up to 15 weeks after the end of exposure to measure SCE rates in peripheral lymphocytes. Lymphocytes taken from rabbits exposed at 50 ppm and 250 ppm showed statistically significant increases in mean number of SCE per cell (9.47 and 13.17, respectively, after 12 weeks of exposure) over lymphocytes from unexposed controls (mean number of SCE after 12 weeks was 7.26 per cell). Fifteen weeks after exposure ceased, the mean SCE levels in rabbits exposed to 50 or 250 ppm of EtO had declined but continued to remain above their baseline SCE levels. Mean SCE levels in the rabbits exposed to EtO at 10 ppm did not increase significantly above the baseline level. Yager and Benz concluded that EtO exposure results in a dose-related SCE effect.

Studies of Occupationally Exposed Workers

Several studies have demonstrated that mutagenic effects similar to those seen in animals can occur among humans exposed to EtO. Ehrenberg and Hallstrom (Ex. 2–38) examined lymphocytes taken from the blood of seven workers who were accidentally exposed to high (otherwise unspecified) levels of EtO for about 2 hours, and who had experienced acute symptoms. Two of these workers required hospitalization due to respiratory difficulties. Eighteen months after this accidental exposure, the authors observed a greater number of chromosomal aberrations (breaks, gaps, and exchanges) in the exposed workers than in an unexposed control group of persons from the same factory (p less than 0.05).

Pero and colleagues (Ex. 6–13) examined the effects of exposure to EtO on unscheduled DNA synthesis induced by N-acetoxy-2-acetylamino fluorene (2–AAF), a measure of repair of damage to DNA, and on chromosomal aberrations in the peripheral lymphocytes of women employees in a Swedish factory that manufactured disposable medical equipment. Seventeen EtO-exposed workers and 11 matched controls working at the same plant were examined. Group A consisted of 12 packers exposed to an average of 0.5 to 1 ppm EtO throughout each working day for 8 years. Group B was composed of 5 sterilizer technicians who had been exposed for 0.8 to 3.0 years at EtO concentrations of 5 to 10 ppm for 1 hour per day. Chromosomal aberrations were scored for both breaks and gaps. Significant increases in the number of total aberrations and the number of breaks were found for Group B alone and for Groups A and B combined, as compared to controls. 2–AAF-induced unscheduled DNA repair synthesis was inhibited significantly in Group A employees. Pero and coworkers verified these findings in *in vitro* studies of EtO-induced unscheduled DNA synthesis in human lymphocytes. Based on these tests of the effects of EtO *in vivo* and *in vitro*, Pero and colleagues reported that EtO can both induce and inhibit DNA repair and suggested that inhibited repair might play a role in the development of leukemia that has been reported among EtO-exposed workers.

In another study, Pero and coworkers (Ex. 6–12) examined the effects of EtO exposure on unscheduled DNA synthesis induced by 2–AAF in peripheral lymphocytes. Blood samples were obtained from five male workers, employed as sterilizing, packing, or truck-driving personnel, who were exposed to EtO at 8-hour TWA concentrations of 0.5 to 1 ppm for 0.3 to 5 years. Control samples were obtained from 12 men employed in a nearby facility where no known mutagens were in use; controls were matched with the exposed group for age and smoking history. A significant decrease in DNA repair proficiency was observed in the EtO-exposed workers when compared to controls. These results, when taken in conjunction with other study results, imply that EtO not only can induce genetic lesions but inhibits their repair. The two studies by Pero et al. indicate that exposure to EtO at average levels as low as 0.5 ppm can cause alterations in the genetic material of human cells, including significant increases in chromosomal breaks and aberrations.

The Pero studies (Exs. 6–12, 6–13) were criticized on the basis that the workers were exposed to methyl formate as well as EtO (Ex. 71). OSHA points out, however, that EtO was not mixed with methyl formate in the *in vitro* studies reported by Pero et al. (Ex. 6–13), which demonstrated similar effects of EtO. OSHA believes it is unlikely, therefore, that methyl formate elicited the *in vivo* effects.

Garry and coworkers (Ex. 6–14) studied a group of 15 employees who worked in an EtO sterilization facility. Clinical symptoms of the upper respiratory tract and central nervous system had been reported periodically by many of these employees. Air samples taken over a period of one-half hour or more revealed a maximum EtO concentration of 36 ppm at a distance of 15 feet from the sterilizer. Concentrations of EtO greater than 1,500 ppm during the purge cycle were reported near the open drain. Measured TWA concentrations of EtO were reported to be less than 50 ppm. Four of the employees reporting symptoms a significantly increased number of sister chromatid exchanges at 3 weeks and 8 weeks after their last known exposure to EtO as compared to a group of 12 employees who worked in an adjacent operating room. Another group of 8 EtO-exposed workers reporting fewer clinical symptoms showed a significant increase in the number of SCE as late as 9 weeks after their last EtO exposure.

A company using EtO in the manufacture of health care products reported the results of cytogenetic evaluations of 75 workers with potential EtO exposure at nine facilities (Ex. 2–39). A group of 37 workers with no known EtO exposure, who were employed at one of the facilities, served as controls. Exposure data indicated that the facilities had complied with the OSHA EtO PEL of 50 ppm as an 8-hour TWA, although there were instances when short-term exposures exceeded 75 ppm, the NIOSH recommended short-term limit at that time. Routine physical

examination showed no unusual clinical findings among EtO-exposed persons. However, the number of chromosomal aberrations was significantly increased in peripheral lymphocytes from exposed workers when compared to the number in the unexposed group. Chromosomal aberrations in exposed workers included quadriradials, a rare form of aberration. The frequency of sister chromatid exchanges was also significantly increased in exposed workers when compared to the unexposed group.

Shortly after these results were reported, Johnson & Johnson initiated a study to determine whether employees potentially exposed to EtO showed more chromosome changes than employees thought to be unexposed. Johnson & Johnson submitted results from the 24-month Pilot Research Chromosome Study of workers exposed to EtO at three facilities (Ex. 4–17, Ex. 137 A, B, C). The worksites selected were chosen on the basis of potential employee exposures to EtO prior to September 1980, with one site (Plant III) representing high exposures (5–200 ppm, 8–hour TWA), another site (Plant II) representing moderate exposures (1–10 ppm, 8–hour TWA), and the third site (Plant I) representing low exposures (less than 1 ppm, 8-hour TWA). Study participants wer employed in sterilizing areas and were classified according to whether their potential exposure to EtO was high or low for their particular worksite. Controls were randomly selected from other areas of each plant and matched by age and gender with exposed workers; in addition, an outside (community) control group was selected for the study conducted at Plant III (the high exposure worksite). Peripheral blood samples were collected at the start of the study and at 6–, 12–, and 24–month intervals. Chromosome studies included assays of the frequency of sister chromatid exchanges (SCE) and chromosomal aberrations. Study participants were interviewed to obtain information on work history, medical history, demographic data, and exposure to other agents considered to be potential confounders of a chromosome effect.

Preliminary results of initial testing and 6-month follow-up (Ex. 4–17) indicated that at Plants II and III a dose-related trend was observed for increases in SCE. All use of EtO at Plant III was discontinued after the first survey. In spite of the cessation of exposure at this plant, there was no significant reduction in SCE scores by the time of the 6-month follow-up study. Dose-related increases in the frequency of complex chromosomal aberrations were also observed at this plant (III). No significant differences in SCE scores were noted between potentially exposed and control groups at Plant I (the low exposure plant). Workers at Plant I were not sampled at the 6-month period.

In August 1983, Johnson & Johnson submitted to OSHA the 24-month SCE Report of the Pilot Research Chromosome Study, which completed the analysis of SCE data through the 24–month follow-up period (Ex. 137A). The aberration data through the 6-month follow-up period were also submitted (Ex. 137C).

At Plant I, where exposures were estimated to be below 1 ppm, when the results were adjusted for smoking habits, gender, and age, SCE levels for the high-exposure group were significantly higher than those of worksite controls at the initial examination only; there were no significant differences in adjusted SCE levels between the high-exposure, low-exposure, or control groups at Plant I at any of the other survey periods, nor were there differences in the unadjusted SCE level at this worksite at any survey period.

At Plant II, where exposures were estimated to range between 1 and 10 ppm, the ajusted SCE levels for the high-exposure group were significantly higher than those of worksite controls and the low-exposure group at the initial and 12-month surveys but were not significantly different at the 6-month or 24-month surveys.

Adjusted SCE levels at Plant III for both the high-exposure and low-exposure groups were significantly higher than worksite control levels at the initial and 6-month surveys. In addition, a clear dose-response trend was evident in the findings for this worksite. Although the use of EtO was discontinued at Plant III after the initial chromosome survey, adjusted SCE levels among the high-exposure group remained significantly higher than worksite control and community control levels throughout the 24-month testing period. Community controls were tested at the 6- and 24-month follow-up periods. SCE levels for the low-exposure group remained significantly higher than those of worksite controls at the time of the 6-month survey, but not at the 12- or 24-month survey; they were significantly higher than community controls at both the 6-month and 24-month follow-up.

Johnson & Johnson (Ex. 137A) concluded that an increase in the number of SCE in human peripheral lymphocytes is associated with EtO exposure and that the occurrence of this effect is related to exposure levels. Johnson & Johnson considers the persistence of high SCE levels among employees at Plant III, where exposures were highest for the three plants studied, to be the most striking observation of its study. It also concludes from results at Plant I that environmental control of EtO can prevent SCE levels that are above baseline even among workers in "high risk" jobs such as sterilizer operators.

Results of the 6-month aberration analysis (Ex. 137C) for this study are similar to those for the initial study. However, the analysis of aberration data for the 12- and 24-month follow-up periods had not been completed by Johnson & Johnson by the close of the rulemaking record.

Johnson & Johnson also prepared a summary of a chromosome surveillance project (Ex. 137D) conducted at three other plants (plants A, B, and C) independent of the Pilot Research Chromosome Study. For this study, historical EtO exposure information was collected from 1977 until the date the first blood samples were drawn for chromosome testing in 1981. These exposure histories include data from 8-hour TWA personal monitoring samples, short-term exposure samples, and exposure data collected for each employee on the date of blood sampling. The high potential EtO exposure group at Plant A had an increased frequency of SCE when compared to controls. The low potential exposure group did not have an increased frequency of SCE. The 8-hour average exposure levels on the date of blood sampling appear to be virtually the same for the high and low exposure groups. The high exposure group employees appear to have experienced higher short-term peak exposures (median short-term peak of about 9 ppm) than did the low potential exposure group (median short-term peak of about 2 ppm), based on available data for short-term exposure levels for Plant A between 1976 and 1981.

The effect of EtO exposure on SCE levels in humans was also studied by Yager and coworkers (Ex. 4–10, 6–15). The study population consisted of 14 sterilizer operators employed in two hospitals. Short-term breathing zone EtO exposures for these workers were rigorously characterized. EtO exposure for each worker and for each task was expressed as an estimated cumulative dose for the 6-month study period, on the basis of results of breathing zone samples and estimated EtO uptake. The cumulative EtO doses of the 14 workers studied ranged from 0 to 744 mg. For 30 observations of short-term exposure, the

mean concentration of EtO was found to be 82 ppm averaged over 3.5 minutes. Three sterilizer operators with cumulative doses of 0 mg were subsequently included in the control group. Control subjects were selected from clerical and administrative staff of the hospitals and two nearby research institutions. Exposed and control subjects were matched for smoking habits. Linear regressions of SCE with dose showed a positive slope and intercept (Ex. 6–18). The mean frequency of SCE per cell was significantly higher in workers with cumulative EtO doses exceeding 100 mg (10.69 SCE per cell) than for workers with cumulative doses of less than 100 mg (7.76 SCE per cell) or for controls (7.56 SCE per cell). Moreover, the emergence of a cell population with very high frequencies of SCE was evident in the high exposure group when the frequency distributions of pooled cells from the two worker populations were compared. This observation was analogous to the cell frequency distributions seen among highly exposed groups in the rabbit study reported by Yager and Benz (Ex. 22). Yager suggested that this shift in the SCE distribution may be attributable to the effect of cumulative unrepaired lesions in the non-dividing population of long-lived circulating lymphocytes.

The mutagenic potential of EtO and the relative importance of the results of investigations concerning its mutagenic potential received numerous comments during the hearings. There was little dispute that EtO is a mutagen and that the investigations indicated that this material has a genotoxic mode of action, that is, it directly affects the DNA.

For example, Leon Golberg testified for the EOIC with regard to EtO's mutagenic effects:

> In view of the alkylating properties of ethylene oxide it is not surprising that it gives rise to gene mutations and chromosomal aberrations in very short time test systems. Genotoxic effects observed in vivo include dominant lethality and inheritable translocations (Tr. 487).

Comments centered around three related issues. These are: (1) The exposure levels and durations that are associated with EtO-induced cytogenetic effects in humans, (2) the relationship between induction of chromosomal aberrations or SCE and health impairment, and (3) the usefulness and necessity of routine cytogenetic testing for EtO-exposed workers (see Medical Surveillance discussion in the Summary & Explanation Section). Arguments pertaining to the first two issues are discussed in the following sections.

Exposure Levels Associated With EtO-Induced Human Cytogenetic Effects

Testimony and comments received on the issue of the cytogenetic dose-response relationship and the relevance of the results of these studies to the promulgation of a specific PEL focused on the human studies conducted by Yager and coworkers (Ex. 6–15) and by Johnson & Johnson (Ex. 137). After a thorough review and evaluation of this evidence, OSHA finds that these studies indicate that chromosomal aberrations and SCE are induced in workers exposed to EtO levels between 1 and 10 ppm as an 8-hour TWA.

In reviewing the Johnson & Johnson study, Marvin S. Legator, testifying for OSHA, stated:

> The study conducted by Johnson & Johnson will probably rank as one of the most well conducted investigations in this area. The protocol is excellent, confounding factors were controlled, and an expert committee was convened to consult on this investigation. . . . The significance of this well conducted study can be appreciated better when one realizes that the pronounced effect was seen with a limited population. In one of the three plants studied, eight workers were considered in the high exposure, five in the low exposure and eleven in the control. A dose-related response and persistent effect was found at a TWA of 1–10 ppm. I know of no other chemical which, in a well conducted study, a persistent effect was detected at this low a concentration (Ex. 21–2).

Relationship Between Human Cytogenetic Effects and Health Impairment

Concern over the application of mutagenic investigations and/or testing centered on the ability of the Agency to use the mutagenicity data available to determine occupational risk in terms of current or subsequent disease. Legator testified as follows:

> In the area of toxicology, some of the most serious adverse health outcomes are those induced by chemicals that cause genetic damage. Following the initial chemical exposure, the induced genetic lesion may lead to irreversible, transmissible damage. The effects on somatic (body) cells include cancer, cellular senescence, behavorial anomalies (if neural dysfunction is involved), among other conditions. The effects of genotoxic agents on germinal cells may include aspermia and oligospermia, spontaneous abortions, congenital anomalies, diseases with chromosomal anomalies, and multifactoral conditions (Ex. 21–2).

Although at the present time, quantitative predictions of the human disease that may be induced by chromosomal or mutagenic changes cannot be made, it is clear that chromosomal abnormalities indicate an adverse effect on DNA. Furthermore, as a biological monitor, chromosomal changes indicate that changes have occurred in the genetic material of the cells and hence serve as an indicator of systemic tissue exposure and response in the DNA of the cells. Evidence in the record indicates that, in humans, changes in the genetic material and alterations in its repair occur at average EtO exposure concentrations of 1 ppm or less (Exs. 4–10, 6–12, 6–13, 6–15 173–D).

Comments on the use of the results of cytogenetic studies as a basis for promulgating a specific PEL centered on OSHA's ability to determine the risk of disease associated with EtO-induced cytogenetic effects. OSHA believes that the cytogenic effects of EtO exposure are of serious concern, particularly when viewed in combination with its carcinogenic and reproductive effects. Nonetheless, the Agency has determined that at the current state of scientific knowledge, the cytogenetic data cannot be used to quantify the excess risk of disease caused by EtO exposure.

Several commenters (Exs. 11–74, 11–135, 66, 141–A, 150, 153) questioned the nature of the health impairment resulting from cytogenetic changes associated with EtO exposure. On this issue, Johnson & Johnson commented that:

> (T)here is agreement in the scientific community that (correlations between chromosome changes and human health effects) have *not* been established with regard to ethylene oxide specifically, and that in general the mechanism of cancer induction has *not* been defined (Ex. 150).

Speaking for the EOIC, Julian Preston of Oak Ridge National Laboratory testified that increased frequencies of SCE or chromosomal aberrations "have not been associated with any subsequent health effects, such that they are not quantitative predictors of adverse health effects" [Tr. 1009]. Janice Yager commented that:

> A sister chromatid exchange (SCE) is the visual manifestation of a four-stranded exchange in the DNA. The number of such exchanges in eukaryotic chromosomes has been shown to be increased upon *in vitro* or *in vivo* exposure to agents that damage DNA by forming covalent adducts or distorting the bases by intercalation or formation of dimers. Many such compounds are known mutagen—carcinogens * * *. An association between SCEs and chronic health effects such as cancer has not been established. However, the biological significance of increased exchange rates may be of importance since SCEs appear to reflect perturbations during the synthesis phase of the cell cycle, and further, increases in SCE rates occur upon exposure to many mutagen/carcinogens

which also increase response in other tests for DNA damage (Ex. 2–13].

Regarding the uncertainty associated with predicting specific health outcomes from the appearance of SCE or chromosomal aberrations, Marvin Legator testified as follows:

(E)ven though the (correlation between chromosome abnormalities and cancer in experimental animals) is extremely good we are talking about the early stage in a multi-stage process. Therefore, we don't know the final, clinical outcome. We simply haven't got that data in front of us.

What we do know is, given a chemical that causes chromosome abnormalities in any biological system—this is a prime indicator of exposure to a carcinogen * * * if we're talking about ethylene oxide * * * not only do we have the animal data, but we show that this compound is also functioning and biologically active in man. And that kind of takes away a lot of the uncertainties in extrapolation, because we have biological effects in man at the cytogenetic level * * * multiple studies with ethylene oxide, where indeed we have had effects below ten parts per million.

I can't emphasize to you strongly enough * * * how unique this is. Again, I know of almost no chemical that would cause that effect at that low level (Tr. 68)

On the basis of the evidence in the record, OSHA concludes that EtO exerts a persistent and potent cytogrenetic effect in humans as well as in experimental mammalian and non-mammalian systems. EtO has been found to interact directly with DNA, most likely by an alkylation reaction. Cytogenetic findings in humans exposed to EtO have included unscheduled DNA synthesis and deficiencies in DNA repair, sister chromatid exchanges, and chromosomal aberrations, including quadriradials, a relatively rare aberration. Moreover, the mutagenic and cytogenetic findings described above support and strengthen OSHA's conclusion that EtO is a carcinogen.

C. Reproductive Effects

Experimental Studies

Four studies have assessed the reproductive and teratogenic potential of EtO in rodents. Snellings and coworkers (Exs. 2–23, 54) exposed groups of 30 male and 30 female Fischer 344 rats to 100, 33, or 10 ppm of EtO vapor for 6 hours per day, 5 days per week, for 12 weeks prior to mating. Males and females were exposed 6 hours per day, 7 days per week during the 2-week mating period, after which the females were exposed for 6 hours a day, 7 days a week from day 0 through day 19 of gestation. Two air-exposed control groups were used. The median number of pups born per litter in the 100 ppm exposure group (4) was significantly lower ($p < 0.001$) than the median number for either control group (9 or 10). The median number of implantation sites per pregnant female in the 100 ppm exposure group (6) was significantly lower than the median of 10 or 11 for the control groups. The percentage of females that became pregnant and the percentage of males proven fertile for the 100 ppm exposure group were lower than those for the control groups, but these differences were not statistically significant. No treatment-related effects were noted among dams or their litters in the 33 or 10 ppm exposure groups.

Hackett et al. (Ex. 6–10) exposed 50 female Sprague-Dawley CD rats to 150 ppm of EtO for 7 hours per day, 5 days per week, for 3 weeks prior to mating. After the mating period, the pregnant females were exposed to the same regimen through the 16th day of gestation. Two other previously unexposed groups of pregnant rats were exposed to 150 ppm of EtO from day 7 through day 16 of gestation, or from day 1 through day 16 of gestation. There was a significant increase in fetal deaths (resorptions) in the group receiving both pregestational and gestational exposure when compared with either of the groups receiving gestational exposure alone or the control groups. Ossification of fetal skulls and sternebrae was significantly reduced among EtO-exposed rats compared with non-exposed rats.

In the third study (Ex. 55), groups of 17–22 pregnant Fischer 344 rats were exposed to 100, 33, or 10 ppm of EtO vapor for 6 hours per day on days 6 through 15 of gestation. No significant differences were found between EtO-exposed groups and control groups in the number of dead fetuses per dam or the number of resorption sites per dam. However, there was significant weight reduction among fetuses in the 100 ppm exposure group compared with controls. The percentages oflitters and of fetuses in the 100 ppm exposure group having variations in ossification of distal thoracic vertebral centra were elevated compared with controls, but the difference was not significant. No gross abnormalities were noted among fetuses in any group. The authors interpreted the variation in ossification and depressed fetal weight in the 100 ppm group to be consequences of maternal or embryonic toxicity, not teratogenic effect.

LaBorde and Kimmel (Ex. 2–24) administered 75 or 150 mg/kg intravenously to pregnant CD–1 mice at one of four periods during gestation: days 4–6, days 6–8, days 8–10, or days 10–12. Mice administered the 150 mg/kg dose showed signs of toxicity, and a significant reduction in mean fetal body weight was noted for all four treatment periods compared with controls. A significant increase in the number of malformed fetuses per litter was observed among mice treated during days 6–8 or days 10–12 of gestation. The majority of defects involved the thoracic and cervical skeleton.

Two studies are available that examined the teratogenic potential and reproductive toxicity of EtO in rabbits. Hackett and coworkers (Ex. 6–10) exposed pregnant New Zealand white rabbits to 150 ppm of EtO by inhalation for 7 hours per day from day 7 through day 19 or day 1 through day 19 of gestation. No evidence of maternal toxicity, fetal toxicity, or teratogenicity was detected in exposed rabbits.

In another study conducted by Jones-Price and coworkers (Ex. 6–9), artificially inseminated New Zealand white rabbits were administered intravenous doses of 9, 18, or 36 mg EtO/kg/day on day 6 through day 14 of gestation, or doses of 18 or 36 mg/kg/day on day 6 through day 9 of gestation. Fifteen to 22 dams per group were evaluated at sacrifice on day 30. Among groups treated on day 6 through day 9 of gestation, maternal toxicity was minimal and no evidence of fetal toxicity or teratogenicity was observed. Administration of EtO on day 6 through day 14 of gestation resulted in a dose-related decrease in maternal body weight gain and gravid uterine weight. There were significant dose-related increases in the percentage of resorptions and dead fetuses per litter, and decreases in average live litter size. No evidence of a teratogenic effect was observed at any of the doses administered.

The studies described above demonstrate that at doses sufficient to cause signs of materials toxicity, EtO is fetotoxic in rabbits, mice, and rats, and teratogenic in mice, when administered during the gestation period. At doses below those that cause maternal toxicity, EtO is fetotoxic in rats when both males and females are exposed prior to and during mating, followed by exposure of females during the gestation period (Ex. 2–23). In addition to the fetotoxic effect of EtO , OSHA belives that the study by Snellings and coworkers (Ex. 2–23) indicates an effect on the male reproductive capacity. This is supported by studies (discussed in the section on Mutagenic and Cytogenetic Effects) showing the induction of dominant-lethal effects to EtO-exposed rats (Exs. 2–35, 2–36), increased levels of unscheduled DNA synthesis in the

testes of exposed male mice (Ex. 2–37), and reduced sperm count and motility in EtO-exposed monkeys (Ex. 6–6). Furthermore, the OSHA analysis (Ex. 6–18) of the Bushy Run one generation rat reproduction study (Exs. 2–33, 54) indicated that the adverse reproductive responses could be correlated with specific EtO exposure levels.

In its "Health Assessment of Ethylene Oxide" (Ex. 47), the EOIC emphasized two important facts with regard to EtO reproductive effects: 1. Evidence from a number of experimental studies indicates that EtO does reach and penetrate into the reproductive organs (Appelgren et al., 1977; Ehrenberg et al., 1974; Cumming et al., 1981; Sega et al., 1981). 2. EtO does cause damage to the gonads including testes and sperm (Hollingsworth et al., 1956; NIOSH 1982; Lynch et al., 1983; Embree et al., 1977; Cumming and Michaud, 1979; Generoso et al., 1980; Sega et al., 1981).

Considered as a body of evidence, OSHA believes that these experimental studies strongly indicate that EtO presents a potential reproductive hazard when males or females are exposed.

Epidemiologic Studies

Comment and testimony concerning the issue of EtO-induced reproductive toxicity focused primarily on a report published by Hemminki and coworkers (Ex. 6–7), which suggests that women exposed to EtO may be at an increased risk of spontaneous abortion. Postal questionnaires were sent to supervising nurses at all general hospital (about 80) in Finland to identify female workers using EtO, glutaraldehyde, or formaldehyde to sterilize medical instruments. Six months later, questionnaires were sent to all hospital staff engaged in sterilizing activities and to an equal number of unexposed nurses (controls) chosen by supervising nurses from nurse auxiliaries in the same hospitals. The response rate was greater than 90 percent for both groups. Information collected in the questionnaire permitted the researchers to adjust for age, parity (number of live-born children), decade of reported pregnancy, coffee and alcohol consumption, and smoking habits using a linear logistic regression model. The total number of reported pregnancies among the sterilizing staff and controls was 1,443 and 1,179, respectively.

No significant difference in crude spontaneous abortion rate was detected between sterilizing staff and controls (11.3 percent versus 10.6 percent). However, when pregnancies of sterilizing staff were stratified according to employment status at time of conception, significant increases ($p <$ 0.001) in both crude and adjusted spontaneous abortion rates were observed among sterilizing staff who were exposed during pregnancy compared with sterilizing staff who were not exposed during pregnancy (15.1 percent versus 4.6 percent, adjusted rates). The controls had an intermediate adjusted spontaneous abortion rate of 10.5.

The effects of exposure to different sterilizing agents on the frequency of spontaneous abortion were analyzed. Although the number of pregnancies in exposed women was relatively small for some of the exposure categories when compared with the number of pregnancies in non-exposed women, significant increases in the spontaneous abortion rates were observed for the following categories: (1) Pregnancies among women exposed to EtO with and without other agents, (2) pregnancies among women exposed to EtO or glutaraldehyde, and (3) pregnancies among women exposed to EtO alone. (In the report, the category "ethylene oxide (with glutaraldehyde)" should read "ethylene oxide (or glutaraldehyde)". Correction explained in Ex. 6–25). No significant increases in adjusted spontaneous abortion rates were found among women exposed to glutaraldehyde (with and without other agents), formaldehyde (with and without other agents), or glutaraldehyde alone.

An examination of the trend in spontaneous abortion rates covering the period 1950–1981 revealed a significant increase in those rates for all pregnancies in the later decades. This result was interpreted by Hemminki and coworkers as being due perhaps to aging of the population or a potential bias resulting from the failure of women to recall spontaneous abortions that occurred 20–30 years ago. There appeared to be a slightly lower adjusted rate of spontaneous abortion among non-exposed sterilizer operators than among controls for each decade covered by the study. This difference was not explained by the authors, but may have been related to employment status, as many of the unexposed sterilizer operators were not employed during unexposed pregnancies, whereas many of the nurse auxiliaries (controls) were employed during pregnancies.

When the authors examined data on the pregnancies of the sterilizing staff and controls from the Finnish hospital discharge register, covering the period 1973–1979, they found a significantly higher rate of spontaneous abortion among EtO-exposed staff (22.6 percent) compared with the rate for controls (9.2 percent). The spontaneous abortion rate for non-exposed sterilizing staff was 9.9 percent. The ratio of the number of spontaneous abortions to the number of live births was also significantly higher among EtO-exposed staff (33.3 percent) compared with controls (11.8 percent). Since spontaneous abortion is known to affect the outcome of future pregnancies, data on one EtO-exposed woman and two control-group women who had had two or more spontaneous abortions were eliminated from the analysis (Ex. 6–25). After this adjustment, the spontaneous abortion rates were 17.2 percent for EtO-exposed women as compared with 8.2 percent for controls. The findings from the hospital register thus appear to corroborate the findings based on the postal questionnaire and suggest that a prior history of spontaneous abortion does not significantly affect the trend seen in the total register data set.

Exposures to EtO between 1976–1981 in Finnish hospitals were estimated to be 0.1 to 0.5 ppm TWA, with the highest recorded peak reaching 250 ppm. Exposure levels of other sterilizing agents were not reported.

The investigators had no measurements of exposure concentrations before 1976, but stated that no major changes in technology or instrumentation in these sterilizing units have taken place since 1964 when the present EtO gas mixture was introduced. However, on the basis of information obtained from supervisors of sterilizing units, they believed exposures to EtO may have been higher in the past because less information was available on EtO's harmful effects, and less caution, was taken in its use.

In response to comments on the appropriateness of the comparison group and the need for further age adjustment, Hemminki et al. performed an additional analysis of the interview data (Ex. 29), comparing only those pregnancies that began during hospital employment for both women exposed to sterilizing agents and unexposed nursing auxiliaries from the same hospitals. Data were age-adjusted by 5 year age groups. The rate of spontaneous abortion was found to be highest for pregnancies with exposure only to EtO and was significantly different (p less than 0.05) from the rate for controls working during pregnancy. In addition, Hemminki et al. found, using hospital discharge data, that the rate of spontaneous abortion for controls working in hospitals during pregnancy was not significantly different from the rate for all controls. These authors reiterated that in various tabulations, exposure to EtO, rather than to other agents, correlated with the highest rate

of spontaneous abortions. Hemminki et al. further addressed criticisms regarding potential sources of bias and concluded that none of these could explain the consistent increases in rate of spontaneous abortion with exposure to EtO.

Several concerns over possible limitations of the Hemminki study surfaced during the hearings and comment period. Much of this testimony was the result of a visit to Dr. Hemminki by representatives of the EOIC and HIMA, which was conducted to examine supplemental data (Exs. 63, 64). Concerns expressed by commenters fall generally into three categories. These include: (1) The possibility that participants in the study knew of its purpose, resulting in biased selection of cohort members and reporting of pregnancy outcomes, (2) inadequate control of confounding factors relevant to the induction of spontaneous abortion, and (3) the lack of industrial hygiene data that would relate exposure levels and durations to spontaneous abortion rates. Testimony and comments received by OSHA on these issues are summarized in the following sections.

Control of Potential Recall and Reporting Biases

Several commenters (Exs. 11–74, 11–135, 61, 67, 141–E, 141–E–2, 141–E–3, 152, 153, Tr. 622, Tr. 689) expressed the opinion that the methods used by Hemminki and coworkers could have resulted in a biased selection of study participants as well as a biased recall of pregnancy outcomes. On the recall bias issue, Susan Austin of the EOIC commented in a letter to the editor of the British Medical Journal:

> If the questionnaire stated that the study was investigating sterilization gases, this could have introduced a stimulus for differential reporting of adverse outcomes between controls and sterilizers and * * * between the sterilizers' exposed and unexposed pregnancies. The direction of the bias * * * would be consistent with the observed excess of spontaneous abortions among exposed pregnancies. Although the hospital discharge data suggest that the observed elevation in abortion rates may be real, the data shown in Table 3 (of the Hemminki study) were crude, rather than adjusted rates and were based on smaller numbers of pregnancies than encompassed by the questionnaire. (Ex. 62, Attachment II.)

This comment was reiterated by the EOIC in its written assessment of the Hemminki study (Ex. 63).

Similarly, Otto Wong and Robert Morgan of Environmental Health Associates stated in a report to the EOIC that:

> Once the woman received a questionnaire, she might be more likely to report reproductive failure if she understood the purpose of the study * * * and that she was exposed (Ex. 67).

However, two other commenters suggested in letters to Austin that the extent of any recall bias is minimal. Jennie Kline of Columbia University pointed out that, because the data from the hospital discharge register are consistent with the questionnaire data, "* * * it seems unlikely that the increased risk of abortion among pregnancies exposed to ethylene oxide compared to those unexposed is owed in any large part to differences in recall" (Ex. 61). Bernard Pasternack of New York University School of Medicine stated that:

> (After adjustment for decade of pregnancy) the time-dependent recall effect appeared to be roughly equivalent for exposed sterilizers, unexposed sterilizers, and controls * * *. A selective recall bias may have existed to some extent as many of the non-exposed sterilizers were unemployed during their first pregnancies. The degree to which employment status affected recall or awareness of miscarriages would determine the importance of this factor. (Ex. 141E–2).

In response to the criticism that bias may have been present because many nonexposed sterilizers were unemployed at the time of their first pregnancies, Hemminki conducted a new analysis of the questionnaire data, including only those pregnancies that had occurred during hospital employment (Ex. 29). Spontaneous abortion rates, adjusted by 5-year age groups, were 20.4 percent among women exposed to EtO alone, as compared with 11.3 percent among non-exposed hospital workers ($p < 0.05$).

From this analysis, Hemminki concluded, "* * * we are unaware of any such bias that could explain why exposure to ethylene oxide rather than to glutaraldehyde or formaldehyde would correlate with an increased rate of spontaneous abortions * * *" (Ex. 29).

On the issue of the potential for selection bias among supervising nurses who were requested to identify control and sterilizer cohort members, Susan Austin commented as follows:

> [Dr. Hemminki] states that the covering letter to supervising nurses specified that the control group was to be selected preferably, from one clinic, which would inhibit them from selecting women based on a knowledge of their reproductive history. (Tr. page 725, lines 12–13). The actual wording of the questionnaire does not bear this out. It states: "For the control group, we wish you to choose assistant nurses who do not work in equipment maintenance, X-ray or operating rooms. There should be the same number of assistant nurses as there are of the individuals studied. This group could include, for example, all assistant nurses who work in a certain department. We hope that you will decide in advance (without consulting with the individuals in question) which assistant nurses are chosen for the study." These instructions permit a great deal of flexibility on the part of the supervisory nurses on the actual selection method which they could use. It does *not* specify how controls *must* be selected and therefore introduces a strong possibility that selection bias may have occurred. Dr. Hemminki further asserts that this letter to the supervisory nurses "did not give any specific information to the supervising nurses of the exact idea of the study" (Tr. page 727, lines 9–13). However, the letter does in fact explain very clearly the specific purpose of the study. To quote: "The purpose of the second part of our study is to concentrate on the possible harmful effects connected with the use of ethylene-oxide, glutaraldehyde and formaldehyde. For this, we are asking for information directly from those individuals who use these substances and from their control group." Therefore, bias could have been introduced as a result of this knowledge (Ex. 141–E).

In responding to this criticism, Hemminki testified as follows:

> * * * I should like to emphasize that the hospitals in Finland are fairly large. There are hundreds of nursing staff for each supervising nurse * * * It requires very much imagination to think [that] the supervising nurses would be aware of the pregnancies of all their staff * * * These matters are not openly discussed in Finland * * *. So, on this point I would say that * * * chances for selection * * * would be very minimal (Tr. 726).

Pasternack agreed with this assessment, commenting that:

> The authors rightfully pointed out the fact that (selection bias) was not likely to be a factor. As mentioned earlier, each supervisor had an excess of 100 employees, making contacts infrequent. Besides, it is apparently a custom in Finland not to openly discuss matters pertaining to pregnancies and miscarriages at work (as per Dr. Hemminki's testimony). In addition, the exposing agent information was obtained six months prior to the questionnaire distribution (Ex. 141E–2).

Kline commented that:

> Although the introductory paragraph to the questionnaire indicates a focus on the effects of exposure to instrument caretaking gases on fertility and health of offspring, response rates were similar and high for the sterilizing workers and comparison workers. We cannot, however, exclude the possibility that the reproductive experiences of these women who declined to complete the questionnaire differed for sterilizing workers and comparison workers. The somewhat greater proportion of women who had been pregnant at least once among the sterilizing workers who responded to the questionnaire than among the comparison workers who

responded is consistent with this possibility. With the data at hand, it is unclear whether or not response rates varied with exposure status (including sterilizing agent) and reproductive experiences for women who had been pregnant at least once (Ex. 61).

OSHA agrees with the comments and testimony of Hemminki, Pasternack, and Kline. Although, because of the wording of the letters to supervising nurses and of the questionnaires, there was a potential for recall and selection biases in the Hemminki study, it is unlikely that these biases significantly affected the results. This is suggested by the results obtained by Hemminki and coworkers . from the hospital discharge register, which is relatively free of such biases, indicating that exposure to EtO is associated with an increased risk of spontaneous abortion. In addition, if significant recall and selection biases were present, one would expect that they would be reflected similarly in the adjusted spontaneous abortion rates among pregnant women exposed to glutaraldehyde or formaldelhyde. This is, in fact, contrary to the findings of Hemminki and coworkers.

Control of Factors Related to Spontaneous Abortion

Several commenters (Exs. 11–74, 11–135, 63, 64, 65, 67, 141C, 141E–2, 152, 153) expressed the opinion that there was inadequate control of confounding factors in the study by Hemminki and coworkers. Confounding factors that were discussed include age, prior reproductive history, and smoking and drinking habits. For example, the EOIC assessment of the Hemminki study reported as follows:

Although the rates reported in Tables I and II (of the Hemminki report) are adjusted for a number of variables including age, parity, year (or decade) of pregnancy, coffee drinking, smoking status and alcohol consumption, the adjusted rates for the two non-exposed groups continue to reflect considerable disparity. This could suggest that the adjustment procedure used was inadequate. The age control is of questionable usefulness given that 80 to 90 percent of all pregnancies fell within the 20 to 34 years of age group, and within this category, no further age adjustment was made. No control for employment status or history of previous spontaneous abortion was included and controls for alcohol, smoking and drinking habits related to a woman's "current" habits and not to her habits at the start of each pregnancy. These considerations suggests that disparities in the distribution of risk factors between groups may not have been completely corrected. (Another) concern is that this study focuses on "pregnancies" rather than "women" * * *. The analyses presented in the study require the assumption that the pregnancies are independent observations, which they are not (Ex. 63).

On the issue of appropriate control of the effects of age on reproductive outcome, Susan Austin added for the EOIC that:

The differential age distribution between the exposed and unexposed pregnancies of the sterilization workers is reported to have been "rather small" by Dr. Hemminki (Tr. page 767, lines 8–13). Table A–6 of the Trip Report (OSHA Ex. 64) contradicts this assertion * * *. When ethylene oxide exposed pregnancies are compared to the non-exposed sterilant workers pregnancies, the difference in maternal ages is quite marked. Sixty-four percent (64.5%) of the EtO exposed pregnancies were [among women] greater than 30 years of age compared with only nineteen percent (19%) of the non-exposed pregnancies. Such a large difference in maternal age distributions calls into question the adequacy of the method used to control [f]or age in this study (Ex. 141E).

The disparity between spontaneous abortion rates of non-exposed women and controls was also cited by the EOIC (Ex. 63) as evidence of improper control of age and other confounding factors. On this point, Kline responded as follows:

The Ethylene Oxide Industry Council critique points out that the frequency of abortions among the unexposed pregnancies of the sterilizing workers is lower than that among the pregnancies of the control group. Several possible sources for this disparity are suggested including insufficient analytic control of year of pregnancy, maternal age and parity, and differences in employment status (working/not working) during pregnancy. With regard to the conjecture that there was insufficient analytic control, the data at hand do not permit a full evaluation. I think it unlikely that differences in the distributions of pregnancies over time explain the disparity between unexposed and control pregnancies because Figure 1 (of the Hemminki study) suggests that the disparity has been relatively constant over time * * *. With respect to maternal age, in most populations the rates of spontaneous abortion between ages 21 and 34 years are fairly constant, increasing by about 25% during the interval. Thus it seems unlikely that a disparity between the unexposed pregnancies of sterilizing workers and controls is due to inadequate analytic control of maternal age. Parity was analyzed as a continuous variable, and *thus any disparities between unexposed pregnancies to sterilizers and controls that might exist have probably been controlled for adequately. We should note that these three factors undoubtedly vary together and so that even if there was inadequate control of all, the effects would be unlikely to be additive (emphasis added) (Ex. 61).*

Criticism of inadequate control for lifestyle and prior reproductive or medical history focused on the fact that information only on current health was sought on the questionnaire. As discussed by Austin, "* * * the factors smoking, drinking and coffee consumption, could not have been well controlled as they reflected the womans' [sic] habits at the time she answered the questionnaire—not at the time of her pregnancy" (Ex. 141E).

The lack of control for prior medical history was discussed by Shirley R. Andersen of H. W. Andersen Products, Inc.:

The Finnish questionnaire failed to collect crucial information concerning maternal health. Examination of the etiology of spontaneous abortions emphasizes the importance of this factor * * * maternal chronic diseases which affect the outcome of pregnancy (e.g., hypertension, diabetes, heart or renal disease), drug therapy or use of narcotics, and family history of illness * * * intercurrent illness during pregnancy (e.g., toxoplasmosis, herpes simplex or mycoplasma infections) and blood (ABO) incompatibilities. No sections of the Finnish questionnaire addressed these factors, which exert more influence than use of tobacco or alcohol, on the outcome of pregnancy (Ex. 11–135).

OSHA agrees that these factors may influence the outcome of pregnancy. However, many of the illnesses listed by Dr. Andersen are associated with late pre-natal and post-natal adverse effects such as low birth weight and neonatal morbidity and mortality.

Their influence on the rate of spontaneous abortion is not well defined. Second, the purpose of including comparison groups in the study is to control, via the design of the study, for other factors which might influence pregnancy outcome, and which could be assumed to be distributed randomly among EtO-exposed and unexposed groups of women.

A comment by Austin was typical of comments received on the issue of inadequate control for prior reproductive history:

Dr. Hemminki argued that multiple spontaneous abortions were not confounding factors in his study. (Tr. page 759, lines 107). However, it is possible that the distribution of women who had multiple spontaneous abortions could have differed sufficiently between the groups being compared to have produced artificial differences in rates. Dr. Hemminki produced data which suggested that this was not a problem with the subset of pregnancies hospitalized but no such data have been made available with respect to the much larger set of self-reported pregnancies. Since the risk of spontaneous abortion nearly doubles after a woman's first spontaneous abortion, failure to consider this problem in the analysis must be considered a great weakness of this study (Ex. 141E).

As pointed out by Kline, prior reproductive history and the issue of whether women or pregnancies are the proper unit of analysis are difficult

problems to resolve in conducting human studies like that of Hemminki and coworkers. Kline states:

As the Ethylene Oxide Industry Council critique notes, the unit of analysis was pregnancies, not women. One assumption of maximum likelihood logistic regression is that observations are independent. This assumption was violated, and it is unclear what effects, if any, this might have on the results of the analysis. Studies of spontaneous abortions pose a particularly difficult problem since not only are characteristics of the woman, such as maternal age, related to abortion risk, but also characteristics of successive pregnancies; that is, women with one spontaneous abortion are at increased risk of a subsequent abortion. There is not even a modest experience in the literature to draw on which compares analyses of pregnancies versus analyses of women (Ex. 61).

In spite of these analytical problems, many commenters agreed that the results of the Hemminki study, taken in combination with animal data that demonstrate the fetotoxic potential of EtO, suggest that occupational exposure to EtO results in an increased risk of spontaneous abortion. For example, Kline commented as follows:

In sum, I consider that the data presented by Hemminki et al. (1982) raise the possibility that working during pregnancy in a hospital job which involves exposure to ethylene oxide may increase the risk of spontaneous abortion. In spite of the several questions which we have discussed, the data show a good deal of internal consistency. Similar results were obtained from an analysis based on questionnaire data and one which was based on recent pregnancies ascertained in the hospital discharge data. The association was similar for registered nurses and for full-time instrument caretakers (data provided by Dr. Hemminki). Given that it appears that the increased risk of abortion related to work with ethylene oxide is greater than that related to work with glutaraldehyde, these data raise the possibility that the association is owed to exposure to the agent, ethylene oxide, rather than to employment during pregnancy (Ex. 61).

Similarly, Pasternack commented that:

In spite of several problems in the study design, it is possible that EtO was responsible for an excess of spontaneous abortions (especially if supported by animal studies * * *). The fact that two other sterilizing agents did not result in a statistically significant excess of spontaneous abortions further supports this finding * * * (Ex. 141E-2).

After reviewing the Hemminki report NIOSH concluded that Hemminki's findings cannot be discounted, even though the study was not as definitive as desired. (Ex. 40).

The EOIC (Ex. 47) reported an investigation by Yakubova *et al.*, who examined the effects of EtO exposure in female production workers and reported an increased incidence of gynecological disorders among those with EtO exposure. Two hundred eighty-two exposed workers (equipment operators and laboratory assistants) were compared to plant administrators (259) in the same factory and 100 other nonexposed workers from other institutions. The level of EtO exposure was said not to have exceeded 1 mg/m^3 (approximately 0.5 ppm). The increased incidence of gynecological disorders (described as diseases of the cervix and uterus) was reported to be highest among equipment workers and was attributed to exposure to higher concentrations of EtO for longer periods during a working day than was the case for the laboratory assistants. Other effects on pregnancy, such as threat of miscarriage and toxemia, were reported to have occurred in equipment operators and laboratory assistants at a higher frequency than in the nonexposed groups. Because of insufficient information on either the study design or the methods of assessing exposure or outcome, and an inadequate description of the study groups, this study is very difficult to evaluate and can only serve as suggestive supporting evidence for the findings of Hemminki et al. that EtO exerts an adverse effect on reproduction in females.

Although several commenters (Ex. 47) have characterized the reported findings on reproductive effects as attributable to a variety of other chemicals, the record evidence, especially that pertaining to the work of Hemminki and his co-investigators, suggests that reproductive disturbances do occur as a result of exposure to EtO. Moreover, these findings are supported by extensive evidence from experimental studies conducted at several institutions (Exs. 2-23, 2-36, 6-10).

The proper interpretation of reproductive animal data is a subject of debate among toxicologists. Little information is available as to the appropriateness of using animal reproduction data as a basis for the quantitative assessment of risk in humans. OSHA notes, however, that the excess adverse reproductive responses shown by the Bushy Run reproduction study are consistent with the excess in spontaneous abortions demonstrated by the Hemminki data.

Although it is possible to find methodological shortcomings in any one of these reproductive investigations, it is prudent to consider these findings as a body of evidence that provides additional support for the Agency's decision to take regulatory action on EtO. OSHA concludes that there is sufficient qualitative evidence in the rulemaking record to indicate that EtO poses a reproductive hazard for both men and women.

D. Other Health Effects

The ACGIH TLV of 50 ppm was established in 1968 on the basis of the toxic effects of EtO encountered in industry resulting from cutaneous contact with aqueous solutions of the compound (Ex. 6-3). These solutions cause primary irritation and sensitization of the skin. Chronic intoxication of humans by EtO had not been reported prior to 1968.

The ACGIH's 1966 documentation did discuss several experimental studies involving laboratory animals that showed that exposure to high concentrations of EtO vapor (204-841 ppm) caused irritation of the respiratory passages, growth depression, and injury to various organs. Repeated exposures for 6 or 7 months (at 113 or 49 ppm) in rats caused no effects except for a growth depression and a moderate increase in lung weight at 113 ppm. The 1966 documentation also noted that repeated exposure of dogs, rats, and mice at 100 ppm for six months caused no significant effects except for slight anemia in the dogs.

In the preamble to the proposal, OSHA requested additional information on all health effects resulting from exposure to ethylene oxide, including cancer. Several participants in the rulemaking submitted information and testimony about the neurotoxic and sensitization effects which can result from EtO exposure. Considerable evidence in the rulemaking record suggests that reducing the 8-hour TWA to 1 ppm will not only reduce the risk of EtO-related cancer but will also decrease the risk that workers will experience these unpleasant and potentially dangerous effects of exposure. Several of these effects have been observed in both animals and humans and will be discussed below.

Several animal species have shown the effects of peripheral neurotoxicity due to EtO exposure. The EOIC noted that:

This (effect) takes the form of a paralysis and subsequent atrophy of the muscles of the hind limbs, with an associated decrease in pain perception and reflexes, also in the hind limbs. In those studies where post-exposure observations have been sufficiently prolonged, it has been observed that there is a slow but apparently full recovery within 3 to 6 months of the cessation of exposure to EO vapor. The species in which this peripheral neurotoxic effect has been described are rat, mouse, rabbit, monkey, dog and cat (Ex. 47).

A discussion of the neurotoxic effects seen in the EtO-exposed primates used in the NIOSH inhalation study (dose groups of 50 and 100 ppm) was described in the preamble to OSHA's proposed standard as follows:

Two of the monkeys in each exposure group were sacrificed for neuropathological evaluation. The only significant finding was an increase of axonal dystrophy in the nucleolus [SIC, nucleus] gracilis of the experimental monkey as compared to the two controls and demyelination of portions of the gracile tract in one of the monkeys in each of the low and high dose groups (Ex. 6-8).

In its "Hazard Assessment", the EOIC also described the loss of reflex responses and neuromuscular function in mice exposed to EtO at 100 and 50 ppm (Ex. 47). The authors report that there were no effects at 10 ppm EtO and that histomorphological changes were not observed at any level. OSHA cannot evaluate the significance of these results because the detailed report of these findings is not available to the Agency at this time. OSHA is able to point out, however, that based on available evidence, the threshold for effects in mice, if one exists, is below 50 ppm, the level of the current OSHA PEL. Furthermore, the lack of neuromorphological changes in rodents at comparable concentrations suggests that primates may be more sensitive to neurotoxicity induced by EtO.

The EOIC further noted that (Ex. 47):

* * * The lowest concentrations of EO likely to produce clinical evidence of hind-limb paralysis lie above 200 ppm, with no-effect concentrations having been demonstrated in the range of 100 to 115 ppm. It follows that the threshold concentration for the induction of paralytic neurotoxic effects for most species is in the range 100-200 ppm. This accords with the absence of clinical signs of neurotoxicity in Fischer 344 rats exposed to EO vapor at concentrations of 10, 33 and 100 ppm for 6 hours a day, 5 days a week for up to 2 years (Snellings *et al.*, 1981). Additionally, primates exposed to 50 or 100 ppm of EO for 6 hours a day, 5 days a week for (a) total of 24 months showed no clinical evidence of neurotoxicity, * * *. However, demyelination was seen in the distal portion of the fasciculus gracilis in 1 of 2 monkeys of both the high- and low-dose EO groups, and the presence of axonal dystrophy was also noted in the nucleus gracilis (Sprinz *et al.*, 1982).

However, when the early signs of neurotoxicity are considered, the no-effect level in animals is lower than that reported for obvious neurotoxic effects such as peripheral paralysis. Mice repeatedly exposed to EtO vapor at various concentrations in the range 10-236 ppm showed a dose-related trend in their responses on several neurobehavioral measures included in the Irwin neurobehavioral screen (Ex. 47). The EOIC (Ex. 47) reported that the threshold for induction of borderline neurotoxic effects, such as abnormal gait and locomotor activity, was 48 ppm, and the no-effect level was 10 ppm.

In humans, the most frequently cited effects of acute EtO overexposure include the following reversible effects: Eye and respiratory tract irritation, lassitude, nausea, vomiting, diarrhea, vertigo, headache, loss of consciousness, convulsions, and occasionally, disturbances of behavior (Ex. 47). Many of these effects appear to be neurotoxic in origin. For example, the EOIC (Ex. 47) noted the fact that nausea and vomiting occur following percutaneous absorption as well as inhalation of EtO. It suggested that these effects may be neuropathologic in origin, because substantial relief is obtained if anti-emetics are given intravenously. Dizziness, coma and convulsions are often also ascribed to a central depressant effect because they may occur even when lung function is not compromised.

The EOIC further discussed the matter of neuropathology when it reported that:

The first credible clinical description of peripheral polyneuropathy occurring in man as a result of occupational overexposure to ethylene oxide (EO) vapor was not published until 1979 (Gross *et al.*, 1979). However, it had been appreciated since the 1930's that EO is capable of producing centrally mediated pharmacologic and behavioral effects. Now the number of published observations on exposed animals or clinical cases of overexposure to EO suffices to confirm that, under appropriate exposure conditions, inhalation of EO vapor can produce pharmacologic and toxic effects on the nervous system that present as sensorimotor central or peripheral signs and symptoms which may be accompanied by behavioral changes. (Ex. 47)

Although the effects of repeated exposure to EtO were reported in the literature as early as 1937, the first clear clinical description of peripheral neuropathy caused by such exposure was provided by Gross and his co-workers (1979), who examined four workers employed in a sterilizing facility that had a leaking sterilizing unit (Ex. 47). The EOIC reported that:

* * * There was one case of acute encephalopathy with normal nerve conduction studies, two cases having both clinical and neurophysiological evidence of peripheral neuropathy affecting the upper and lower limbs, and one asymptomatic individual who had evidence of sensorimotor polyneuropathy on electrophysiological examination. The amplitude of muscle action potentials, moderate decrease in conduction velocity, and signs of denervation were compatible with an axonal degenerative neuropathy. In the symptomatic cases there was marked subjective improvement within two weeks of terminating EO exposure, but over a period of 10 months there was improvement in conduction studies in only one of the three individuals originally found to have abnormalities. The concentrations of EO to which the workers were exposed are unknown but all intermittently smelled the vapor, indicating an exposure on such occasions to at least 700 ppm, the mean detection odor concentration (Jacobson et al., 1956).

Two recent case studies of sterilizer workers exposed to EtO have come to OSHA's attention (Finelli et al., 1983 and Kuzuhara et al., 1983) (Ex. 47). Kuzuhara et al. found axonal degeneration with changes in the myelin sheath; unmyelinated nerves were also involved in the degenerative process; and muscle tissue showed typical denervation atrophy. The morphological degeneration was accompanied by electrophysiologic changes which implied axonal neuropathy. EOIC cites the authors as commenting that:

Our experiences indicate that chronic repeated exposure to ethylene oxide can cause sensorimotor polyneuropathy of axonal type, even if each exposure is very brief. To eliminate the hazards, ethylene oxide levels should be monitored strictly, and a safety limit for peak exposure should be established. The ventilation system should efficiently reduce the ethylene oxide gas that diffuses from the sterilizer when the door is open in loading and unloading (Ex. 47).

The EOIC reported that Finelli et al. (1983) described similar peripheral nerve conduction abnormalities (Ex. 47). These authors noted that the changes detected by electromyogram as well as the signs and symptoms of neurological damage to be reversible, as NIOSH has previously noted. In commenting on the current OSHA standard, Finelli et al. (1983) stated:

As in other toxic neuropathies, individual vulnerability to EtO is suggested by the involvement of only some exposed workers. The US standard for occupational exposure to EtO is 50 ppm for an eight-hour time weighted average. However, the concentration to which humans may be exposed safely is uncertain. In addition to measuring the concentration of EtO, it is suggested that when symptomatic cases of EtO-induced polyneuropathy are identified, fellow workers should be examined clinically and electrodiagnostically to determine the incidence of asymptomatic neuropathy in that particular facility. This may help to identify susceptible persons for whom removal from exposure to EtO would be advisable.

The lowest concentrations of EtO that have been reported to produce the early symptoms of neurotoxicity in humans were observed by Garry and colleagues

(Ex. 6–14), who conducted a study of 12 exposed employees working in a hospital sterilization area. The maximum EtO concentration to which these workers were exposed was stated to be 36 ppm. The investigators reported incoordination in 2 of the 12 exposed employees, dizziness in 3, weakness in 4, nausea and difficulty of speech in 5, headaches in 6, and diarrhea and conjunctival irritation in 7. None of the persons who served as controls in this study reported any of these symptoms (Ex. 6–14). However, there is little quantitative documentation concerning the concentrations of EtO that cause these effects in humans. The EOIC (Ex. 47) concluded that, "Since sensory irritant effects are often present, and because it has been stated that EO (in these cases) could be smelled, the signs and symptoms noted above probably only occur in man at EO concentrations of several hundred ppm."

During the informal public hearing, several witnesses described neurotoxic effects caused by repeated exposure to EtO at concentrations below 50 ppm. June McMahon of the Service Employees International Union, AFL–CIO, reported that several workers in Local 715 complained of tingling sensations in their extremities, headaches, and skin lesions, although air samples showed that exposure levels were below the 50 ppm limit prescribed by Table Z–1 (Tr. 1247). One of these workers was diagnosed as having neurological problems of unknown cause (Tr. 1247).

Eric Frumin of the Amalgamated Clothing and Textile Workers Union, AFL–CIO, testified that at Johnson & Johnson Company facilities, where an internal standard of 1 ppm as an 8-hour TWA has generally been met, there are still a substantial number of EtO-exposed workers who complain about eye irritation, dizziness, nausea, extreme fatigue, disorientation, and, in some cases, rashes (Tr. 1307–1308). Although the company does not believe that EtO is the cause of these complaints, the workers are convinced that they are caused by EtO (Tr. 1307).

Peter A. Roy, a Certified Industrial Hygienist from the University of Minnesota, testified about two cases of EtO-related peripheral neuropathy in his experience, one of which also resulted in permanent lung damage (Tr. 268). Roy (Ex. 36) and others also submitted information suggesting that EtO exposure may cause occupational EtO sensitizations in susceptible individuals. He noted that in one facility there were medically verified cases of damage to the sense of smell, which was attributed to nerve damage in the nasal epithelium.

Roy also testified (Tr. 269) about several cases of sensitization personally known to him that occurred as a result of relatively constant occupational exposures of 10–15 ppm as 8-hour TWA's in areas where sterilized products were being stored. According to Roy (Tr. 270–271), "Some of the people who developed the sensitizations * * * indicate that * * * (these) sensitization(s) kept getting worse and even levels similar to the existing or proposed PEL could still elicit the (sensitization) response."

In his written testimony, Roy (Ex 36) indicated that in numerous cases:

> Sensitizations were severe enough to require the affected employees to avoid all subsequent contact with ethylkene oxide. These health effects have resulted in workers compensation claims, difficulties in finding new employment, disruption of lifestyles, and apparent cross-sensitization susceptibilities in individuals that were so sensitive that other irritant or sensitizing chemicals would also have an effect.

According to Roy (Ex. 36), EtO sensitization symptoms

> * * *Included pulmonary sensitization, similar to asthma, and the development of skin rashes and facial swelling similar to "hives." This skin reaction to airborne EtO is, I presume, a systemic reaction to EtO exposure, and is not likely a direct skin contact phenomenon [sic]. My original reports of apparent EtO sensitizations were questioned by some, but I submit that if one analyzes the chemical activity of ethylene oxide, and its ready ability to alkylate other organic chemicals, including body proteins, then an immune allergic response via the "Hapten" mechanism, similar to that of many other small highly reactive molecules, is not hard to envision for EtO. In my opinion the occupational allergic illnesses, irritations I have seen (occur) at levels below the existing PEL. (Tr. 214)

Some similar reactions resulting from exposure to EtO were summarized by the EOIC (Ex. 47):

> For humans exposed to ethylene oxide vapor (EO), sensory warning signs, such as odor, cannot be detected until high concentrations of EO occur. Continued exposure results in olfactory fatigue (Cawse *et al.*, 1980). Other sensory warning signs, including irritation of the upper respiratory system, have been reported to be undetectable in humans accidentally exposed to high concentrations of EO (Thiess, 1963).
>
> Some of the problems encountered in human exposure to EO have resulted from cutaneous contact. Not only is EO a potent skin irritant (Taylor, 1977), but it has been reported in a study with humans, under laboratory research conditions, to result in delayed hypersensitivity following dermal exposure (Sexton and Henson, 1950). However, the authors of this report stated that these types of allergic reactions have not been observed in the workplace with employees who have had frequent contact with EO over a period of many years. Other reports of human signs from acute exposure to high concentrations of EO have included observations of diarrhea, delayed nausea, and vomiting (Thiess, 1963).

On the basis of the above evidence, OSHA believes that adverse neurotoxic and sensitization effects are occurring as a result of exposure conditions permitted by OSHA's current 50-ppm EtO standard. Regarding the neurologic effects, it is likely that these effects occur from chronic exposures at EtO levels lower than 50 ppm. Although current information does not permit the no-effect exposure levels for EtO neurotoxicity and sensitization to be determined with certainty, the record as a whole clearly suggests that lowering the TWA will significantly reduce the risk that employees exposed to EtO will experience these effects.

E. Conclusions

OSHA's determination that EtO is a potential occupational carcinogen was based primarily on the positive findings of the chronic inhalation studies performed at the Bushy Run Research Center and for NIOSH. This is supported by the strongly suggestive epidemiological findings of Morgan et al. and Hogstedt et al. Many positive effects from *in vitro* mutagenic investigations establish the genotoxic mechanism of cancer induction. The work of Calleman et al. suggests that EtO may elicit this action by alkylation of DNA.

The work of Pero et al. and the data submitted by Johnson & Johnson establish that EtO exposure at relatively low levels produces effects in man related to its probable carcinogenic mechanism.

The recent report of Hemminki et al. suggests that EtO exposure may cause an increase in spontaneous abortions. The fetotoxic hazard of EtO with regard to exposure of the female is supported by positive findings in the animal studies performed by Hackett et al., Jones-Price et al., and La Borde and Kimmel. This type of effect could be induced by changes in the DNA and which are known to be produced by many alkylating agents such as EtO. OSHA feels that the adverse spermatogenic effects of EtO on the primates alone, which are consistent with EtO's effects on DNA, are suggestive of an effect on the male reproductive capacity. This conclusion is supported by the one generation study in rats conducted at the Bushy Run

Research Center. Furthermore, the establishment of the dominant lethal effect by Embree et al., heritable translocations by Generoso et al., and alteration of DNA in testes of experimental animals establish the hazard of heritable changes following exposure of the male.

In summary, findings in humans and experimental animals exposed to EtO are indicative of damage to the genetic material (DNA). These include hemoglobin alkylation, unscheduled DNA synthesis, sister chromatid exchange, chromosomal aberrations, and functional sperm abnormalities. In addition, evidence from *in vivo* studies shows that in animals and man, DNA damage may occur in the form of increased incidence of cancer, mutation in offspring, and spontaneous abortions following exposure to EtO. Other adverse effects from EtO exposure such as neurotoxicity and sensitization, and acute effects such as skin lesions, eye irritation, dizziness and nausea have also been observed.

V. Quantitative Risk Assessment

As discussed in the proposal, OSHA's approach to risk assessment is guided by recent Supreme Court interpretations of the OSH Act, namely decisions involving benzene (*Industrial Union Department, AFL–CIO* v. *American Petroleum Institute*, 448 U.S. 607 (1980)); and cotton dust (*American Textile Manufacturers Institute* v. *Donovan*, 452 U.S. 490 (1981)). The Court has ruled that OSHA may not promulgate a standard unless it has determined, based on substantial evidence in the record considered as a whole, that there is a significant risk of health impairment at existing permissible exposure levels and that issuance of a new standard is necessary to achieve a significant reduction in that risk. Although in the cotton dust case the Court rejected the use of cost-benefit analysis in setting OSHA standards, it reaffirmed its earlier holding in the benzene case that a risk assessment relating to worker health is not only appropriate, but is, in fact, required in order to identify a significant worker health risk and to determine whether a proposed standard will achieve a reduction in that risk. Although the Court did not require OSHA to perform a quantitative risk assessment in every case, the Court implied, and OSHA as a policy matter agrees, that such assessments should be put in quantitative terms to the extent possible (48 FR 17292).

OSHA has presented its views on risk assessment in detail in several proceedings (48 FR 1867, 48 FR 45956, 48 FR 51124), as well as in the rulemaking record for EtO, including the preamble to the proposed standard and the preliminary quantitative risk assessment for ethylene oxide (48 FR 17292, Ex. 6–18). A summary of OSHA's approach to quantitative risk assessment is offered below as introduction.

Several approaches have been used to estimate cancer risk from exposure to toxic agents. A standard approach uses mathematical models to describe the relationship between dose (such as airborne concentration) and response (e.g., cancer). Generally, curves are fit to the data points observed at different exposure levels and these curves are used to predict the risk that would occur at exposure levels which were not observed. The shape of these curves is varied, ranging from linear extrapolations from the observed points through the origin (zero exposure and zero risk) to curves which may deviate far from linearity at the very highest and very lowest doses. The use of a particular model or curve can be justified in part by a statistical measure of "fit" to available data points, that is, a statistical test which measures how closely a predicted dose-response curve is to the actual observed data.

In all cases it is assumed that the mathematical curves are reflective of biological processes that control the biological fate and action of the toxic compound. To date, many of these factors have not been quantitatively linked to the mathematical models. Biological factors which may play important roles in the risk assessment are: (1) Dose of the material at the sensitive tissue; (2) the sensitive tissue(s) itself; (3) the nature of the response(s); (4) rates and sites of biotransformation; (5) toxicity of metabolites; (6) chronicity of the compound (cumulative nature of the material or its actions); (7) pharmacokinetic distribution of the material (especially effects of dose on the distribution); (8) the effect of biological variables such as age, sex, species and strain of test animal; (9) and the manner and method of dosing the test animals (48 FR 45969).

It is clear that all of these factors cannot be easily incorporated into a single mathematical model. Therefore, careful selection of the data for evaluation in the model is important to the risk assessment in order to make use of as much information as possible. In cases where several data sets are available, such as the case of EtO, the results of different approaches applied to different data sets should provide a guide as to the optimal approach to risk assessment, and they should compare logically with each other.

Several different mathematical models are discussed in this preamble. Most of the models are based on theories of cancer development, such as the onehit, the multistage, and the gamma multihit models. Other models commonly used for risk assessment (such as the probit, logit, and Weibull models) have developed from tolerance curves of responses to toxic substances. These are often applied in the prediction of cancer but have also been used to predict risk for other actions of toxins. A linear model is generally used for epidemiologic data due to its biological plausibility and simplicity of use. Details on the form of these mathematical models can be found in OSHA's preliminary quantitative risk assessment (Ex. 6–18).

A number of participants in the ethylene oxide rulemaking commented on OSHA's approach to quantitative risk assessment (QRA) in general, particularly noting the need for human data on which to base a quantitative assessment of risk (Exs. 4–18, 4–22, 11–39, 11–110). However, the Court specifically noted in the benzene decision that "imposing a burden on the Agency of demonstrating a significant risk of harm will not strip it of its ability to regulate carcinogens, nor will it require the Agency to wait for deaths to occur before taking any action" (448 U.S. at 655). This holding by the Court strengthened OSHA' confidence in proceeding with the quantitative risk assessment based on animal data.

In the preamble to the proposed standard, OSHA outlined its approach to the quantitative estimation of risk from exposure to EtO, including the selection of the data base, general assumptions and models used. On the basis of its preliminary quantitative risk assessment, OSHA concluded that the best estimate of occupational risk from exposure to EtO 50 ppm was 634 to 1,093 excess cancer deaths per 10,000 exposed workers. This figure was used to support OSHA's finding that exposure to ethylene oxide represented a significant risk to workers.

Some commenters disagreed with OSHA's quantitative approach to risk assessment, specifically the reliance on results from mathematical models and experimental data in predicting human response (Exs. 4–51, 11–110). However, the comments submitted by BASF Wyandotte, a producer of EtO, expressed the views of many participants and recognized the suitability of OSHA's approach; BASF Wyandotte concluded that:

OSHA must perform formal risk assessments based on valid animal tests. The Agency must: (1) Extrapolate from the higher dose levels of response to the much lower exposure levels normally found in the workplace, and (2) extrapolate from the animal species to man. The methodology of extrapolations necessarily includes the use of mathematical models. This procedure is necessary in order for the Agency to establish a new standard which minimizes the possibility of adverse health effects from exposure to ethylene oxide based on cost-effective control measures (Ex. 4–54).

While a number of commenters expressed concern over certain aspects of the OSHA risk assessment, in general the comments noted the clear inadequacy of the 50 ppm PEL and the need to lower the PEL based on assessments of risk (Exs. 4–28, 11–68, 11–71, 11–110, 11–131, 11–133, 47).

The following discussion reviews OSHA's risk assessment as presented in the proposal, summarizes and evaluates comments submitted on that risk assessment, including alternative risk assessments, and offers OSHA's final assessment of the level of risk posed by occupational exposure to ethylene oxide.

A. Experimental Evidence Available for Risk Assessment.

The Bushy Run Research Center Carcinogenicity Study

OSHA's prelminary quantitative estimates of risk were derived from results of a two-year inhalation study on rats performed at the Bushy Run Research Center (Snellings et al., BRRC study, Bushy Run study) (Ex. 2–9). The study was selected for the quantitative assessment of risk because it provided at that time, by far, the most precise quantitative information available from any study on ethylene oxide. In the study, Fischer 344 rats were exposed to airborne concentrations of 100, 33, or 10 ppm of ethylene oxide vapor for six hours per day, five days per week, for approximately two years. Two control groups were exposed only to air under similar conditions. Initially, 120 rats per sex group were exposed, and at each six-month interval a portion of the animals was sacrificed to determine possible exposure-related effects.

The investigators employed two independent control groups in the study to gain a better assessment of variability in the unexposed animals. Results in the two control groups (for the tumors of interest) were not significantly different and the two groups were combined for purposes of the OSHA quantitative risk assessment.

In the preamble to the proposed standard, OSHA characterized the suitability of the BRRC study for risk assessment (48 FR 17293). OSHA concluded that the data were appropriate for risk assessment purposes for the following reasons:

(A) High quality of information (FDA good laboratory practices inspection);

(B) Statistical significance of observed increases in neoplasm incidence;

(C) Availability of concurrent control information;

(D) Dose-response relationships that were observed in both sexes;

(E) Well-documented specifics of the dosing regimen;

(F) Availability of information on ages of individual rats at death; and

(G) The inhalational dosage which is the major route of human exposure.

The usefulness of this study for quantifying risk was also attested to by the Ethylene Oxide Industry Council (EOIC) in its "Hazard Assessment of Ethylene Oxide":

> The results which are best able to support a quantitative assessment of human cancer risk are those of the Bushy Run study, with a preference expressed for use of the incidence data on peritoneal mesotheliomas. The leukemia data, while capable of supporting a quantitative risk assessment, offer a lower level of confidence in the results because of the higher spontaneous incidence of MCL than peritoneal mesothelioma in Fisher (sic) 344 rats (Goodman *et al.*, 1979), the possible specificity of this disease for this strain of rat, and the late-occurring nature of the disease (Ex. 47).

Several commenters raised a number of issues involving the suitability of using the results of the Bushy Run study as indicative of a carcinogenic effect of EtO, and the applicability of risk estimates derived from these data to the human situation. Several of these issues were well-delineated by the Health Industry Manufacturers Association (HIMA) in its review of the Bushy Run study (Ex. 11–74), and they include discussion of the effects of possible differences in dosage, dynamics of exposure, metabolism, pharmacokinetics and repair mechanisms between species. The questions raised concerning the use of this animal study for risk assessment purposes are not specific to ethylene oxide. These issues often present themselves in the task of extrapolating risks derived from animal data to man. The issue of the carcinogenicity of EtO has been discussed in detail in the Health Effects section of this preamble where OSHA concluded with confidence that EtO should be considered a potential human carcinogen. Moreover, in terms of the appropriateness of applying risks derived from animal data to the human situation, Crump testified that:

> * * * So, I would not certainly hold to the idea that regulation must wait until positive human data are available. I believe that animal data do provide an adequate basis for quantifying human risk (Tr. 142).

He noted that support for this comes from the fact that:

> Estimates of human risk from animal data are based upon the imperical (sic) observation that there is a quantitative relationship between chemical effects in animals and chemical effects in humans.
>
> Actually, this really forms a basis of toxicological investigations with animals. If there were no quantitative relationship between animal responses [and human responses], then the results obtained from animal data would be very limited. But there is a quantitative relationship which has been observed imperically (sic) and has been observed for carcinogenesis. (Tr. 143).

Although these issues may increase uncertainty in the final numerical risk estimates, they do not discount using animal studies for quantitative risk assessment purposes when epidemiologic data of sufficient quality are not available. Furthermore, there was little indication in the record to dispute the choice of the experimental animal data as the most appropriate data upon which to base the quantitative estimates of cancer risk from EtO exposure.

As Crump noted in his testimony (Tr. 142):

> The human studies available on Ethylene Oxide are limited in terms of size. They are also limited in terms of exposure. I believe that to be their principle (sic) limitations as far as quantitative risk assessment is concerned and quantification of risk assessment * * * I believe in the case of Ethylene Oxide, the animal data currently provides the strongest basis for doing quantitative risk assessment.

Therefore, OSHA concludes, as stated in the preamble to the proposal, that the Bushy Run study remains an appropriate data base on which to rely in making quantitative estimates of risk.

At the time of the proposal, the BRRC study reported that a statistically significant increased incidence over the control levels had been observed for two different neoplastic lesions: peritoneal mesothelioma in the male rats and mononuclear cell leukemia in the female rats. These lesions also showed significant dose-related trends (the p value for the one-sided Cochran-Armitage test was less than 0.00001 for both groups) (Ex. 34). As Crump testified, "For mesothelioma in male rats, and mononuclear cell leukemias in female rats, these tests are highly indicative of a dose-related carcinogenic effect of EtO" (Ex. 34).

The results of mathematical extrapolations based on these two tumor types formed the basis of OSHA's preliminary prediction of risk. As stated in the proposal, using the multistage model, OSHA predicted an excess lifetime risk for cancer from exposure to EtO at 50 ppm to be 634 to 1,093 per 10,000 workers, with 95% upper confidence limits on the excess risk of 1,008 to 1,524 deaths per 10,000 workers. The risk estimated at 1 ppm was approximately 12 to 23 excess deaths per 10,000, with 95% upper confidence limits of 21 to 33 excess deaths per 10,000.

As was noted in the preamble to the proposed standard, the increase in the incidence of mononuclear cell leukemia in male rats was not statistically significant at any level when a Bonferroni correction was applied to correct for multiple comparisons. Likewise, the Cochran-Armitage test for linear trend was not significant (the p value was 0.15) (Ex. 34). But, as Crump pointed out:

> * * * this lack of significance is chiefly due to a shortfall in response in the 100 ppm group. When this group is omitted from the analysis both the trend test and Fisher's exact test with the Bonferroni inequality are significant at the 0.05 level. The shortfall in the high dose group can be explained by the absence of these leukemias in the 100 ppm animals sarcificed at 18 months (10 and 33 ppm dose group animals sacrificed at 18 months were not examined for tumors). For cancers such as leukemia which can be detected for only a brief period before they are fatal, it is preferable to analyze fatal and incidental tumors separately (IARC, 1980). Such an analysis would probably detect a significant dose-related effect for mononuclear cell leukemia as suggested by the significant findings when the 100 ppm dose group is omitted.
>
> Considering these issues, in my judgement there is a dose-related increase in mononuclear cell leukemia in male rats and I have used these data as well to make risk estimates (Ex. 34).

Support for this analysis comes from several other commenters to the record. For example, the EOIC "Hazard Assessment for Ethylene Oxide" noted that "mortality-adjusted trend analysis revealed either an increased rate or an inceased incidence of MCL (mononuclear cell leukemia) in male rats ($p < 0.010$)" (Ex. 47) and employed these same data to calculate estimates of risk (Ex. 47).

OSHA has examined the impact of incorporating the male mononuclear cell leukemia data into the risk assessment. Crump presented the predictions of risk based on the male mononuclear cell leukemia data alone in Table 3 of his testimony (Ex. 34). This table shows that an excess risk of 284 deaths per 10,000 workers is predicted at 50 ppm, and 5.8 excess deaths per 10,000 are predicted at a PEL of 1 ppm. These estimates of risk are less than half the estimates of risk predicted from results at other tumor sites. However, it should be noted that the 95% upper confidence limits on these risk estimates are 717 and 14.9 excess deaths per 10,000, respectively, which fall within the range of OSHA's preliminary "best" estimates. (That is, this level of risk cannot be ruled out by the data.)

OSHA has considered the option of including the estimates of risk from the male MCL data in its overall estimates of risk. The tentative nature of the fit of all of the models to the female leukemia data was noted in the preliminary risk assessment (Ex. 6–18). The fit of the male MCL data is no better ($p=0.11$). In his testimony, Crump also noted that:

> * * * for both mononuclear cell leukemia in both males and females, the response at 100 ppm is below that suggested by the trend of the data at lower doses. This plateau effect suggests that uptake and distribution pathways for EtO may be saturated and the "effective internal dose" of EtO is less than 100 ppm. If this is the case, it would be reasonable to omit the 100 ppm data from the calculations. (Ex. 34).

OSHA refit the curves to the male mononuclear cell leukemia data excluding the responses at 100 ppm. This resulted in a much better fit to the one-hit model than when the 100 ppm data were included (p value for the chi-squared goodness-of-fit test rises from 0.11 to 0.53.) As anticipated, much higher predicted risks are given when the 100 ppm data are not included in the analysis. This approach gives an excess risk of 1,694 excess deaths per 10,000 at 50 ppm and 37 excess deaths per 10,000 at 1 ppm, with 95% upper confidence limits of 2,914 and 69 excess deaths per 10,000, respectively. This represents an almost 6-fold increase over the estimates predicted with the 100 ppm data points included in the curve-fitting, and approximately a 1.5-fold increase over the risk predicted by the female leukemia data, as reported in the proposal.

In its "Hazard Assessment of Ethylene Oxide," the EOIC also performed a quantitative evaluation of the risk posed by exposure to ethylene oxide. It based this assessment on the results of the BRRC study utilizing both the male and female mononuclear cell leukemia data and the male peritoneal mesothelioma data, as well as the mononulcear cell leukemia data from the NIOSH study, to be discussed below.

The EOIC calculated "continuous lifetime equivalent" doses based on parts per million (ppm) of ethylene oxide, rather that a body weight conversion (OSHA used the latter in its preliminary quantitative risk assessment), but it did not explain its objections to the use of a body weight conversion, nor did it offer a rationale for a preference for the ppm approach to dose. The EOIC did employ a scaling factor very similar to that used by OSHA to "normalize" exposure periods and noted that "Such a procedure is strictly a mathematical convenience to permit intercomparison of data * * *" (Ex. 47). The effect of different approaches to scaling factors for dose will be discussed below.

In making its estimates of risk, the EOIC employed a one hit model as the most appropriate mathematical dose-response function. The EOIC noted:

> Where more than one model fits the data, the basic criteria for selection and weighting results are the goodness of the fit and the reasonableness of the assumptions underlying the models in relation to the known data. * * * Numerous models have been proposed * * * However, the one-hit model provides an excellent fit to the four data sets for EO * * * Therefore, only the one-hit model will be used here initially (Ex. 47).

Based on the data described above, the EOIC predicted an excess risk of 18 to 79 deaths per 10,000 for on-the-job exposures of 1 ppm, approximately 1.5 to 3 times higher than OSHA's preliminary estimates of risk. The EOIC did not quote estimates of risk for exposure at 50 ppm.

The NIOSH Study. In addition to the BRRC study, at the time of the proposal there were preliminary results from a two-year chronic inhalation study on male rats conducted by NIOSH (Ex. 6–6). Since that time, more detailed results of the effects observed in this study have been reported (Exs. 11–146, 15, 40).

Though there were increases in the incidence of mononuclear cell leukemia in the rats, these increases were not statistically significant and the data were not employed in OSHA's preliminary quantitative risk assessment. The EOIC, however, did employ the leukemia data from the NIOSH study (using dose in ppm and a one hit model, the same methodology as it used for the BRRC data) to make predictions of risk. The estimates of risk based on the mononuclear cell leukemia data from this study produced risks comparable to those produced by the mononuclear cell leukemia data in the BRRC study that is, an approximate excess risk of 250 per 10,000 at 10 ppm.

Given the similarity with the BRRC data, the EOIC did not quote specific risks for this data set at all dose levels; however, based on the similarity of the BRRC and NIOSH data, OSHA has determined that the NIOSH MCL data will predict a risk of 35 excess deaths per 10,000 at 1 ppm.

Perhaps more important than the observation of leukemia in this study was the finding of a statistically significant increase in the incidence of peritoneal mesothelioma in the rats exposed to ethylene oxide. This finding also correlates directly with the finding of peritoneal mesothelioma in the BRRC study. As reported in NIOSH's testimony, the incidence of peritoneal mesothelioma was 3 out of 76, 9 out of 77 and 17 out of 77, for rats exposed at 0, 50 and 100 ppm, respectively (Ex. 40). (p values for Fisher's Exact test were 0.068 and 0.0007 when comparisons were made to the controls for the 50 and 100 ppm groups, respectively.) These data also showed a statistically significant linear trend (p value for linear trend test was 0.00048).

Using the same methodology as it employed for the BRRC data, OSHA fit a one-hit model to these data so that the results could be incorporated in the quantitative risk assessment. Based on these data, OSHA predicts an excess risk of 690 excess deaths per 10,000 workers from exposures at 50 ppm (95% upper confidence limit of 930 per 10,000). For exposures at 1 ppm, extrapolations based on these data show an excess risk of 14 deaths per 10,000, with a 95% upper confidence limit of 20 excess deaths per 10,000. These estimates of risk comport very closely with those predicted from the peritoneal mesothelioma data in the BRRC study and fall within the range predicted by OSHA in its preliminary quantitative risk assessment.

Primary Brain Neoplasms. In addition to the leukemia data from the NIOSH study, there was an increase in the incidence of primary brain neoplasms in the male rats. The BRRC researchers, after reexamining their data, have also reported a finding of primary brain neoplasms in their study. The incidence of this tumor in these two studies is given in Table 1. In the NIOSH study, the increase in primary brain neoplasms was not statistically significant when a Bonferroni correction was applied, but there was a statistically significant linear trend (P value 0.035). Since the increased incidence was not statistically significant, these data were not used for mathematical extrapolations when predicting risk.

For the BRRC data, there was a dose-related trend in primary brain neoplasms in both males and females; the linear trend was statistically significant when the Cochran-Armitage trend test was applied to the combined data from the rats sacrificed at 18 and 24 months and from animals dying spontaneously ($p=0.0003$ for males and $p=0.014$ for females) (Ex. 34). A statistically significant increase in gliomas were seen in the male rats exposed at 100 ppm (p equals 0.0024).

Crump combined the BRRC male and female data for risk assessment. Applying the multistage model (chi-squared goodness of fit test, $p=0.43$), the estimated lifetime excess cancer risk at 50 ppm is predicted as 185 excess cancers per 10,000 with a 95% upper confidence limit of 280 excess cancers per 10,000. At 1 ppm, the model predicts 3.7 excess cancers per 10,000, with a 95% upper confidence limit of 5.7 excess cancers per 10,000.

Sielken, a consultant to the EOIC, also performed an analysis on the brain tumors, analyzing two subsets of tumors: (1) Primary brain neoplasms, which include granular cell tumors, astrocytomas, and glial cell tumors, and (2) malignant reticuloses and glial cell tumors (which included all brain neoplasms except granular cell tumors). He fit the multistage model as well as the probit, logit, Weibull, and multihit models to these subsets of data using the mg/kg/day scale as defined in OSHA's preliminary quantitative risk assessment. Risk was quoted as additional risk (P(d)–P(O)) rather than excess risk (P(d)–P(O))/1–P(O)), but Sielken noted that in the case of brain tumors, these two measures of risk were "nearly identical" (Ex. 141–F). This seems likely due to the low spontaneous rate of brain neoplasms observed in this population. Using the multistage model, Sielken predicted estimates of risk at 1 ppm to be approximately 2 to 6 per 10,000 for all primary brain cell neoplasms in rats alive at 17 months, and approximately 1 to 5 per 10,000 for all rats. Sielken did not quote estimates of risk for exposure at 50 ppm. A comparison of these estimates with those made by Crump show that they are very similar; the estimate of 3.7 excess deaths per 10,000 made by Crump falls within the range suggested by Sielken.

The observation of primary brain tumors in these two studies has biological importance. Qualitatively, the occurrence of a tumor with low spontaneous incidence lends support to OSHA's finding that EtO is a carcinogen. As discussed in the section on Health Effects, some commenters have argued that ethylene oxide is only a promoter, not an initiator. If this were true, it would be inappropriate to use models which are linear at low doses (such as the onehit and multistage models) to make extrapolations, and applying these models to promoter data would greatly overstate the risk. OSHA concluded in the Health Effects section that there is sufficient evidence that EtO is indeed an initiating carcinogen. These findings were based on evidence of EtO's DNA alkylation and mutagenic properties, but in particular, on the observation of these very rare brain tumors. However, it should be noted that the same property that lends support to the finding of carcinogenicity (i.e., the rarity of the tumors) causes these data to yield low estimates of risk if they are used to predict human risk. Because these tumors occur so infrequently, the excess risk predicted on the basis of these data is low, approximately one-third the excess risk predicted using data from the other tumor sites.

In general, when making estimates of risk, OSHA makes no assumption of a direct correlation between the tumor sites observed in experimental animals and those expected to occur in man, although on occasion the tumor sites in several species (including humans) may coincide. (For example, there is some evidence that exposure to ethylene oxide gives rise to leukemia in both humans and rats.) The predictions of human risk made by OSHA are usually for "excess cancer," without regard to site. In other words, based upon the animal data, OSHA is not predicting that humans will contract brain cancer, leukemia, or mesothelioma, but only that humans will contract cancer. Thus, one way of incorporating the estimates of risk from the glioma data would be to include these estimates in the range of estimates over all sites, just as the mesothelioma data and leukemia data were combined in making OHSA's preliminary estimates of risk. This would change the lower limit of risk from 634 per 10,000 excess cancer deaths to 185 per 10,000. OSHA believes that it would be inappropriate to adopt the risks predicted on the basis of the brain tumor data as the lower end of the range of risk because there is some indication that OSHA's preliminary estimates of risk (634 to 1,093 per 10,000) may be, in fact, underestimates. (This is discussed further below.)

OSHA has considered other ways of incorporating the estimates of risk derived from the glioma data into estimates of the "total risk" of cancer. Crump noted in his testimony (Tr. 164) that in some sense, the estimates of risk from the glioma data should be *added* to the estimates of risk that were made from other sites. Although this is not

possible explicitly because of the possibility of double counting (the data for "total malignant tumors" did not include the gliomas), OSHA nevertheless believes that this position has important implications for the Agency's choice of a "best" estimate. In light of these data, OSHA does not feel it would be appropriate to *lower* its range of risk based on the inclusion of estimates of risk derived from the glioma data. In fact, considering these data in terms of the risk from all cancer, OSHA believes that its preliminary estimates of risk may have underestimated the total cancer risk to exposed workers.

B. Time-to-Tumor Analysis

Although most of the alternative risk assessments submitted to the record involved the use of quantal mortality data for the prediction of risk (Exs. 34, 44, 47, 141–F), Crump, OSHA's witness, and Sielken, testifying on behalf of the EOIC, both suggested a time-to-tumor analysis as an appropriate alternative approach. This approach was also recommended by the Union Carbide Corporation in its prehearing submission, which noted that:

> In view of the nature of the tumorigenic effects of ethylene oxide as learned from the Bushy Run study, i.e., that of a late-in-life enhancer of kinds of tumors to which the species under study is naturally prone, it would, in retrospect, have been more useful to conduct the animal studies with the "time-to-tumor" model, or a model to take into account the latency of the (presumed) cancers as part of the experimental design (Ex. 11–133).

Crump elaborated on the usefulness of a time-to-tumor analysis:

> When time-to-tumor data are used for risk assessment, there is a built-in method for correcting for differential mortality patterns in different dose groups, and consequently it is not necessary to resort to *ad hoc* methods such as deleting animals that die before the first tumor is discovered. Use of time-to-tumor also facilitates distinguishing between fatal tumors and incidental tumors (Ex. 34).

Further, Sielken noted that "Both (the OSHA and EOIC) quantitative hazard assessments can be strengthened by more fully including the role of time" (Ex. 53).

Crump conducted a time-to-tumor analysis of data from the BRRC study using the multistage-Weibull model (multistage in dose, Weibull in time). Based on leukemia mortality in both male and female rats, the excess risk of death from exposure at 50 ppm is predicted to be 484 to 546 excess deaths per 10,000, with 95% upper confidence limits of 866 to 1,135 excess deaths per 10,000. The estimates of risk made from the time-to-tumor analysis on the male leukemia data are approximately 1.8 times higher than the risks predicted by the analogous quantal data; the estimates of risk from the time-to-tumor analysis on the female leukemia data are approximately 2.2 times smaller than those estimated from the quantal data.

Crump also used the time-to-tumor approach to analyze the excess mortality from "all" cancers using the total number of (malignant) tumor-bearing animals provided in the BRRC data. (The primary brain tumors were not counted in this analysis.) Crump commented that "In terms of human risk, increased incidences of all malignancies are important rather than just increased numbers of cancers of a single type.* * * This is particularly true in view of the recent finding of Haseman (1982) that, in NTP studies involving rats, increases in tumors of one type are frequently associated with decreases in tumors of other types, with very little effect, if any, upon the total crop of tumors" (Ex. 34). The results of the time-to-tumor analysis of mortality due to "all malignant tumors" show an excess mortality of 637 to 727 deaths per 10,000 from exposure at 50 ppm, with 95% upper confidence limits of 1,070 to 1,600 excess deaths per 10,000. This estimate of risk is very similar to the excess risk predicted in the OSHA preliminary risk assessment.

In addition, Crump also conducted a time-to-tumor analysis on the incidence of cancer in the experimental animals for leukemia and separately for "all malignant tumors." Incidence refers to the occurrence of new tumors and does not refer to the mortality of the animals. The results of the analysis on the incidence of leukemia were 501 to 1,679 excess cancers per 10,000 from exposure to EtO at 50 ppm, with approximate 95% upper confidence limits of 1,032 to 2,233 per 10,000 respectively. The time-to-tumor analysis on the "all malignant tumors" incidence data produced an excess risk of 1,213 to 1,476 excess occurrences of cancer per 10,000 workers, with upper confidence limits of 1,941 to 2,210 excess cancers per 10,000. For three out of four analyses (males or females with leukemia or with "all malignant tumors"), the excess risk of occurrence (incidence) of cancer is substantially larger than the prediction of excess cancer mortality (approximately two to three times larger). Only the analysis of mononuclear cell leukemia in the male rats produces estimates of risk of the incidence of leukemia that are slightly smaller (546 versus 501 excess cases per 10,000) than the predicted estimates of mortality from leukemia.

Sielken took a different approach to the inclusion of time in the hazard assessment. In his pre- and posthearing submissions (Exs. 53, 141–F), he looked at several different measures of the effect of exposure to ethylene oxide on tumorigenesis: (1) The mean number of months until prescribed percentages of rats died from a particular tumor, (2) the mean number of months without a response during the entire 25-month experiment, (3) the mean number of months without a response for those rats surviving to 17 months. The overall trends seen in these different methods are similar and OSHA has only discussed the results of method (2) as a representative example. Measure (2) was chosen because of the comparability of these data and the data used by Crump in his time-to-tumor analysis.

Sielken calculated the average length of time, as a percentage of the experimental periods survived by rats in various dose groups in the BRRC study. He commented:

> * * * it seems reasonble to combine all undesirable responses and simply consider the time to death at the different dose levels. * * * These percentages include the impact of brain neoplasms as well as all other potential causes of death. * * * Of course, any effects of brain neoplasms on the time of death are a contributing factor to the time of death data (Ex. 141–F).

These percentages are given in Table 2.

TABLE 2.—AVERAGE LENGTH OF TIME, AS A PERCENTAGE OF THE EXPERIMENTAL PERIOD, SURVIVED BY RATS IN THE BRRC STUDY[1]

EtO dose, ppm	Male rats (percent)	Female rats (percent)
0	94.2	94.5
10	94.6	93.8
33	89.5	90.8
100	88.8	83.7

[1] Ex. 53, Table 1.3.

In his prehearing submission, Sielken examined the life-shortening effect of three tumors: Mononuclear cell leukemia in both male and female rats, peritoneal mesothelioma in male rats, and pituitary adenoma in both male and female rats. These tumors "were judged by the Bushy Run scientists to be 'nonincidental' " and it was noted that the pituitary adenomas were included because of their anatomical location. Sielken concluded, "The information in Table 1.2 (Ex. 53) clearly suggests that the mean time without a response is virtually the same at 0 and 10 ppm and hardly decreased even at 33 ppm." However, Sielken failed to note the decrease in the mean percentage of experimental period without response

observed in the 100 ppm groups, the experimental group in which the statistically significant increases in incidence generally occurred. Sielken also did not point to any statistical tests to determine if such decreases were or were not statistically significant. He merely stated that the decreases seemed small.

OSHA has calculated the statistical significance of the decrease in mean survival period for both male and female rats (Ex. 53, Table 1.3) and has determined that there is a statistically significant dose-related linear (downward) trend in survival times for both male and female rats (p values were 0.002 for female rats and 0.054 for male rats). After reviewing Sielken's discussion of the survival data, OSHA concludes that there is a definite dose-response relationship between exposure to ethylene oxide and survival time, that is, that exposure to EtO is associated with decreased survival in both male and female rats.

C. Equivalent Doses

Much material was submitted to the record on the subject of mathematical adjustments of dose in order to extrapolate from the animal carcinogenicity data in making risk predictions for humans. The EOIC noted that "such a procedure is strictly a mathematical convenience to permit intercomparison of data" between the exposures in experimental animals and workers (Ex. 47). As discussed in the proposal (48 FR 17293), OSHA employed a milligram per kilogram body weight per day adjustment to scale the animal doses to "equivalent human doses." These scaling factors were discussed in detail in the OSHA preliminary risk assessment (Ex. 6–18, Appendix B).[1]

A number of commenters suggested changes to these adjustment factors. Crump examined the impact of several changes in the assumptions on the OSHA estimates of risk (Ex. 34, Table 4). For example, both Crump and HIMA (Ex. 11–74, Appendix D) point out that when one averages dose over a complete lifespan rather than over the remaining livespan after first exposure (OSHA used the latter in its preliminary risk assessment), the estimates of risk computed under a linear model would be only 75% as large as those presently computed.

Crump and HIMA also raised some concerns about values that OSHA assumed were "standard" breathing rates. Crump pointed out that if different assumptions on the breathing rates of the animals had been used, the estimates of risk under a linear model would be 1.5 to 2.5 times higher. HIMA commented that OSHA had overestimated the total volume of air that a worker would be expected to breathe in a normal working day. HIMA estimated that the correct volume should be 7.2 m^3/workday, rather than the 9.3 m^3/workday, assumed by OSHA. Such a change would reduce the equivalent human dose by approximately 23%. As noted in the preliminary quantitative risk assessment, the value of 9.3 m^3/day, agrees with values from "Recommendations of the International Commission on Radiological Protection," 1977, and is a standard breathing rate employed by many regulatory agencies.

In addition, Crump examined the impact of different choices of scaling to achieve "equivalent human doses." As discussed in the proposal, OSHA relied on work by Crump and Howe (Ex. 6–17) in choosing mg/kg/day as the correct scaling procedure for ethylene oxide. As Crump reiterated in his testimony, "this work suggests that use of mg/kg/day body weight may be the most appropriate of the 4 dose measures for extrapolating from animals to humans, and that the other methods tend to overestimate human risk" (Ex. 34, p. 16). In its Hazard Assessment, the EOIC chose not to make such an adjustment based on body weight, but assumed dose in ppm to be an appropriate expression of equivalent dose. Crump had calculated that, had OSHA calculated risks on the basis of ppm in air (as the EDIC did), the estimates of risk would be less than 25% the magnitude of the risk presently predicted by OSHA. The EOIC did not elaborate on this choice of dose expression, but noted that "in establishing continuous lifetime equivalents, absorption dissemination elimination parameters between species (including man) are not taken into account" due to a lack of pertinent data (Ex. 57). After review of the record, and in light of Crump's testimony, OSHA believes that mg/kg/day is the most appropriate dose expression for assessing risks due to occupational exposure to ethylene oxide. Due to the systemic nature of the tumors used in the quantitative analysis (the tumors were not contact tumors), OSHA believes an expression of dose which in some way reflects the distribution of EtO tumors is more appropriate than expressing dose in terms of concentration at the site of contact (ppm). OSHA recognizes that much of the data on absorption and dissemination of EtO throughout the body is still lacking, but expressing the dose in mg/kg/day is a best attempt to incorporate this type of data.

Crump also calculated the effect on the estimates of risk if OSHA had used milligrams of intake per surface area per day, an expression of dose used routinely by the Environmental Protection Agency, instead of milligrams per kilogram of body weight per day. He calculated that this expression of dose would increase the estimates of risk approximately 5- to 6-fold. There was no other discussion of this expression of dose in the record, and as Crump noted above, dose measures other than mg/kg/day tend to overstate human risk. Hence, OSHA has not considered it appropriate to change its risk assessment in terms of dose measure and has calculated risk on the basis of milligram per kilogram of body weight per day.

In addition to using dose in ppm, the EOIC did mathematically adjust for differences in lifetimes and dosing regimens between the two animal studies and humans, adjusting for dose over a complete lifespan (72 years) rather than lifespan after first exposure (54 years, as was done by OSHA). In his testimony, Crump estimated that adjusting for complete lifespan would reduce estimates of risk by approximately 25%, when risk is computed under a linear model.

Another issue raised by several commenters was the use of 45 years of exposure as the basis upon which to make estimates of risk. HIMA (Ex. 11–74) expressed the views in many of the submissions:

> * * * OSHA's standard use of a 45-year exposure period is felt to be overly conservative; job changes occur, on the average, much more frequently than twice per lifetime and one should be willing to accept a 20-year period as a maximum time in any one position. This would lead to a 2.2-fold (20/74 vs. 45/74) reduction in risk.

HIMA has based its conclusion on the premise that by reducing the dose to which an individual is exposed (by decreasing the length of time he is exposed), one will lower the risk to that individual in a proportionate manner. While this may be the case for individual risks, it is not true when predicting population risks, as is pointed out by AFSCME (Ex. 44). In its prehearing submission, AFSCME noted that when there is a high turnover rate among workers in a particular industry (as there is in the health care industry),

[1] OSHA assumed a typical working lifetime of 8 hours per day, 5 days per week, 46 weeks per year, for 45 years out of a working lifespan of 54 years (assumes that a person begins work at age 20, retires at age 65, and lives 74 years).

an estimate of risk using, as OSHA did, a cumulative dose model may produce *lower* estimates of risk "than the estimate derived from evaluating successive independent periods of exposure to EtO" (Ex. 44). AFSCME noted that this approach may, in fact, be less protective in terms of overall health impact on a population of workers.

OSHA has recognized when discussing the disadvantages of worker rotation in earlier rulemakings that exposures of shorter duration may not necessarily have a lower total population risk than the risk produced by exposing a single population for the entire 45 years (49 FR 14125). Although HIMA notes that 20 years may be the maximum time spent in any one job position, a shorter job tenure implies that the population at risk will be more than doubled. The resulting risk experienced by the exposed population may consequently be the same, or even greater.

The submission by AFSCME offered an alternate interpretation of this problem. AFSCME presented the formulation by Day and Brown (1980), which is an extension of the Armitage-Doll multistage model of carcinogenesis. AFSCME pointed out that:

> This model assumes that there are one or more separate and distinct stages in the transformation of a normal cell into an observable tumor. Eariler stages involve permanent alteration in the genetic material. Later stages involve the replication of the altered cell into a detectable mass. Day-Brown provides a mathematical model for estimating excess risk of cancer to exposed human populations, taking into account the stage at which the substance acts, the age at which exposure starts and the duration of exposure.

AFSCME noted that because EtO acts directly on the DNA, at least with respect to the animal data, it appears to be an early stage carcinogen (Ex. 44). Consequently, under the formulation by Day and Brown (1980),

> Employee turnover, which leads to repeated exposures to different early stage carcinogens such as EtO may have a very important effect on the risk assessment. * * * Individual workers are unlikely to work for a full working lifetime of 45 years as sterilizer operators. In fact, workers may experience a period of exposure to EtO followed by subsequent periods of employment involving exposure to other early stage carcinogens. Such an employment profile would serve to increase that worker's lifetime probability of developing leukemia in excess of a profile involving no employee turnover (Ex. 44).

Thus, while HIMA may disagree with OSHA's choice of 45 years as a "working lifetime," OSHA feels confident that the level of risk assigned to a population of workers who are assumed to experience 45 years of exposure is reasonable, and may well represent an underestimate of the risk experienced by such a population if employee turnover rates are high.

Another type of mathematical adjustment to the estimates of risk was suggested by the American Federation of State, County and Municipal Employees (AFSCME) (Ex. 44). In its review of the OSHA preliminary risk assessment, AFSCME commented that the study was "flawed by its failure to take fully into account the difficulty in translating risk estimates obtained from experiments using genetically uniform laboratory animals to genetically varied human populations." AFSCME contended that test results from genetically uniform animals will yield "an underestimation of the human dose response curve at low exposure levels due to the relatively steeper slope of the test animal dose response curve" (Ex. 44).

AFSCME suggested that a safety factor of from 10 to 100 should be applied to such estimates from animal data to "generate prudent human risk" (Ex. 44). Employing such a safety factor would bring the estimates of risk from the animal data into approximate agreement with those that AFSCME computed from the epidemiological studies, as discussed below.

D. Epidemiologic Evidence Available for Risk Assessment

OSHA's preliminary determination was that the BRRC data "provided the most appropriate data on which to base the risk assessment" (48 FR 17294). At the time, it was felt that the epidemiologic evidence of risk to workers exposed to EtO was not strong enough to support a quantitative determination of risk. AFSCME expressed concern about this, however, when it noted that: "OSHA by apparently relying completely on laboratory data (i.e. experimental animals) to estimate the risk of developing cancer from lifetime exposure to EtO has seriously underestimated the total number of excess cancers which can be anticipated from various levels of workplace exposure to EtO" (Ex. 44). Crump noted that "* * * these (epidemiologic) studies do contain some useful information to aid in quantifying risk" (Ex. 34). Upon review of the record, OSHA has determined that risk assessments based on the epidemiologic data, the Hogstedt studies in particular, may be useful in the determination of the level of risk which may be experienced by workers exposed to EtO.

Crump calculated risk based upon the hogstedt et al. study (Hogstedt I, Ex. 2–8) of a population of Swedish workers exposed to EtO in the sterilization of hospital equipment from 1968 to 1977 (approximately 10 years). Three deaths from leukemia were observed among 230 workers. Based on information in the study, Crump assumed that average exposures in the population were 20 ppm, and that the minimal latency for environmentally induced leukemia was three to four years, suggesting an "effective" exposure duration of 6.5 years (10–3.5).

Using a linear model to describe the relationship between relative risk for leukemia and exposure, Crump predicted that exposure to EtO at 50 ppm would lead to a lifetime probability of leukemia mortality of 0.300 (3,000 per 10,000), with an 80% confidence limit of 0.125 to 0.50 (1,250 to 5,000 per 10,000) (Ex. 34). Recognizing the uncertainty in these estimates, Dr. Crump nonetheless concluded that "It does not appear that the Hogstedt et al. study suggests that the extimates from the animal data are too large" (Ex. 34).

As discussed in the proposal, the Environmental Protection Agency-Carcinogen Assessment Group (EPA–CAG) performed a quantitative assessment of risk based on the same report of leukemia in 3 out of 230 workers (Hogstedt I, Ex. 2–8). Based on an occupational exposure of nine years, CAG predicted a lifetime probability of dying from leukemia from breathing 1 mg/m^3 (0.56 ppm) of EtO of 1.2 deaths per 10,000. In the preamble to the proposed standard, OSHA noted CAG's discussion of various uncertainties with estimates derived from the Hogstedt et al. study (48 FR 17294).

AFSCME (Ex. 44) commented that the CAG analysis "assumed continuous lifetime exposure to EtO," and thus it submitted an alternate analysis to correct "for EPA's clear overestimation of the risk of occupational exposure to EtO." First, AFSCME adjusted the exposure level reported in the Hogstedt study by a factor of 9/45 to account for the relatively short period of follow-up in the study and to obtain an "equivalent working daily dose." Using this method of adjustment, AFSCME predicted an excess lifetime risk of leukemia at 1 ppm of 0.033 (330 per 10,000).

AFSCME also submitted a risk assessment based on the apparent genotoxic nature of EtO and the methodology of Day and Brown (1980) discussed earlier.

> * * * Their (the Day and Brown) model predicts that 58% of the excess risk resulting

from exposure to an early state (sic, stage) substance like EtO will develop from an exposure duration of 10 years. (Ex. 44).

Using this formulation, and scaling for an exposure of nine years, AFSCME suggested that the 20 ppm exposure be adjusted to accommodate the fact that 53% of the relative risk expected in a working lifetime was expressed in nine years. Using this method, AFSCME predicted a lifetime probability of leukemia as 0.012 (120 per 10,000) at a 1 ppm exposure. Similarly, if it is assumed that not all of the members of the Hogstedt study cohort worked for a full nine years, but rather an average of 5 years, then the effective dose would be even lower, and the excess lifetime risk of leukemia at 1 ppm is predicted to be 0.019, or 190 excess deaths per 10,000.

AFSCME noted that "the EPA model, by assuming purely cumulative equivalence of dose and time, appears to have underestimated the effective EtO dose and thus overestimated the lifetime EtO risk" (Ex. 44). In addition, AFSCME pointed out that employee turnover "can have a significant impact on the overall risk assessment" in light of the Day and Brown formulation of risk.

E. Risk Assessment by Rad-equivalence

In the proposal, OSHA discussed another approach to risk assessment introduced by Calleman and colleagues (Ex. 6–19) wherein they compare the degree of alkylation of histidine in the hemoglobin in EtO-exposed workers and workers exposed to ionizing radiation. The authors calculated the "red-equivalence" for certain alkylating agents, that is, the number of rads of acute gamma radiation that gives the same effect as a unit dose of the chemical. Using this approach, and based on EtO exposure profiles, Calleman et al. estimated that exposure to 1 ppm per hour of ethylene oxide resulted in a risk of 10 mrad-equivalents of effects in a genetic mechanism.

Thus, in industrial work environments with an average exposure level in the range of 5 to 10 ppm of EtO, Calleman et al., estimated that the midpoint of the range would correspond to approximately 120 rad-equivalencel per hear. On this basis they predicted that a group of 100 workers exposed at the 5 to 10 ppm level for 10 years could expect 3.6 cases of leukemia, one of which would be expected to appear before the end of the 10 year period (48 17294).

There were mixed reviews of this approach to risk assessment. Commenters such as HIMA (Ex. 11–74, Appendix D) pointed out that "* * * there are simply too many differences between the mechanisms of mutation induction by radiation compared to that by chemicals" and that this method "assumes that cancer in man is initiated by forward mutations in somatic cells," an assumption HIMA felt oversimplified the mechanism of cancer initiation.

At this time OSHA is unable to determine the ultimate advantage or disadvantage of this approach to risk assessment. In OSHA's view, calculation of rad-equivalence does not yet represent a generally accepted method for quantifying risks. Moreover, in light of the quality of the bioassay data and their suitability for making quantitative estimates of risk, OSHA is confident that the methodology that was used in performing its quantitative risk assessment, as applied to the available experimental data, represents the best available means of quantifying the risk of EtO exposure.

F. Conclusions

In this preamble OSHA has attempted to address the major issues relating to risk assessment which were presented in the comments and testimony of the ethylene oxide rulemaking. The range of all estimates submitted to the record is very wide (16-fold), from a low estimate of 185 excess deaths per 10,000, to 3,000 excess deaths per 10,000. This range covers both the experimental and the epidemiology data, all tumor types, all models, and all endpoints of mortality as well as incidence.

OSHA has examined the individual estimates of risk offered by participants in the rulemaking. OSHA's preliminary estimates of the risk from exposure to EtO at 50 ppm ranged from 634 to 1,093 excess deaths per 10,000, based only on the mortality from peritoneal mesothelioma and mononuclear cell leukemia observed in the Bushy Run study. Since that time, the observation of primary brain neoplasms in the rats of the Bushy Run Study, as well as the observation of tumors in the subjects of the NIOSH study has broadened the data base upon which to rely in making estimates of risk. Several participants in the rulemaking have made predictions of risk from these data sets, as well.

In summary, using quantal models, Crump estimated a risk of from 185 to 1,093 excess deaths per 10,000 workers from exposure to 50 ppm, and from 284 to 1,093 excess deaths per 10,000 when the brain tumor data are not included as the basis for independent estimates of risk. Using time-to-tumor models, his predictions of risk at 50 ppm range from 484 to 727 excess deaths per 10,000 based on mortality data, and 501 to 1,679 excess cases per 10,000, based on incidence data. In addition, Crump made estimates of risk based on the epidemiology data and predicted that exposure to EtO at 50 ppm may result in 3,000 excess deaths per 10,000 workers. Crump noted that there was a wide band of uncertainty around this estimate and that the estimate of risk from these data may be as low as 1,250 excess deaths per 10,000 or as high as 5,000 per 10,000.

The other participants in the rulemaking did not present their estimates of risk in a form which made them easily comparable to the preliminary estimates of risk made by OSHA. Many of them did not estimate the risk that may be posed by exposure to the current PEL of 50 ppm, the level at which OSHA must make a threshold finding of significant risk. However, almost all participants made predictions of the risk from exposure to 1 ppm, the proposed 8-hour TWA.

OSHA's preliminary estimates of risk at 1 ppm ranged from 12 to 23 excess deaths per 10,000. Crump's predictions of risk ranged from 3.7 to 23 per 10,000, including estimates made from the primary brain tumors. The EOIC made predictions of risk based on both the Bushy Run study and the NIOSH data and calculated an excess risk of 18 to 79 deaths per 10,000 workers from exposure to EtO at 1 ppm. Sielken calculated estimates of risk based only on the gliomas and predicted an excess risk of approximately 1 to 6 per 10,000 at 1 ppm.

HIMA's estimates of risk, based only on 20-year exposures, predicted a risk of 1.5 excess deaths per 10,000 at 1 ppm. AFSCME presented estimates of risk using several different approaches to risk assessment, employing both the epidemiologic and experimental data. Based on the epidemiologic leukemia data, AFSCME predicted estimates of risk of approximately 120 to 330 per 10,000 as the lifetime probability of developing leukemia from exposure to EtO at 1 ppm. Based on the experimental data, AFSCME has predicted a risk of 10 per 10,000 for exposures in the range of 0.05 to 0.1 ppm (10 times lower than OSHA's preliminary estimates of risk). After reviewing the record as a whole, and the many estimates of risk offered by participants in the rulemaking, OSHA has concluded that its original estimates of risk, as presented in the proposal, still validly project the risks from exposure to ethylene oxide over a working lifetime. That is, OSHA's best estimate of risk is approximately 634 to 1,093 excess deaths per 10,000 workers exposed to EtO at 50 ppm, and the risk at 1 ppm is approximately 12 to 23 excess deaths per 10,000 exposed

workers. The Agency's confidence in these estimates was greatly increased when predictions made from the data in the NIOSH study were found to agree closely with these estimates of risk. Uncertainties in these estimates as well as estimates of risk derived from the human data indicate that the risk may be approximately five times larger.

Taken as a whole, OSHA believes that the assumptions made in the Agency's preliminary quantitative risk assessment are reasonable and appropriate. Crump concluded that overall "assumptions made by OSHA produce risks which fall near the mid-range of those produced by other plausible assumptions; that is, other reasonable assumptions could produce risk estimates which fall within an order of magnitude in either direction of those estimated by OSHA" (Ex. 34).

Crump's evaluation is borne out by a comparison of the various risk estimates submitted to the record. The estimates proffered by other participants in the rulemaking did not differ substantially from those given by OSHA in the preamble to the proposal. The EOIC noted that:

> It is apparent in these comparisons that the estimates of excess risk are essentially of the same magnitude or differ by up to circa three-fold (as those produced by OSHA). * * * In view of the uncertainties outlined elsewhere in this chapter regarding translation of observed animal effects to calculation of risks to man, in addition to the lack of information regarding comparative pharmacokinetics, it is surprising that the results of these different approaches are as similar as they are (Ex. 47).

In determining the appropriateness of its risk assessment for EtO, OSHA considered the relative merits of making predictions of risk from epidemiologic data versus chronic inhalation bioassays in rodents. The human data offer the advantage that there is no need to extrapolate from animals to humans, and thus estimates of risk derived from these data may be more appropriately applied to workers. Likewise, exposure conditions experienced by the study cohorts (problems of mixed exposure, intermittent exposures, etc.) may more accurately represent the industrial scenario under which risk should be assessed. These are important advantages. On the other hand, the animal bioassays allow exact determination of administered dose and careful control of extraneous environmental factors which may influence carcinogenicity. These properties enhance the ability to tie response directly to dose in a causal manner.

In the case of ethylene oxide, it should be noted that the epidemiological studies are very small (three deaths in one, two deaths in another) and that small sample size leads to a great deal of statistical uncertainty in the estimates of risk. This was demonstrated by Crump when he pointed out that the 80% confidence interval around the estimate of risk for the Hogstedt et al. study was 125 to 500 excess deaths per 10,000 (a four-fold range) (Ex. 34). In addition, there were other methodological problems with the epidemiologic studies that further increase the uncertainty. However, upon consideration of the predictions of risk from the epidemiologic studies, it can be stated with reasonable assurance that the estimates of risk derived from the animal data do not overstate the risk from lifetime exposure to ethylene oxide, and, in fact, may understate the risk.

In choosing its best estimate of risk, OSHA considered both the risks derived from quantal data and the risks computed from time-to-tumor models. In addition, OSHA examined the estimates of risk from site-specific data versus data on total numbers of tumor-bearing animals. In general, the ranges of risk computed from these data overlapped.

The inclusion of the glioma data in the data for the risk assessment had little quantitative impact on the overall estimates of risk. The estimates of risk derived from these data are lower (by approximately 3-fold) than the estimates of risk derived from the other sites or total tumor-bearing animals. (The tabulations based on "all malignant tumors" did not include the mortality caused by the gliomas, and thus, these tumors did not contribute to these overall estimates of risk.) Given the rarity of this type of tumor, the glioma risk should be added to the risks from other causes, though this could not be done directly because the data on other tumors in animals with gliomas were not available. OSHA believes that using the estimates of risk derived from the glioma data as the lower end of the range of risk would greatly underestimate the total expected cancer risk from exposure to ethylene oxide.

There were participants in the rulemaking who felt that OSHA had overstated the risk. For example, HIMA (Ex. 11–74) concluded that once the "necessary biological and workplace corrections to yield a more correct estimate of the risk involved" were incorporated, the prediction of risk at 1 ppm would be reduced approximately 8-fold, from 12 per 10,000 (1 ppm for 45 years of exposure) to 1.5 per 10,000 (1 ppm for 20 years of exposure). HIMA's objections to this conclusion were discussed in detail earlier. Given the other submissions to the record, and the weight of evidence concerning the preliminary estimates, OSHA cannot agree with this characterization. Most indications lead to the conclusion that the risk is not overstated. Although OSHA does not believe HIMA's approach to be valid for these purposes, it should be noted that even the lower level of risk proposed by HIMA would still constitute a "significant" risk, as discussed in the following section.

The importance of these risk estimates, and their implications for justifying the permanent standard will be discussed in the section on significance of risk.

VI. Significance of Risk

OSHA's overall analytical approach to making a determination that workplace exposure to hazardous chemicals presents a significant risk of material health impairment takes into consideration a number of factors that are consistent with recent court interpretations of the OSH Act and rational, objective policy formulation. As prescribed by Section 6(b)(5) of the OSH Act, OSHA examines the body of "best available evidence" on the toxic effects of hazardous chemicals to determine the nature and extent of possible health consequences resulting from workplace exposure to the substance under consideration. Quantitative risk assessments are performed where possible and considered with other relevant information to determine whether the substance to be regulated poses a significant risk to workers at the current permissible exposure level. OSHA considers whether reduction of the permissible exposure level for the substance will substantially reduce the risk.

OSHA has reviewed the toxicologic and epidemiologic literature and the record evidence on EtO described in the Health Effects section of this preamble. The record, as summarized herein, clearly shows that EtO exposure is associated with a wide range of health effects; those effects include cancer, possibly of the blood as well as other organs; spontaneous abortions among exposed pregnant women; other reproductive effects among males and females; mutagenic and cytogenetic effects; neurotoxic effects; and sensitization reactions.

Of all the toxicologic evidence presented in the record, the evidence showing that EtO is carcinogenic is the most impressive. Three epidemiological

studies (Exs. 2–8, 2–22, 6–5) provide supportive evidence that EtO is carcinogenic in humans; although the groups of workers studied were small, two of these studies (Exs. 2–8, 2–22) described significant increases in deaths from leukemia among EtO-exposed workers. One described significant increases in deaths from stomach cancer (Ex. 6–5), another showed significant increases in pancreatic cancer and Hodgkin's disease.

In addition, a number of experimental studies provide evidence that EtO is carcinogenic. The Bushy Run study (Ex. 2–9) revealed both statistically significant and dose-related increases in peritoneal mesothelioma in male rats and mononuclear cell leukemia in female rats exposed to EtO by inhalation. In addition, an excess incidence of gliomas, a rare tumor in the Fischer 344 rat was detected. Although criticisms of this study were raised on specific methodological points, all interested rulemaking participants agreed that the study was conducted in accordance with good laboratory practices was well-suited for use as the basis for quantitative assessment of cancer risk related to EtO exposure. Because of these considerations and because the mode of exposure was by inhalation of EtO at concentrations both above and below the current PEL of 50 ppm, OSHA chose the Bushy Run bioassay as the basis for its quantitative risk assessment, as discussed in the previous section. The results of the Bushy Run study were supported by positive findings of EtO-induced cancer in four other bioassays (Exs. 2–18, 2–19, 6–16, 15, 19); furthermore NIOSH (Ex. 15), reported an increased incidence of gliomas among EtO-treated rats, further strengthening the findings of the Bushy Run study.

The first element established in the Supreme Court's Benzene decision (*IUD* v. *APA* 448 U.S.) for determining significant risk, that of demonstrating that exposure at the current PEL constitutes a significant risk of material health impairment, is clearly and definitively established by the rulemaking record for EtO. Based upon the quantitative risk assessment, OSHA has determined that the best estimate of excess risk of cancer at 50 ppm EtO (the current PEL) is between 634 and 1,093 cancer-related deaths per 10,000 employees. In making a determination that this risk is significant, OSHA relies, in part, upon the Supreme Court's indication of when a reasonable person might consider a risk significant and take steps to decrease that risk. The Court stated:

> It is the Agency's responsibility to determine in the first instance what it considers to be a "significant" risk. Some risks are plainly acceptable and others are plainly unacceptable. If, for example, the odds are one in a billion that a person will die from cancer by taking a drink of chlorinated water, the risk clearly could not be considered significant. On the other hand, if the odds are one in a thousand that regular inhalation of gasoline vapors that are 2 percent benzene will be fatal, a reasonable person might well consider the risk significant and take the appropriate steps to decrease or eliminate it. (*IUD* v. *API* 448 U.S. at 655).

The estimated cancer mortality attributed to EtO exposure at the current PEL must be considered significant using virtually any reasonable basis for such a determination.

It is also evident that the estimates of cancer risk for EtO at the current 50 ppm exposure limit are significant when compared to risk estimates judged significant by OSHA for other hazardous substances in previous rulemakings. For example, the risks from EtO exposure at the current PEL are a higher than those for coke oven workers (10 cancer cases per 1,000 workers) which OSHA determined were sufficient to justify lowering the coke oven emissions standard (41 FR 46755). The risk from EtO exposure are near those from arsenic exposure at the former PEL (148–425 cases per thousand, as reported in the supplemental statement of reasons for the final rule for occupational exposure to arsenic (43 FR 19584)). The excess risk of cancer from EtO exposure also approaches the level of risk of byssinosis (130 cases per thousand) resulting from exposure to cotton dust at the former PEL.

Further insight into the significance of the magnitude of the risk can be gained by reviewing occupational accident fatality statistics. Such an analysis was performed previously by OSHA for the arsenic standard (48 FR 1864–1903).

Accident fatality rates are not directly comparable to the estimated excess cancer deaths resulting from EtO exposure. Fatality statistics represent deaths from accidents reported by the employers. They are calculated on an annual basis, and reflect accidents that have occurred due to all causes combined. To increase the comparability, annual BLS fatality accident rates were adjusted to be equivalent to a 45 years working lifetime. The reported annual accident fatality rates are lower than the estimated lifetime fatality rates given below. If OSHA calculated the excess cancer risk associated with a single year exposure to EtO, the excess cancer risk would also be lower than the 45 year lifetime risk. Smaller numbers would result for all statistics if a shorter time period, such as one month, is used as the basis for the comparison. A common time basis using a lifetime exposure associated with the comparison appears to be a logical approach. (In addition, see the discussion below regarding use of a 20 year working lifetime).

OSHA believes that the accident fatality statistics gives a general view of the conditions in the work environment that can place in perspective, to some extent, the types of situations that are considered very risky, and some that are not. As such, it can be seen that the cancer risks associated with EtO exposure are significant. EtO risks at 50 ppm are higher than accident fatality risks from all types of accidents combined, in most industries. Typical lifetime fatality risks for all manufacturing was 27 per 10,000 and for service employment was 16 per 10,000. Typical fatality risks in electrical equipment industries was 4.8 per 10,000 and 0.7 per 10,000 in retail clothing (48 FR 1902).

Although OSHA ultimately relied upon the multistage and one-hit model to determine risk from exposure to EtO at the current and proposed permissible exposure limits, the Agency also examined the results from other mathematical models. At the current exposure limits, maximum likelihood estimates based on the other models varied between 63 to 173 cancer cases per 1,000 workers. The Agency points out that with regard to the estimates of risk based on the finding of leukemia in female rats, use of these models gave higher maximum likelihood estimates of risk than did use of the one-hit model. Results of risk estimation based on these models support OSHA's determination that significant risks exist from exposure to EtO at the current PEL.

In accordance with the second element of the Supreme Court's Benzene decision on determination of significant risk, OSHA has determined that lowering the PEL for EtO from 50 ppm to 1 ppm is reasonably necessary to reduce the cancer risk for EtO exposed workers. OSHA's risk assessment indicates that the reduction in risk resulting from lowering the 8-hour TWA to 1 ppm will be dramatic. The best estimate, as determined by the risk assessment, is that the risk at 1 ppm will be between 12 and 23 cases per 10,000. The upper confidence limits for this assessment are 21 to 33 deaths per 10,000 workers.

In developing estimates of risk for occupational exposure to EtO, OSHA had the benefit of numerous

independent risk assessments that were submitted to the record, in addition to its own assessment. Although the estimates of the risk varied from one assessment to another, all of the assessments indicated that the excess cancer risk from EtO exposure at 1 ppm over a working lifetime are significant. Based upon the discussion referred to above, OSHA has determined that significant risk is *not* eliminated by lowering the TWA to 1 ppm.

Some participants have suggested that OSHA calculate the cancer risks to individuals attributable to EtO exposure for 20 years of exposure rather than 45 years of exposure. For example, HIMA (Ex. 11–74) noted that OSHA had greatly overstated the risk by computing risks on 45 years of exposure. HIMA suggested that 20 years would produce a more plausible risk estimate because most exposures to EtO in the hospital sector are for far less than 20 years, and therefore HIMA suggested using 20 years, not 45 years, as a maximum length of exposure in risk calculations.

There was discussion of the reasons for selection of the 45-year working lifetime in the quantitative risk assessment section of this document, which concluded that calculations of population risk based on 20 years of exposure may not necessarily reduce the risk calculated for a population which is exposed for 45 years.

Another reason for using the 45-year exposure as the lifetime risk is the use of comparative risk analysis when evaluating the importance of the magnitude of the risk. To gain a perspective on the significance of the risk, OSHA has examined occupational risks relative to one another. The data on work-related illnesses are very scanty and often OSHA must resort to comparisons with the risks of occupational injuries. In doing these relative comparisons, OSHA has chosen a common unit of time used for determining "occupational lifetime" risks, that is, 45 years. The common time basis for comparison is necessary because risk to an individual from exposure to a hazard for 45 years will be greater than risks from exposure for only 20 years, and similarly, risks to an individual exposed to a hazard for twenty years will be greater than the risks of exposure for only one year. OSHA believes it is appropriate (and necessary) to compare lifetime risks from EtO to lifetime risks from other causes, as long as the periods of "exposure" are the same.

The use of the 45-year lifetime is based upon guidance given in the OSH Act. As found in section 6(b)(5): "The Secretary, in promulgating standards dealing with toxic materials or harmful physical agents under this subsection, shall set the standard which most adequately assures to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life." It is reasonable to assume that a person will begin work at age 20 and work until the age of 65 years old, a 45-year working lifetime, although the person may not work at the same job or be exposed to the same toxic substance for the entire 45 years. Changing jobs may result in increased risk from worker turnover.

As OSHA noted in the quantitative risk assessment section of this preamble, although the use of a 20-year lifetime risk will be lower than the 45-year risk for any single individual, the overall risk to the population will increase. Though workers will be exposed for shorter periods of time, the population at risk will increase dramatically, because turnover causes the exposure to be spread among several individuals (that is, two workers exposed for 20 years each, compared to one worker exposed for 40 years). Worker turnover is believed to increase the risk for the population to a level greater than that associated with individual risks. (See discussion in quantitative risk assessment. AFSCME has stated that, due to turnover, risks should be increased by a factor of ten.

OSHA has not made the adjustments suggested either by HIMA or AFSCME. OSHA believes that adding more factors for analysis in the significant risk determination is not necessary. In addition, calculating 20-year risks rather than 45-year risks increases uncertainties. The risks of 45 years of human exposure are comparable to the lifetime dosing pattern in the Bushy Run and NIOSH studies that were used as the basis for the quantitative risk assessment. If a 20-year human exposure is taken as the lifetime at risk, adjustments would have to be made to take into account the period of nonexposure. Because information is not available on which to base those adjustments further assumptions would have to be made in order to obtain estimates of risk. Although these assumptions might be reasonable they would, nonetheless, add uncertainty to the 20-year estimate that does not exist for the 45-year estimate. Finally, with the exception of HIMA, OSHA's approach to determining significant risk has been virtually unchallenged. OSHA's approach is consistent with other risk assessments previously conducted.

In conclusion, OSHA believes its approach, using a 45-year exposure as an occupational lifetime is an appropriate method for analyzing the significance of risk. Although risk from a 20-year exposure for any individual appears to be smaller than a 45-year exposure risk, when using comparative risk analysis, the regulatory decision remains the same. That is, that risks are significant at the existing 50 ppm PEL, that the new standard reduces the risks, and that the new 1 ppm TWA limit does not eliminate significant risks. In addition, using a 20-year exposure as lifetime rather than a 45-year lifetime means that more workers will be exposed to EtO, which will have the effect of increasing the risk to the population as a whole. If a 20-year lifetime were used, this turnover factor would have to be included in the significant risk determination. Evidence has not been sufficient in this rulemaking to adopt this type of population analysis for the significance of risk. It seems, however, that such an approach would, if used, lead to greater estimates of risk, and thereby provide further justification for the standard.

In accordance with the Supreme Court's guidelines, OSHA has attempted to quantify the risk of exposure to EtO by determining which levels of exposure constitute a significant risk to employees. However, as acknowledged by the Court, significant risk determinations involve more than mere mathematical treatment of the available health data. The use of mathematical risk assessment models is only one tool, though an important one, in the overall risk evaluation performed by OSHA in developing health standards. The Agency must evaluate all of the health evidence, including those data which do not readily lend themselves to quantification of risk, to determine necessary and appropriate protective provisions for exposed employees.

OSHA believes that the record evidence describing EtO's carcinogenic effects, along with the findings of the quantitative risk assessment, provide overwhelming evidence that a significant excess risk of cancer mortality is associated with EtO exposure and supports the need to reduce the PEL for EtO. In addition to this evidence, the record evidence showing that EtO exposure is associated with reproductive and cytogenetic effects buttresses the need to lower the PEL, although the available data do not permit development of reliable quantitative risk assessments for these

health effects. Evidence on reproductive effects include a study by Hemminki and coworkers (Ex. 6–7), who reported an increased incidence of a spontaneous abortion among pregnant EtO-exposed women, as well as findings from animal bioassays (Ex. 2–23, 6–9, 4–60, 6–10, 6–16) describing increased incidences of fetotoxicity, decreased fertility, and effects on sperm count and motility. Despite criticisms of these studies, many commenters (Exs. 21–261, 141E–2, 40) agreed that the results of the Hemminki study, taken in combination with the animal data describing fetotoxic and genotoxic effects resulting from EtO exposure, indicate that EtO poses a reproductive hazard for both men and women.

The genotoxic effects of EtO exposure described in the record include mutation of cells in culture, dominant-lethal mutations, heritable translocations, (Exs. 2–37, 2–352, 2–36), unscheduled DNA snythesis in germ cells of rodents, and increased frequency of chromosomal aberrations and SCE's in monkeys, rabbits (Exs. 4–60, 6–16, 22), and in humans occupationally exposed to EtO below the current PEL of 50 ppm. (Exs. 2–38, 6–13, 6–12, 6–14, 2–39, 137, 6–15) These effects are not surprising given that EtO is a highly reactive chemical and is capable of alkylating DNA. Although it is clear that the findings of chromosomal aberrations and SCE's in exposed humans stem from EtO acting upon DNA in human cells it is not clear what clinical manifestations would result from these effects. Nonetheless, the fact that EtO acts to alter the basic structure of genetic material, and resulting in alternations in ways that are both rare and persistent, and for which the clinical outcome is uncertain, is serious cause for concern.

The wide spectrum of effect attributable to EtO exposure is striking both in the number of test systems for which positive effects were found and in the relatively low exposures associated with those effects. These findings, taken together with the evidence on cancer, suggest similarities in the mechanism by which EtO induces mutagenic, carcinogenic, and reproductive effects. It is well established in the scientific community that most carcinogens have also been found to be mutagens when tested in *in vitro* and *in vivo* systems. For example, Legator testified:

> * * * we can talk at great length about the correlation between compounds that cause chromosome abnormalities * * * (and) cancer and the correlation is extremely impressive * * *" (Tr. 68).

Similarily, NIOSH has stated that the evidence that EtO exposure is associated with spontaneous abortion is supported by EtO's genotoxic activity. (Ex. 40).

Although the mechanisms by which EtO induces cancer or spontaneous abortion have not been precisely determined, the mutagenic activity of EtO suggests a mechanism by which EtO may cause these other effects. In evaluating the need to regulate occupational EtO exposures, OSHA must consider these elements in addition to the finding that a significant excess cancer mortality risk exists at the current 50 ppm EtO PEL. OSHA agrees with Legator's testimony that EtO is unusual in the breadth of its related toxic effects.

> I think you've had all the information that one could possibly gather to make a decision here. We can do all the risk estimates we wish and the answer is going to be that this is an extremely toxic chemical, a uniquely toxic chemical, a chemical that represents, in the pure sense of the word, a mutagenic, carcinogenic substance that does all the things that one would anticipate and one that we very seldom see in terms of (the) entire spectrum of results. (Tr. 81).

OSHA therefore concludes that EtO presents a serious and significant risk of adverse health effects going well beyond those of an excess risk of cancer, and believes that these risks will be substantially reduced by promulgation of the 1 ppm TWA.

Congress passed the Occupational Safety and Health Act of 1970 because of a determination that occupational safety and health risks in the American workplace were too high. Based on this, it is clear that Congress gave OSHA the authority to reduce serious occupational risks when feasible. OSHA believes that the proposed standard for EtO will reduce risk of cancer from a hundred per thousand to nearly one per thousand workers, and therefore, the Agency is carrying out the Congressional intent within the limits of feasibility and is not attempting to reduce insignificant risks.

In accordance both with Congressional intent and the Supreme Court's rationale, OSHA must, if it is feasible, seek to reduce risks below those estimated by the risk assessment to persist at a PEL of 1 ppm. OSHA expects that the final rule will reduce the risk of cancer below that estimated using the mathematical model. The estimates of risk only consider the standard's exposure level and do not take into account the other protective provisions of the standard such as respirators and medical surveillance. The decrease in risk to be achieved by these additional provisions cannot be adequately quantified beyond a determination that they will add to the protection provided by the lower PEL alone. OSHA has determined that employers who fulfill all the provisions of the final rule will provide that protection for their employees from the hazards presented by occupational exposure to EtO beyond that which would be provided solely by reduction of the PEL.

VII. Summary of Regulatory Impact and Regulatory Flexibility Analysis

Introduction

Executive Order (E.O.) 12291 (46 FR 13197, February 19, 1981) requires that regulatory agencies develop a regulatory analysis for any rule having major economic consequences on the national economy, individual industries, geographic regions, or levels of government. The Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*) similarly requires regulatory agencies, including OSHA, to consider the impact of regulatory actions on any small entities that will be affected by the regulation.

In accordance with these requirements, OSHA prepared a Preliminary Regulatory Impact and Regulatory Flexibility Analysis (Ex. 6–22) to accompany the proposed standard for EtO. The Agency has also developed a combined Regulatory Impact and Regulatory Flexibility Analysis for the final EtO standard. Rulemaking comments received on the Preliminary Regulatory Impact Analysis and on the economic and technological feasibility of the standard are addressed in the summary sections below. The principal findings of each of the chapters of the final Regulatory Impact Analysis, and any differences between the Agency's preliminary and final analyses, are also discussed in the following sections. The Regulatory Impact and Regulatory Flexibility Analysis is available in the rulemaking docket for inspection and copying.

The Secretary has determined that this regulation does not constitute a major regulatory action, as defined by the criteria of section 1(b) of E.O. 12291. The Secretary also certifies that this action will not have a significant impact on a substantial number of small entities.

In accordance with the Paperwork Reduction Act of 1980 (Pub. L. 96–511), the reporting or recordkeeping provisions that are included in this regulation will be submitted for approval to the Office of Management and Budget (OMB). They are not effective until OMB approval has been obtained and the public notified to that effect through a technical amendment to this regulation.

Summary of Industry and Exposure Profiles

Information received from the Health Industry Manufacturers Association (HIMA) (Ex. 89, Tr. 240) has caused OSHA to reevaluate its original estimates of the numbers of directly and incidentally exposed employees potentially affected by this standard. OSHA estimates that the EtO standard covers approximately 71,196 directly exposed employees and 69,175 incidentally exposed workers in five industry sectors. Directly exposed workers are defined as those exposed to EtO as part of their regular work assignments. Incidentally exposed employees are defined as those exposed on a non-routine basis, such as might occur if an employee walked through an area where EtO was present. For example, an incidental exposure occurs when an employee inhales airborne EtO that is off-gassing from a product previously sterilized with EtO, or when a poorly functioning ventilation system permits EtO to accumulate in an area normally free of EtO.

The majority of employees covered by the standard work in five industry sectors: EtO producers, ethoxylators (firms using EtO to manufacture other chemical products), health care providers (hospitals that use EtO as a sterilant), manufacturers and sterilizers of medical products (hereafter termed medical products manufacturers), and spice manufacturers. The producer industry is comprised of 13 large firms, only 3 of which had annual sales under $1 billion in 1979. OSHA has identified 38 of the 50 firms that were estimated by the Ethylene Oxide Industry Council (EOIC) to comprise the ethoxylator industry. The 38 ethoxylator firms and the 13 producers identified use approximately 98 percent of all EtO produced in the United States to synthesize other chemicals, such as the ethylene glycol used in antifreeze, and polyester resins and fibers. The smallest ethoxylator firm by revenue (of the firms that were identified) had annual sales of $15 million and employed 350 workers in 1981. A total of 3,676 employees are currently estimated to be directly exposed in the producer and ethoxylator sectors.

Three of the industries affected by the standard—hospitals, medical products manufacturers, and spice manufacturers—use EtO to sterilize other products. Although the sterilant uses of EtO consume only 2 percent of all EtO produced in the United States, these applications are responsible for most occupational exposures to EtO. OSHA estimates that EtO is used as a sterilant in 7,700 sterilizers in 6,237 hospitals. In all U.S. hospitals, approximately 62,370 employees are estimated to be directly exposed, and 25,000 are estimated to be incidentally exposed.

In addition, 5,000 and 41,750 employees are directly and incidentally exposed to EtO, respectively, in the 125 medical products manufacturing firms that are estimated to use EtO. In the Preliminary Regulatory Impact Analysis, OSHA estimated that 300–400 firms in this sector sterilized with EtO and that 14,000 and 116,900 employees were directly and incidentally exposed, respectively, in this sector. However, HIMA reported (Ex. 89, Tr. 240) that fewer firms in this sector are currently using EtO to sterilize medical products. Among the firms identified by OSHA in this industry were very large companies such as Johnson & Johnson (with sales of $4.8 billion and employment of 42,000) and relatively small firms such as Edward Weck and Company, Inc., with 400 employees and annual sales of $30 million.

An estimated 25 spice manufacturing firms use EtO to sterilize spices. These firms have a total of 150 directly exposed employees. OSHA revised its estimate of the number of EtO-using firms and exposed employees in this sector based on information submitted to OSHA's rulemaking docket by the American Spice Trade Association (ASTA) (Ex. 11–130). The Preliminary Regulatory Impact Assessment estimated that there were 27 EtO-using firms and 162 directly exposed employees in this sector. Fifty-seven percent of the firms identified in this industry sector have more than 1,000 employees. The two smallest firms identified have 28 and 95 employees and annual sales of $20 and $14 million, respectively.

Summary of Costs

OSHA examined both the annualized and present value costs (in 1982 dollars) of compliance with a 1 ppm TWA and a 10 ppm.

These costs were determined for each of the affected industry sectors and represent the annualized and present value costs that would be incurred assuming that the start-up dates of the engineering provisions in the standard are 1 year from the effective date of the rule. The present value of the costs was estimated using a 10 percent discount rate and a 50-year time period. Costs are presented in this regulatory analysis for the engineering controls necessary to achieve exposure levels of 1 ppm as an 8-hour TWA, and for other provisions of the standard, such as medical surveillance, exposure monitoring, training, and hazard communication.

OSHA estimates that total annualized costs, which include capital costs as well as annual operating costs, are $35.45 million for all affected sectors. The total annualized costs for the five industry sectors are: producers, $1.27 million; ethoxylators, $0.97 million; health care providers, $16.68 million; manufacturers of medical products, $16.38 million, and spice manufacturers, $0.15 million. The present value of the costs of the final standard over the next 50 years, assuming a 10-percent discount rate, is estimated to be $351.52 million for the five affected industry sectors.

OSHA's Preliminary Regulatory Impact Assessment reported higher costs than those presented here. OSHA estimated that the total annualized costs for all sectors for the proposed standard would be $72.4 million, distributed by industry sector as follows: producers, $1.56 million, ethoxylators, $1.03 million; health care providers, $23.65 million; manufacturers of medical products, $45.99 million; and spice manufacturers, $0.17 million. OSHA has revised the estimated compliance costs for the producers sector based on submissions suggesting that two companies had already achieved compliance with a 1.0 ppm TWA (Exs. 4–40, 11–68) and, therefore, would incur no costs for engineering controls. Costs in the health care providers sector were revised based on information submitted to OSHA by the American Hospital Association (AHA) (Ex. 11–115) showing that 40 percent of the hospitals participating in the AHA's survey reported that they had already achieved a 1.0 ppm TWA and, therefore, would incur no costs for engineering controls. Costs in the manufacturers of medical products and spice manufacturers industry sectors have also been changed based on revised estimates of the number of firms using EtO and the number of exposed employees (Exs. 11–130, 89).

Summary of Economic Impacts

In the EtO producer and ethoxylator sectors, OSHA estimates that the annualized compliance costs of the final standard are approximately 0.2 and 0.1 percent of total annual sales for these sectors, respectively. Costs of this size will not have a substantial impact on the firms in these two sectors, since these firms are large, multi-product, multi-facility, and financially sound companies.

In the sectors using EtO as a sterilant (medical equipment manufacturers, hospitals, and spice manufacturers), the

estimated annualized compliance costs per firm ranged from $1,475 to $131,040. The estimated cost of the standard per directly exposed employee in the spice manufacturing, hospital, and medical equipment manufacturing sectors is $1,000, $267, and $3,276, respectively. OSHA believes that, since the demand for the products produced by these sectors is relatively price inelastic, firms in these sectors will be able to pass these costs forward to their customers.

In the medical equipment manufacturing sector, where an additional 41,000 employees are believed to be incidentally exposed to EtO, firms will probably be able to pass a part of their costs forward to their customers in the hospital sector. As described above, OSHA believes that the hospitals, in turn, will pass these costs through to the consumers of hospital services.

In conclusion, OSHA has determined that the compliance costs associated with the final EtO standard will not have a significant impact on the market structure of any of the affected industries. In addition, the impact of the rule on inflation will be negligible, accounting only for approximately 0.001 percent of the GNP for 1982. Further, since OSHA has found that few if any firms will be forced to cease doing business because of the standard, no impacts on employment or regional concentration are anticipated. Finally, the permanent standard for EtO should not have a discernible impact on the balance of payments, since the U.S. producers of EtO who compete with foreign producers are clearly capable of absorbing the costs of the standard.

Summary of Benefits

The illnesses and premature deaths prevented by the implementation of the final EtO standard represent some of the expected benefits of this standard. Some aspects of these benefits can be quantified, such as the excess risk of cancer due to direct exposure to EtO. Other EtO-related health impacts, such as chromosome damage and neurotoxic effects, have not been quantified due to data limitations.

Among the non-quantifiable health effects attributable to EtO exposure are several types of chromosome damage including increased frequency of sister chromatid exchanges (faulty exchanges of genetic material among chromosomes), chemical alteration of the DNA, failure of the DNA repair mechanism, and quadriradials (a visually detectable, rare, and complex chromosome aberration). Mutagenic and reproductive effects of EtO exposure have been observed in experimental animal studies involving increases in the frequency of fetal resorption, teratogenic effects, and dominant-lethal effects. In addition, increases in the number of spontaneous abortions were observed in an epidemiological study of exposed hospital sterilizer technicians in Finland. Exposure to EtO can also have serious neurotoxic and sensitization effects. The neurotoxic effects of EtO can range from centrally mediated nausea and dizziness to peripheral paralysis. Employees who become sensitized to EtO often have to avoid all subsequent contact with the chemical.

Using a quantitative risk assessment based on the Bushy Run experiments, OSHA has estimated the number of excess cancer cases that are expected to occur among directly exposed workers during the next 50 years. The risk assessment model assumed that workers are exposed to EtO 8 hours per day, 5 days per week, 46 weeks per year, for 45 years. The 50-year time period represents the remaining life expectance of a worker whose first exposure occurs at the age of 25 years. The directly exposed population accounts for approximately 71,196 of the estimated 140,371 employees exposed to EtO. Based on current exposure levels, OSHA estimates that compliance with the 1 ppm TWA will reduce the number of excess EtO-related cancers over the next 50 years from a range of 532 to 1,017 to a range of 75 to 146, an 86 percent reduction.

Summary of Technological Feasibility

Several issues were raised and discussed at length as to the technological feasibility of certain provisions of the EtO standard. These included: the feasibility of achieving compliance with the 1 ppm 8-hour TWA and the ability of available monitoring methods to measure 8-hour TWA EtO concentrations accurately and reliably. The record evidence on each of these issues is summarized below.

Feasibility of the 1 ppm TWA

OSHA concludes that compliance with the 1 ppm TWA is technologically feasible for each of the five industry sectors principally affected. The methods that can be used to reduce employee exposure to EtO in the EtO producer and ethoxylator industry sectors involve conventional technology. Examples include the increased use of exhaust ventilation, double mechanical pump seals, leak detection and repair, and the supplemental use of respiratory protection for selected short-term operations and maintenance activities. This technology is commonly known and presently used by firms in these affected industry sectors. The following sections present evidence and testimony from the record that demonstrate the feasibility of compliance with the 1 ppm TWA, not only in the producer and ethoxylator sectors, but in the medical products manufacturers sector, the spice manufacturers sector, and the health care providers sector.

Processes in which EtO is manufactured or used as a chemical feedstock primarily involve closed systems. Emissions that are of concern from the viewpoint of occupational exposure arise from pump and compressor seals, valves, and flanged joints. According to the JRB, Associates (Ex. 6–22) study of the EtO industry, these exposures can be controlled by the increased use of mechanical seals on pumps and compressors; leak detection and repair, rupture disks for minimizing low-level leakage from pressure relief devices; closed sampling devices at process sampling locations; and vapor-tight unloading connections, magnetic level gauges, and nitrogen purge systems on tank car loading facilities. Based on visits to producer and ethoxylator sites where these controls were being used, JRB concluded that a 1 ppm TWA was technologically feasible if respiratory protection was used for short periods of time during hose-disconnect operations at tank car loading and unloading stations (Ex. 6–22).

Many producers and ethoxylators submitted information supporting JRB's conclusion. For example, Celanese Corporation (Ex. 4–40) adopted a 1 ppm internal 8-hour TWA exposure limit in 1980 and is currently achieving this level at all job locations. Texaco (Ex. 4–47) reported that it is currently "fairly close" to achieving a 1 ppm 8-hour TWA and is preparing to implement additional controls to achieve a 1 ppm standard. The controls used by Texaco include "* * * recovery systems, closed-loop sampling systems, and magnetic level gauges for loading EtO tank cars" (Ex. 4–47).

The EOIC surveyed its member companies on the issue of the feasibility of a 1 ppm TWA (Ex. 4–33). Although the EOIC agrees with OSHA that a TWA of 1 ppm is feasible for the EtO producers and non-producer ethoxylators, they expressed concern that certain non-producer ethoxylators would not be able to achieve the 1 ppm TWA:

> * * * With respect to the non-producer* * * [ethoxylators], * * * it must be emphasized that the EOIC survey response constitutes a relatively small sample of a diverse industry and that 1 ppm

may not be technologically feasible for some members of that industry. (Ex. 4–33)

However, a supplemental submission by the EOIC (Exs. 4–33A, 4–33B) noted that 19 of 26 non-producer ethoxylator firms contacted by EOIC had already achieved 8-hour TWA's of 1 ppm or below. Neither the EOIC nor individual non-producer ethoxylator firms presented evidence to the record to suggest why firms in this sub-sector might have difficulty achieving a 1 ppm PEL. OSHA believes that the processes involved in ethoxylation, the types of equipment used, and the engineering controls employed to reduce emissions from these processes are substantially similar for both EtO producers and producer and non-producer ethoxylators. OSHA concludes, therefore, that compliance with a 1 ppm TWA is feasible for producers and for ethoxylators.

Several commenters (Exs. 11–57, 11–133, 70, Tr. 828, 837) stated that, while a 1 ppm TWA is feasible, respirators might be required for some short-term operations. For example, the EIOC commented that:

> In order for industry to meet a PEL of 1 ppm (TWA), use of respirators in certain circumstances, in addition to maintenance and repair, will be necessary. Producers and * * * (ethoxylators) may need to use respirators during loading and unloading operations. (Ex. 11–57)

Howard L. Kusnetz, Manager of Safety and Industrial Hygiene, Shell Oil Company (Ex. 70, Tr 878), stated that workers in 14 of 16 job categories at Shell were exposed to 8-hour TWA EtO concentrations of less than 1 ppm; in the 2 categories where exposures exceeded 1 ppm, respirators were used for short-term operations. Donald E. Rapp, a Certified Industrial Hygienist with the Dow Chemical Company, also confirmed that 1 ppm can be achieved if respirators are used during tank car loading and unloading and during vessel cleaning (Tr. 837). A submittal by Union Carbide Corporation stated that a 1 ppm level "* * * may be feasible *only* with the extensive use of negative pressure respirators, supplied air equipment, and with a sufficient phased-in compliance period" (Ex. 11–133). Union Carbide goes on to comment that respirators would be required in operations such as "* * * breaking connections, changing filters, cleaning railcars and tank trucks, clearing lines and quality control sampling * * *" (Ex. 11–133).

OSHA agrees with Union Carbide's assessment that a 1 ppm TWA may require the use of respirators in some maintenance operations and tank car loading and unloading. Such operations will need to be evaluated by individual employers on a case-by-case basis to determine whether engineering and work practice controls are feasible. However, OSHA does not agree that respiratory protection will be necessary during process (quality control) sampling. As reported by JRB (Ex. 6–22), Texaco (Ex. 4–47), the EOIC (Ex. 4–33), and the Dow Chemical Company (Tr. 837), employee exposures during process sampling can be controlled effectively by enclosing and ventilating the sampling points.

There was general agreement in the record that a 1 ppm 8-hour TWA exposure limit is achievable for operators of large industrial sterilizers (Exs. 6–22, 11–74; 11–113; 91; 146; Tr. 213, 1068, 1042). In the feasibility study conducted by JRB (Ex. 6–22), a number of engineering controls and work practices were identified that are currently being used in the industry to reduce occupational exposure to EtO. These include chamber evacuation systems, liquid/gas separation units to prevent excessive EtO emissions during chamber evacuation, local exhaust hoods installed over the sterilizer door, local ventilation of aeration chambers, and allowing the sterilizer to aerate for a short period of time after opening the sterilizer door. Because the equipment described by JRB is readily available on new sterilizers or can be retrofitted onto old equipment, JRB concluded that a 1 ppm TWA is feasible for sterilizer operations (Ex. 6–22). Ronald H. Abrahams, Director of the Regulatory Compliance Division of the American Hospital Supply Corporation (Ex. 4–45), commented as follows:

> For us to achieve a 1 ppm or lower level by engineering means, it is our opinion that we would have to construct new facilities with remote material handling capabilities, sterilization cycle modifications, [and] conveyor systems to transport products from the sterilizer area to specially designed degassing areas * * *.

Abrahams also stated that in order to achieve a 5 ppm TWA, chamber purge systems and additional air ventilation would be required (Ex. 4–45). However, OSHA believes, based on the evidence submitted by several medical products manufacturers (discussed above), by Peter Roy (Ex. 36), and by Robert Kramer (Ex. 35), that chamber purge systems and ventilation systems, if properly designed, can reduce 8-hour TWA exposures to 1 ppm and that the extensive use of automation described by Abrahams will not be necessary to achieve a 1 ppm TWA in this sector.

In his written submission to the docket, Peter A. Roy, Assistant Professor of Industrial Hygiene at the University of Minnesota, commented as follows:

> In my opinion, the measures necessary for EtO exposure control * * * to * * * 1 ppm PEL * * * are in fact nothing more than the application of good industrial hygiene practices, which have been well established and proven * * * These control measures include both local exhaust and general ventilation, process isolation, work practice control, equipment modification, and personal protection. (Ex. 36).

Comments submitted by the 3M Company also indicate that a 1 ppm TWA is attainable using new equipment or by retrofitting older equipment. In this regard, 3M stated:

> We believe that both new STERI-VAC equipment and retrofit modifications available for older 3M sterilizers make it feasible for 3M customers to meet the proposed PEL of 1.0 ppm reliably. (Ex. 146).

In addition, in 1981 3M adopted an internal guideline of 1 ppm as an 8-hour TWA in for its own sterilization facilities (Ex. 146).

Like 3M, Johnson & Johnson has already adopted an internal standard of 1 ppm as an 8-hour TWA (Ex. 11–113). In their written submission, they commented as follows:

> Johnson & Johnson adopted internal EtO exposure guidelines of 1 ppm (8 hr. TWA) and 10 ppm (15 min. STEL) in May of 1980 and thus has three years experience in implementing this guideline for exposure. This experience indicates that a PEL of 1 ppm * * * is feasible when coupled with the limited use of respirators * * * (Ex. 11–113).

Frank P. Wilton, President of Ethox Corporation, commented in his written testimony that, after installing new ventilation equipment and constructing a dedicated aeration facility, Ethox "* * * achieved an operating environment with a TWA below 10 ppm" and believes that it "will be able to achieve a TWA of 1 ppm" after installing additional control measures (Ex. 91).

On the issue of when respirators were needed to meet the 1 ppm TWA, commenters generally agreed that limited use of respirators would be required during certain operations (Exs. 11–74, 11–113, Tr. 285, 302, 1042, 1068). For example, G. Briggs Phillips, Vice President of Scientific Affairs for HIMA, testified that:

> HIMA supports OSHA's proposal of the one part per million PEL and believes that compliance is feasible * * * [if] limited use of respirators [is permitted] for short periods. (Tr. 1041).

In its written submission HIMA described the areas in which respirators

may be required to achieve a 1 ppm TWA:

In addition to chamber unloading, respirator protection is essential in degassing rooms, for example, removal of biological indicators from sterilized products, requires the employee to enter the degassing room, where ambient levels from the off-gassing product, even with ventilation, are likely to be above 1 ppm. (Ex. 11-74).

In his testimony, Roy agreed that respirator use may be necessary in the sterilizer chamber and aeration facility:

Based upon my experience even with the engineering controls and ventilation and chamber aeration * * * unloading the pallets from a large sterilizer * * * would require respiratory protection.

[T]ransferring into and entering the heated aeration tunnel or aeration room, depending on the size of the facility * * * would routinely require respiratory protection * * *

[R]emoval of biological indicators in industrial settings, since the indicators were often buried in the pallets somewhere, * * * quality assurance technicians would put a gasmask on * * * (Tr. 302).

OSHA concludes, based on the evidence discussed above, that achievement of the 1 ppm TWA is technologically feasible during the sterilization of medical products, with the limited use of respirators. As is the case with EtO producers and ethoxylators, the employer who sterilizes medical products will have to evaluate his or her operation on a case-by-case basis to determine the feasibility of control technology and the need, if any, for respiratory protection.

The process for sterilizing spices is essentially the same as that for sterilizing medical products. Materials to be sterilized are placed in gas-permeable bags, bales, or containers before being loaded into the chamber. After sterilization,the product is removed from the chamber and stored in a holding area for at least 48 hours. Because the process and sterilization equipment and the available control equipment used in this sector are similar to those used for sterilizing medical products, the JRB study concluded that compliance with a 1 ppm TWA was feasible for spice manufacturers (Ex. 6-22).

Five spice manufacturers (Exs. 4-34, 11-47, 11-49, 11-101, 11-141) and the American Spice Trade Association (ASTA) (Ex. 11-130) submitted comments to OSHA. Only the ASTA submittal commented on the feasibility of a 1 ppm TWA.

Only six [spice manufacturing] firms were contacted by JRB [in its feasibility study of the EtO industry], and only 20 percent of the six can meet a 1 part per million level. It would appear, therefore, that this is a totally unsound basis for judging the industry, as * * * to its ability to comply with the proposed regulation (Ex. 11-130).

However, the JRB study stated that:

All 8-hour TWA levels reported by * * * (the six responding spice manufacturing firms) were below 5 ppm, and 20 percent (of the exposure samples) were less than 1 ppm (Ex. 6-22).

Thus, the information presented by ASTA (Ex. 11-130) from the JRB report does not refer to the ability of spice manufacturing firms to meet the 1 ppm TWA, but instead refers to current EtO exposure levels in spice manufacturing firms, as reported by the firms themselves to JRB. Two spice manufacturing firms submitted cost estimates to the docket for achieving a 1 ppm TWA (Exs. 11-49, 11-141). OSHA believes that a 1 ppm TWA PEL is feasible in the spice manufacturing industry sector since these firms were limiting exposure by using engineering and work practice controls. In addition, the similarity between the sterilizing processes in the spice manufacturing and the medical product manufacturing industry sectors, where evidence shows that 1 ppm is feasible, strongly suggests that 1 ppm is feasible in the spice manufacturing industry sector. OSHA therefore concludes that the 1 ppm TWA is technologically feasible in the spice manufacturing industry sector with the use of engineering controls and the limited use of respirators.

Although the EtO sterilizers used in hospitals are smaller than the industrial sterilizers used by medical products manufacturers and spice manufacturers, the control of EtO exposures in hospitals involves the same principles and types of equipment used for industrial sterilizers. However, as Roy testified, the smaller size of hospital sterilizers makes controlling EtO exposures in hospitals generally easier than in industries using large sterilizers:

In my work [with] sterilizers, ranging from tabletop size to industrial size, I have found the process * * * [and] [t]he exposure patterns are basically the same.

The size and scope of the problem, of course, varies with the size and scope of the operation—more gas, bigger sterilizers, bigger problems; less gas, smaller sterilizers, generally a smaller problem in terms of total exposure (Tr. 240).

In addition, Robert Kramer stated that "* * * [u]sing a continuous purge cycle or a post-vacuum continuous purge * * * [hospitals] can readily achieve a 1 ppm standard" (Tr. 201).

Several hospitals submitted exposure data indicating that they are currently achieving the 1 ppm TWA (Exs. 4-6, 11-5, 11-20, 11-35, 11-37, 11-38, 11-40, 11-60, 11-77, 11-85, 11-87, 11-97, 11-100, 11-132, 11-156, 99). A hospital survey report submitted by the Council Shared Services, Hospital Council of Southern California (HCSC) (Ex. 11-122), showed that 62.9 percent of 426 EtO site surveys conducted in 123 hospitals (August 1978 through March 1983) showed EtO exposure lower than an 8-hour TWA of 1 ppm. In a second set of surveys taken by the Council from March 1982 through March 1983, 75 percent of 148 site surveys taken in 86 hospitals showed EtO exposures below 1 ppm (Ex. 11-122). Malcolm Ridgeway, Director of HCSC, further testified that 50 site surveys conducted using passive dosimeters showed that "* * * 88 percent of sites that we now survey show levels below one part per million * * *" (Tr. 1336).

The results of a survey conducted by the American Hospital Association (AHA) (Ex. 11-115) indicated that 40 percent of 451 hospitals contacted to provide exposure data reported EtO exposures of 1 ppm or less as an 8-hour TWA.

Despite the fact that many hospitals report that they are currently meeting a 1 ppm TWA, some commenters state that extensive facility modifications would be required to achieve 1 ppm (Exs. 4-45, 11-111, 11-127). Gordon E. Whitaker and Collette Keyser, co-chairpersons of the Association for the Advancement of Medical Instrumentation (AAMI), commented that:

Compliance will be difficult for most hospitals, but especially for the smaller, older and not-for-profit institutions. Older institutions may require major modifications in area ventilation and the installation of dedicated exhaust systems. Even the more modern institutions will need time to * * * formulate plans for needed ventilation changes and then to implement these plans to comply with a 1 ppm PEL. (Ex. 11-127).

Although the installation of new and retrofitted ventilation systems may be required to achieve the 1 ppm TWA in some older hospitals, OSHA believes that such modifications can be made without renovation or restructuring of existing facilities. On this point, Peter Roy testified as follows:

* * * Those that argue against the feasibility or practicality of the installation of local exhaust systems in hospitals are * * * (thinking of) facilities where there are "remote" sterilizers * * * (e.g.) far from the roof or from an outside wall * * *.

Although * * * so-called * * * remote locations may be inconvenient, they are certainly not impossible (for the purposes of EtO control). Sterilization equipment in a "remote" central service area is not in a concrete box all by itself * * *. Certainly,

you can drill a hole through a concrete wall and put in a duct. It's done all the time. (Tr. 223).

After reviewing the available evidence in the entire record OSHA believes that a TWA of 1 ppm is technologically feasible in the sectors that will be principally affected by the final rule for EtO. The technologies to achieve this level of control consist of conventional equipment, such as forced ventilation, closed-loop sampling systems, pump seals, local exhaust, and chamber purges, and widely accepted work practices, such as leak detection, delaying sterilizer unloading after opening the door to permit off-gassing of EtO, and training employees to stand upwind during tank car pulling, rather than pushing the cart loaded with sterilized goods. As discussed above, these technologies and work practices are already in use by firms in each of the sectors studied, and have permitted many facilities to achieve compliance with the 1 ppm TWA mandated by the final rule.

Feasibility of Monitoring a 1 ppm TWA and 0.5 ppm Action Level

Many commenters addressed the availability and accuracy of feasible methods to measure employee exposures to EtO (Exs. 4–20, 4–24, 4–28, 11–54, 11–65, 11–74, 11–76, 11–101, 11–127, 11–133, 11–141, 11–147, 37, 75, 109, 142, 146, 151). These commenters raised five issues regarding monitoring:

- Ability to measure concentrations of 1 ppm as an 8-hour TWA.
- Accuracy of monitoring methods.
- Field validation of monitoring methods.
- Inability to measure concentrations below 1.0 ppm accurately.
- Length of time to obtain monitoring results.

Each of these issues is discussed below.

Several commenters stated that the currently available methods for monitoring employee exposures to EtO were not capable of detecting concentrations of EtO at 1 ppm (Exs. 4–35, 11–18, 11–21). For example, Robert R. Everett, Executive Vice President of Louise Obici Memorial Hospital in Suffolk, Virginia (Ex. 11–21), stated:

> We know of no way of determining compliance at the 0.5 and 1 part per million standard. Our monitoring equipment will not detect that small an amount, nor will (other) equipment that we have been able to find on the market.

However, information submitted to the docket shows that there are at least six sampling and analytical methods that have limits of detection sufficiently low to measure 8-hour TWA exposure and action levels. Of the six methods listed below, three are reported to be able to detect 1 ppm as an 8-hour TWA within the ±25 percent and 0.5 ppm as an 8-hour TWA within the ±35 percent accuracy limits specified by the standard: the OSHA method, the Qazi/Ketcham method, and the DuPont Protek passive dosimeter.

OSHA's method 30 has a limit of detection of 0.01 ppm and a reliable detection limit of 0.05 ppm (Tr. 222).

The NIOSH method is a modification of the OSHA method and has a limit of detection of 0.027 ppm (Tr. 325).

The Qazi/Ketcham method has a limit of detection of 0.25 ppm, has been validated over the range of 0.5 ppm to 50 ppm (Ex. 11–133), and is used routinely to measure 1 ppm (Exs. 4–24, 4–28, 11–54, 11–76).

The Miran infrared spectrophotometer, a direct reading instrument, is capable of detecting 1 ppm (Exs. 11–73, 11–79).

The 3M model 3550 passive dosimeter has a limit of detection of 0.25 ppm (Exs. 4–20, 136).

The DuPont ProTek passive dosimeter has a limit of detection of 0.25 ppm (Exs. 11–65, 11–65A, 109).

Each of the above methods is capable of measuring the 1 ppm TWA. All of the methods except the Miran infrared spectrophotometer are capable of measuring the 0.5 ppm action level. The Qazi-Ketcham method, for example, is capable of detecting 0.25 ppm when used to measure an 8-hour TWA. This method has been validated at a flowrate of 20 cc per minute for 6 hours, 40 minutes samples and 500 cc per minute for 15 minute samples (Ex. 11–133).

Several commenters (Exs. 11–76, 11–127, 11–133) noted that the standard OSHA method is inconvenient to use because it requires frequent changing of charcoal tubes during an 8-hour sampling period. For example, William F. Kirchoff, senior attorney for Warner Lambert Company (Ex. 11–76), stated that:

> Since the recommended total air volume (that must be collected) is 1.0 liter at a flow rate of 0.05 liter per minute, sampling tubes would have to be changed every 20 minutes. This would greatly increase the number of samples taken per operator during the course of full shift sampling.

However, to overcome this problem, the NIOSH method uses a larger charcoal tube than the OSHA method, and the NIOSH method has also been validated to 1 ppm (Tr. 219, 325). In addition, the Qazi/Ketcham method, the DuPont ProTek badge, and the 3M passive dosimeter are reported to be able to measure concentrations at the 1 ppm TWA and 0.5 ppm action level (Exs. 4–20, 11–65, 11–65A, 11–113, 109, 146).

Several commenters (Exs. 4–28, 11–54, 11–65, 11–74, 75) questioned the ability of available monitoring methods to achieve the accuracy requirements specified by the standard (± 25 percent at the 95 percent confidence level for the 0.5 ppm action level). Referring to OSHA's proposed accuracy requirements, HIMA (Ex. 11–74) states that "Such levels of accuracy cannot be achieved in practice* * *." However, OSHA received much information showing that the required level of accuracy can be achieved with several of these monitoring methods (Exs. 11–65, 11–105, 11–133, 37, 109, Tr. 222). Information submitted by DuPont (Ex. 11–65) shows that the DuPont ProTek passive dosimeter had an overall system accuracy of ±13.5 percent. The OSHA method 30 has been validated at a concentration of 1 ppm and has been shown to be accurate to ±13 percent (Ex. 37, Tr. 222). Charles P. Blahaus, Vice President, of Environmental, Health and Safety for PPG Industries, states that "laboratory evaluations of charcoal tube samples have reported accuracies at 1 ppm of ±25% and 0.5 ppm ±35% under optimal conditions" (Ex. 11–105).

Union Carbide (11–133) has performed tests to determine the accuracy of the Qazi/Ketcham method and concluded: "OSHA has specified that the EtO sampling and analytical methods must meet the following accuracy requirements at the 95% confidence level: ±25% at the PEL and ±35% at the action level. Under controlled laboratory conditions, the Qazi/Ketcham method appears to meet (OSHA's) accuracy requirements". DuPont has also tested the Qazi/Ketcham method (Ex. 11–65, 109) and found an accuracy of ±25.9 percent for the method in one validation test and ±79.2 percent in another validation test. The first validation test included results of 21 samples of airborne concentrations ranging from 4 to 8 ppm. The second validation test involved results from unreplicated samples taken at each of six concentrations ranging from 0.25 ppm to 10.7 ppm. However, the results of the second validation test are likely to have been compromised by the inclusion of two samples that were at or near the lower limit of detection for the Qazi/Ketcham method. OSHA therefore believes that DuPont's estimate of an accuracy of 25.9 percent for the Qazi/Ketcham method is a more reasonable assessment of the method's performance.

Union Carbide's comments (Ex. 11–133) were typical of those of several commenters (Exs. 4–28, 11–49, 11–54, 11–

65, 11–74, 11–101, 11–130, 11–141, 11–147, 75) who expressed doubt that monitoring methods could achieve their rated accuracies under actual field conditions. Union Carbide (Ex. 11–133) stated that:

* * *Considerable analytical experience and expertise is required to perform the (Qazi/Ketcham) method. Even within Union Carbide, only industrial hygiene laboratories with considerable experience have been able to duplicate the validation data* * *. Thus, while the method is the best we know of, it may be difficult to meet the accuracy requirements of OSHA under field conditions and in inexperienced laboratories.

However, evidence (Ex. 11–133) that some industrial laboratories within Union Carbide have been able to train their personnel to achieve the required accuracy indicates that the skills necessary for accurate determination of EtO concentrations can be learned. Although the method is difficult to use, OSHA is confident that with strict adherence to the published methods and adequate training of laboratory and industrial hygiene technicians, the skills enabling technicians to measure EtO concentrations accurately will be acquired following promulgation of the final standard.

Many commenters (Exs. 11–54, 11–74, 11–101, 11–133, 11–141, 74, 153) stated that none of the currently available sampling and analytical methods for measuring employee exposures to EtO have been field validated. In addition, specific questions regarding field validation of the OSHA and NIOSH methods were raised during the hearing (Tr. 216, 327). DuPont (Ex. 109) provided a definition of field validation procedures:

A new analytical and sampling method* * * (is) field tested and validated against the most commonly used independent monitoring method once that method has been validated in the laboratory under expected field conditions and shown to be precise and accurate. Few methods have been tested in this manner.

Samuel Tucker, Research Chemist from NIOSH (Tr. 330) confirmed that "* * *for (field) validation, one must have an independent method of analysis." At the present time, OSHA knows of no independent EtO monitoring method that has been tested under field conditions that could be used as a reference method against which new sampling and analytical methods for EtO could be validated. Until a method is tested and accepted by an independent organization such as the American Society of Testing Materials (ASTM) Committee D22, new methods cannot be field validated.

However, as Ronald Freking, Director of the Organic Division of OSHA's Analytical Laboratory in Salt Lake City emphasized, the sampling and analytical methods used for most OSHA-regulated chemical substances have not been field validated (Tr. 229). Further, Mathew Gillen, Industrial Hygiene Consultant for the Workers Institute for Safety and Health, observed that "field validation is something that's desirable but isn't absolutely necessary for enforcement purposes" (Tr. 230).

Commenters (Exs. 11–49, 11–101, 11–130, 11–141, 11–147) from the spice manufacturing industry sector indicated that they believed field validation was especially necessary in their industry because of the number of chemicals in their workplaces that might interfere with the validity of monitoring results. For example, ASTA (Ex. 11–130) stated that:

Since our primary reason for existence as an industry hinges on the presence of numerous volatile components and the very atmosphere of our production facilities can contain many of these chemicals, we submit that the possibility of interference by volatile chemicals in current measurement capabilities can be substantial.

However, OSHA has determined that the currently available and commonly used EtO sampling and analytical methods have been tested for interferences. For example, Union Carbide reported that a wide variety of chemical substances do not interfere with the (Qazi-Ketcham) analytical procedure (Ex. 11–133). These chemicals are different from EtO in terms of molecular weight, polarity, and other chemical characteristics, which means that they also have different residence times in the chromatographic columns used to analyze them. OSHA believes that the high molecular weight aromatic compounds that lend flavor and odor to spices are also likely to have residence times that are readily distinguishable from that of EtO.

Although several commenters (Exs. 11–65, 11–133, 37, 109, Tr. 222) provided laboratory validation data demonstrating the accuracy of some of these analytic methods at 1 ppm, no commenters provided data demonstrating the ability of these methods to measure the 0.5 ppm level with an accuracy of ±25 percent at the 95 percent confidence level. Therefore, OSHA cannot demonstrate the feasibility of monitoring alternative TWAs of 0.5 ppm or lower within an accuracy of ±25 percent. Howard Kusnetz, Manager of Safety and Industrial Hygiene for the Shell Oil Company (Ex. 4–28), stated:

Standard analytical methods are available for monitoring EO concentrations in the 1- to 20-ppm range. Should OSHA consider reducing the permissible exposure level below 1.0 ppm, the analytical methods would require modification to provide the necessary sensitivity.

Based on a careful review of the evidence in the record of this rulemaking, OSHA has determined that it is feasible to measure airborne concentrations of EtO at the 8-hour TWA level with the accuracy required by the standard's 8-hour TWA provision. Further, the record indicates that it is possible to measure the 0.5 ppm action level within the accuracy range required by the standard. However, the evidence indicates, and OSHA finds, that it is not feasible to measure EtO concentrations under field conditions, within the limits of error specified in this standard, at levels below the 1 ppm TWA and the 0.5 ppm action level.

Notification of Monitoring Results

The proposals requirement to notify employees of monitoring results within 10 days from the employee's receipt of monitoring results was questioned by some commenters (Exs. 11–25, 11–74, 142). For example, John Kuchta, Vice President and General Counsel of the Kendall Company (Ex. 142) stated that:

* * * the proposed regulation requires that employers provide employees with the results of all EtO personal monitoring within 10 days. This proposal is unreasonable and unrealistic in light of the fact, that in order to comply with other provisions of this standard requiring accurate testing, the samples must often be forwarded to outside laboratories for evaluation and analysis. Experience has shown that this testing requires, at a minimum, three to four weeks.

OSHA did not intend the 10-day period specified in the proposal's notification of monitoring results provision to apply to the interval between monitoring and notification, but to the period between the receipt of monitoring results by the employer and notification of the employee. As written, this requirement would permit employers to send their monitoring results to outside laboratories for analysis. OSHA believes that clarifying the intent of this provision will prevent misinterpretation of this provision in the future.

Another commenter objected that the 10-day interval between the employer's receipt of results and notification of employees was too short. For example, Charles P. Blahaus, of PPG Industries, Inc. (Ex. 11–105), stated that additional time for employee notification of monitoring results would be required to

"allow the employee's work shift to be rotated to where he could be contacted by day supervision and medical personnel * * *."

OSHA agrees with this argument, and has therefore extended the time for employee notification of monitoring results to 15 days after receipt of monitoring results. OSHA believes that 15 days will allow sufficient time for an employee who is monitored on the day shift to be rotated back to the day shift.

Based on the evidence in the entire record, OSHA has determined that a 1 ppm TWA is technologically feasible. The technologies, methods, and work practices are commonly known and presently used by firms in the affected industry sectors. OSHA has also determined that it is technologically feasible to accurately monitor a 1 ppm TWA and a 0.5 ppm action level within the parameters set forth in the standard.

Although the record in this rulemaking does demonstrate that most operations in most facilities can be expected to achieve 8-hour exposure levels of 1 ppm, OSHA cannot demonstrate that most facilities could reliably achieve compliance with an 8-hour TWA (and its accompanying action level) set at a level below 1 ppm.

Environmental Assessment—Finding of No Significant Impact

On April 21, 1983, OSHA published a notice of proposed rulemaking (NPRM) for occupational exposure to ethylene oxide (EtO) (45 FR 17284–17319). At that time, OSHA also published an environmental finding of no significant impact. OSHA has reviewed the docket and has received no additional information on any potential environmental effects of the standard as a result of the public hearing, or as part of the posthearing comments. In addition, OSHA has reviewed the final EtO standard in accordance with requirements of the National Environmental Policy Act (NEPA) of 1969 (42 U.S.C. 4321 et seq.), the provisions of the Council on Environmental Quality (CEQ) (40 CFR Part 1500), and OSHA's DOL NEPA Compliance Procedures (29 CFR 11). As a result of the Agency's review, and based on the information contained in the preamble of this notice, the Assistant Secretary has determined that the promulgation of the rule will have no significant effect on the quality of the human environment external to the workplace in terms of air, water or soil quality, plant or animal life, or land or energy use.

VIII. Summary and Explanation

The following sections discuss the individual requirements of the EtO standard. The sections include an analysis of the record evidence and the reasons underlying the adoption of the various provisions of the standard. The final standard contains a permissible exposure limit for EtO of 1 ppm as an 8-hour TWA. Engineering controls, work practices, and respirators are required where necessary to reach the PEL's, and written compliance plans must be developed. Engineering controls must be completed within 12 months from the effective date of the standard. Several provisions of the standard, including those on exposure limits, respirators, emergencies, medical surveillance, labels and signs and recordkeeping have been revised and clarified as described in detail below.

The language of the standard and the order of the various provisions are consistent with the drafting in other recent OSHA health standards, such as the arsenic final standard (43 FR 19584), and the acrylonitrile final standard (43 FR 45762). OSHA believes that a similar style should be followed from standard to standard to facilitate uniformity of interpretation of similar provisions. Section 6(b)(5) of the Act states that health standards shall also be based on "experience gained under this and other health and safety laws."

Paragraph (a) Scope and Application

The standard applies generally to all occupational exposures to EtO. However, depending on the nature and the extent of the exposure, certain provisions of the final standard may become inapplicable or may have limited applicability.

The standard applies to any workplace where exposures to EtO may be found except those workplaces exempted by paragraph (a)(2). The applicability of several of the provisions of the standard is based on the results of the initial monitoring conducted by the employer or on the availability of other objective data concerning employee exposures or product characteristics.

The final standard contains the same exemption as proposed. Paragraph (a)(2) excludes workplaces that process, handle or use products containing EtO where objective data show that the product cannot release EtO at or above the action level. The criterion for exemption under paragraph (a)(2) requires objective data that show that the material is incapable of releasing airborne EtO at or above the action level under the expected conditions of processing, handling or use that would cause the greatest possible EtO release. OSHA anticipates that the primary producers and intermediate processors of EtO-containing products will be in the best position to test their products and to supply the necessary objective data on the levels of EtO likely to be released by the product to downstream users of the EtO containing material. The final standard does not require downstream employers to generate their own objective data on the EtO levels likely to be released from a product if they can obtain it from producers or other processors. However, as required by paragraph (k)(1) of the standard, the employer must document that this information appropriately supports the exemption, and the employer must maintain a record of this information.

In addition, employers may demonstrate that their employees' exposures are below the action level by using historical monitoring data, i.e., monitoring results for these employees obtained within a one-year period preceding publication of this final rule. When employee exposures can be demonstrated, by means of such objective data, to fall below the action level trigger for many provisions of the standard, employers can use these data to satisfy the initial monitoring requirements of paragraph (d)(2)(ii) of the standard. This alternative to initial monitoring is discussed in greater detail in the monitoring section below.

Some participants suggested specific exemptions for their industries. For example, representatives of an airline company (Ex. 11–117) performing infrequent fumigation of aircraft and representatives of the construction industry (Exs. 11–2, 11–7, 11–11) who claimed EtO is not found in construction operations asked for special exemption. OSHA believes, however, that employees should be protected even where EtO is used very infrequently, especially given the adverse health effects potentially associated with intermittent EtO exposure. For example, it is possible that construction workers could be exposed to EtO during construction activities in or around medical facilities.

Moreover, OSHA notes that the final rule has been structured so that any compliance burden imposed by the standard is related to the extent and duration of the employee exposures in an employer's workplace. One provision (medical surveillance) applies only to workplaces having EtO levels at or above the action level for more than 30 days per year, while other requirements, such as periodic monitoring, annual medical examinations, and labeling,

apply only to workplaces having exposures at or above the action level. OSHA therefore does not believe that any significant compliance burden is placed on employers who either do not use EtO or who have workplaces where employee exposures are below the action level. OSHA also notes that the Construction Advisory Committee on Occupational Safety and Health (CACOSH) voted at its meeting on May 23 and 24, 1983, to have the construction industry covered by the EtO standard.

Paragraph (b) Definitions

In the final standard, the definitions of "Director," "Authorized person," "Assistant Secretary," and "Ethylene oxide" remain unchanged from the proposal.

The definition of an "action level" as an airborne concentration of 0.5 ppm (8-hour time-weighted average) also remains unchanged from the proposal. An action level is an exposure limit above which some provisions, such as monitoring and medical surveillance, apply, and below which fewer provisions apply. The action level may have the effect of providing an incentive for employers voluntarily to reduce exposures to below the action level where possible. However, employers are not required to achieve this exposure level.

Many participants supported the action level concept and suggested that a 0.5 ppm action level would be an appropriate level, given a 1.0 ppm TWA (Exs. 11–25, 11–77, 11–90, 11–143, 129). For example, Vicki L. Martin, Environmental Attorney for Dow Corning Corporation, stated that:

> Dow Corning strongly supports the concept of an "action level" as a means to focus surveillance and monitoring efforts to those work situations where significant exposure is likely to occur; and to relieve those employers of these more burdensome obligations if actual monitoring data shows they are unnecessary. The 0.5 ppm actions level appears appropriate (Ex. 11–143).

As noted by Martin, one purpose of the action level is to lessen any burden on employers by providing a cut-off point for many of the compliance activities required by the standard. If, on the basis of initial monitoring results or other objective data, employee exposures are found to be below the action level, the employer would be permitted to discontinue monitoring (as specified by paragraph (d)). Periodic medical examinations would also not be required for these employees. The action level thus provides an objective means for an employer to determine what provisions of the standard apply.

Use of an action level also improves workers protection while increasing the cost-effectiveness and performance orientation of the standard. Employers able to achieve exposure conditions below the action level will be encouraged to maintain this status to reduce their monitoring and medical surveillance expenses. At the same time their employees will be further protected because their exposures will be less than half of the TWA. Where it is not feasible to reduce exposures below the action level, employees will continue to receive the protection afforded by regular exposure monitoring and periodic medical surveillance.

Some commenters (Exs. 11–5, 11–83, 11–125) argued that achieving the action level should not be reason for allowing employers to discontinue routine monitoring of employees. For example, Merry K. Holthof, Central Service Supervisor for the Grand Rapids Osteopathic Hospitals, observed:

> * * * [I]t is necessary for some type of periodic monitoring to be conducted to insure that the levels of Ethylene Oxide are remaining at the action level. There are variable factors * * * that may have an effect on the levels of Ethylene Oxide (including) equipment breakdown or new employees * * * OSHA (should) set down a recommendation for periodic monitoring to insure that the level of EtO remains at the action level (Ex. 11–125).

The rationale for setting an action level has been discussed in connection with several other OSHA health standards. (See, for example, inorganic arsenic, 1910.1018(b); vinyl chloride, 1910.1017(b); and acrylonitrile, 1910.1045(b)). In brief, although all employee exposure measurements on a given day may be below the TWA, it is possible that on days when no measurements are taken, an employee's actual exposure may unknowingly exceed the TWA. Similarly, where employee exposure measurements are above one-half of the TWA (i.e., the action level), the employer cannot be confident that his employees may not, at some time, be exposed above the TWA (Ex. 6–26). However, requiring periodic exposure monitoring when exposures are above the action level does permit the employer to have confidence that employee exposures are in fact below the TWA when monitoring data so indicate.

It is noted here, however, that even if the employer has controlled exposures to below the action level, paragraph (d)(5) of the final rule requires reinstitution of exposure monitoring "when there has been a change in the production process, control equipment, personnel or work practices that may result in new or additional exposures to EtO or when the employer has any reason to suspect that a change may result in new or additional exposures."

The definition of "employee exposure" incorporates the proposed language which specified that employee exposure means that exposure which would occur if the employee were not using a respirator and that employee exposure measurements are to be made without regard to the use of respiratory protection. Several commenters took issue with this definition, contending that breathing zone sampling does not reflect the actual exposure of an employee who is being protected by a respirator. Although this statement may apply in certain circumstances, it overlooks the fact that exposure monitoring is not a single-purpose activity. It is necessary to know employee exposure levels without the use of respiratory protection to evaluate the effectiveness of the required engineering and work practice controls and to determine whether additional controls must be instituted. In addition, monitoring is necessary to determine which respirator, if any, must be used by the employee, and it is also necessary for compliance purposes.

The potential health effects associated with high EtO exposures have necessitated the adoption of provisions dealing with emergency situations where unexpected significant releases of EtO may occur. The proposal defined "Emergency" as "* * * an unexpected massive release of EtO." However, the meaning of the term "massive" could be confusing and might be difficult to define for enforcement purposes, as pointed out by several commenters (Exs. 11–145, 44, 103, 142, Tr. 364). This is particularly true since EtO is a gas, which means that even "massive" releases would not cause visible leaks or spills. In addition, EtO's warning properties are poor, since levels as high as 700 ppm are required before it has a noticeable odor.

The industrial uses of EtO could give rise to several types of emergencies, but many of these are already covered by existing OSHA standards. For example, emergency situations that could result in an explosive mixture of EtO are addressed in 29 CFR 1910.106, and those that could result in skin burns are regulated under 29 CFR 1910.132. Situations that cause chronic health effects are covered by the PEL provision of the final EtO rule. The emergency situations that OSHA is concerned about preventing with this emergency situation provision are those having the potential to produce acute toxic effects

among inadvertently exposed employees. The acute toxic effects of concern are short-term and reversible effects such as eye or respiratory irritation, skin rashes, headache, nausea and dizziness.

To clarify that the intent of this provision is to protect employees from unexpected and substantial releases of EtO, OSHA has defined "Emergency Situations" as "an occurrence such as but not limited to equipment failure, rupture of containers, or failure of control equipment that may result in an unexpected significant release of EtO." Quantities of EtO sufficient to produce acute toxic effects in exposed employees would constitute such an emergency. Although individual variability among workers makes it difficult to quantify with precision what EtO levels may cause acute toxic effects, acute effects may be expected to occur from exposures resulting from the rupture of a flange, valve or pump seal, failure of a check valve on an EtO tank, or failure of a ventilation system over a sterilization chamber or liquid sampling station.

Paragraph (c) Exposure Limits

In the final rule for EtO, OSHA has revised the permissible exposure limit for EtO by amending the current 50 ppm standard contained in 29 CFR 1910.1000, Table Z-1, for all affected industry sectors. The final standard sets an 8-hour time-weighted average (TWA) limit of 1 ppm in paragraph (c) of § 1910.1047. The basis for promulgating this exposure limits is discussed below.

Permissible Exposure Limit

As discussed in the risk assessment section above, OSHA concludes that occupational exposure to EtO presents an excess cancer risk of 634 to 1,093 deaths per 10,000 employees exposed at the current OSHA limit of 50 ppm (TWA). The final rule, which sets an 8-hour TWA of 1 ppm, will achieve a 98 percent reduction in cancer mortality risk, for an excess of 12 to 23 deaths per 10,000 employees. OSHA believes that the remaining risk at the 1 ppm limit is still significant, but that the 1 ppm limit reduces the risk to the extent feasible. Most rulemaking participants commenting on the PEL agreed that revision of the current PEL was necessary, and many commenters agreed that a 1 ppm PEL was appropriate (Exs. 2-11, 4-21, 4-26, 4-41, 11-25, 11-38, 11-47, 11-57, 11-69, 11-71, 11-74, 11-77, 11-98, 36, 89). The significance of the risk associated with the existing EtO standard has been acknowledged by employers, who have reacted to information regarding the potential health effects of EtO by voluntarily reducing exposure among their employees, as noted above in the Summary of Technological Feasibility.

As discussed in other sections of this preamble, OSHA is confident that an 8-hour TWA of 1 ppm is technologically feasible in the sectors that will be principally affected by the final rule for EtO. The technologies necessary to achieve this level of control consist of conventional equipment and widely accepted work practices. These technologies and practices are already in use by firms in each of the affected sectors, and have permitted many facilities to achieve the 1 ppm level mandated by the final rule. In addition, OSHA has determined that sampling and analytical methods are available to detect an airborne concentration of 1 ppm EtO (8-hour TWA) within the ±25 percent accuracy requirement set forth by paragraph (d)(6) of the final rule.

The final rule also includes an action level of 0.5 ppm (8-hour TWA) with less stringent accuracy requirements for sampling and monitoring. Where it is feasible to do so, OSHA believes that many employers will choose to achieve the action level with engineering and work practice controls, in order to provide additional employee protection and to reduce their compliance expenditures.

OSHA is reserving decision today on the question of whether the standard should contain a STEL. OSHA takes this action largely in response to reservations expressed by the Office of Management and Budget (OMB) to STEL provisions in the draft final standard delivered by OSHA to OMB pursuant to Executive Order 12291. OSHA concurs that these matters are important and merit further consideration. OMB's comments have been entered into the docket of this rulemaking. Ex. 162 OMB has raised questions concerning:

—Quantification of the risk avoided by issuance of the STEL;
—The appropriateness of relying on studies by Hemminki, Yager, and Johnson & Johnson as partial support for the issuance of a STEL;
—A decision by ACGIH not to recommend a STEL for EtO; and
—The economic and technical feasibility of a STEL without the use of respirators.

To develop the fullest possible administrative record, both OSHA's draft final standard and OMB's comments will be submitted to a number of scientifically qualified peer reviewers for comment, analysis, and criticism. The peer reviewers will file statements to be placed in the public docket.

Public comment on the statements filed by the peer reviewers and the issues raised by OMB will be solicited in a **Federal Register** Notice to be published in approximately 30 days. A reasoned decision by OSHA on the STEL will be published by OSHA in the **Federal Register** in about six months.

OSHA notes that the standard does not require installation of engineering controls until one year from the effective date of this rule. A decision on these STEL issues will be made well in advance of that compliance deadline.

OSHA anticipates that, if the process described above results in adoption of a STEL with a feasible engineering control compliance requirement, the deadline for installation of the engineering controls required by the STEL will be a year from the effective date of this standard—the date by which feasible engineering controls must be installed to reduce exposure to 1 ppm 8 hour TWA.

The PEL for EtO has been set at 1 ppm because OSHA believes that this new exposure limit will substantially reduce the significant risk associated with current EtO exposures and that the 1 ppm level is feasible for most operations in most workplaces that use EtO.

Paragraph (d) Exposure Monitoring

Section 6(b)(7) of the Act (29 U.S.C. 665) madates that any standard promulgated under section 6(b) shall, where appropriate, "provide for monitoring or measuring of employee exposures at such locations and intervals, and in such a manner as may be necessary for the protection of employees." The primary purpose of monitoring is to determine the extent of employee exposures to EtO.

Exposure monitoring informs the employer whether the employer meets the obligation to keep employee exposures below the 8-hour TWA exposure limit. Exposure monitoring also permits the employer to evaluate the effectiveness of engineering and work practice controls and informs the employer whether additional controls need to be installed. In addition, Section 8(c)(3) of the Act (29 U.S.C. 657(c)(3)) requires employers to notify promptly any employee who has been or is being exposed to toxic materials or harmful physical agents at levels that exceed those prescribed by an applicable occupational safety or health standard. Finally, the results of exposure monitoring are part of the information that must be supplied to the physician, and these results may contribute information on the causes and prevention of occupational illness.

Paragraph (d) of the final rule contains the standard's requirements related to the monitoring of employee exposure. These provisions are essentially unchanged from the proposal, with one exception. The language of paragraph (d)(1)(ii) concerning the term "representative monitoring" has been simplified in response to comments received into the record.

The final rule contains an 8-hour TWA permissible exposure limit and an action level that acts to alert employers of cases where existing exposures are approaching the PEL. The interrelationship among these three exposure levels determines the frequency at which employers are obligated to monitor employee exposures. There are three possible exposure scenarios that will determine the frequency of monitoring required. The table below lists these three exposure scenarios, along with the monitoring frequency for each.

Exposure scenario	Required monitoring activity
Below the action level	No monitoring required.
At or above the action level, but at or below the TWA.	Monitor exposures 2 times per year.
Above the TWA	Monitor exposures 4 times per year.

As is shown by the table above, the action level trigger largely determines whether employers must monitor employee exposure to EtO.

Under the two possible scenarios where the action level is exceeded, the employer must monitor employee exposures. The frequency required for monitoring such exposures is determined by whether the action level or PEL is exceeded.

The monitoring provisions contained in the proposed standard were addressed by a large number of commenters; two major issues were discussed. First, many participants commented that sampling and analytical methods were not available for measuring EtO with the accuracy and precision required by the proposal (Exs. 4–20, 4–24, 4–28, 11–27, 11–54, 11–65, 11–74, 11–76, 11–133, 11–141, 11–142, 11–146, 11–147, 11–151, 37, 109). Second, commenters addressed the specifications for monitoring frequency contained in the proposed standard (Exs. 11–25, 11–38, 11–48, 11–57, 11–74, 11–125, 11–133).

The availability and feasibility of monitoring methods to measure exposures to EtO accurately and precisely were demonstrated by evidence in the record, which is discussed in the Summary of Economic Impact and Regulatory Flexibility Analysis section of the preamble. In that section, OSHA concluded that there are at least three currently available methods that have sufficiently low limits of detection to measure EtO with the accuracy specified by the standard (at the 95 percent confidence level, ±25 percent at the 1 ppm TWA, and ± 35 percent at the 0.5 ppm action level).

Several commenters requested that OSHA not specify a frequency for monitoring employee exposure levels (Exs. 11–25, 11–57, 11–74, 11–133, 11–141). For example, G.J. O'Rourke, Engineering and Technical Manager for SunOlin Chemical Company, stated:

> We believe there is no need to have a rigid schedule for monitoring. The schedule should merely require employers to monitor according to a plan, which [when] implemented, shows compliance (Exs. 11–25).

The EOIC also addressed this point:

> The EOIC believes that the precise frequency of monitoring should not be specified by OSHA. Instead, OSHA should leave the frequency of monitoring to the judgment of industrial hygiene experts and should only require that monitoring be done according to a written plan that, if implemented will adequately demonstrate that the employer is in compliance with the PEL (Ex. 11–57).

However, OSHA believes that the monitoring frequency specified in the final standard is a minimal requirement, and that many employers will wish to conduct more frequent monitoring to ensure employee protection and compliance with the standard. Clearly, the more frequent the measurements, the greater the reliability of the resulting employee exposure profile. In addition, periodic measurement is appropriate when employee exposures are at or above the action level, because relatively minor changes in the process, materials or environmental conditions might increase the airborne concentration of EtO to levels above the standard's PEL.

Several commenters who submitted information to the docket supported OSHA's requirement for monitoring every 6 months if EtO levels were at or below the TWA and every 3 months if the TWA was exceeded (Exs. 11–38, 11–125). For example, Brian J. Kuske and Deloa Pitt, of St. Mark's Hospital in Salt Lake City, stated:

> St. Mark's Hospital has concluded that * * * (m)onitoring of the environment can be accomplished on a regular basis and recommends a minimum of twice a year * * *. (Ex. 11–38).

Merry K. Holthof, Central Service Supervisor for the Grand Rapids Osteopathic Hospital, commented:

> I feel that OSHA needs to * * * set down a recommendation for periodic monitoring to ensure that the level of EtO remains at the action level. I personally feel that monitoring should take place every six months for this purpose. This would also help avoid employer complacency regarding this issue. It is unfortunate, but also realistic, that rules and regulations are necessary to keep standards high (Ex. 11–125).

The final rule does not require periodic monitoring and measurement for the TWA when initial monitoring data reveal exposures below the 0.5 ppm action level because exposures below the action level provide a margin that makes it unlikely that minor changes in processes, materials or environmental conditions will result in exposures above the PEL.

However, the standard requires that whenever there has been a production, process, or control change that may result in new or additional exposures to EtO, or whenever the employer has any other reason to suspect an increase in employee exposures, the employer shall again initiate the required monitoring for those employees affected by such a change or increase.

The final standard also provides that an employer may discontinue periodic monitoring for those employees for whom two consecutive measurements, taken at least 7 days apart, show exposures to be below the action level. Where employee exposure measurements are at or below the PEL but are at or above the action level, the employer may alter the monitoring schedule for those employees from quarterly to semiannually if two consecutive measurements, taken at least 7 days apart, confirm this reduction in levels.

As previously discussed, Section 8(c)(3) of the Act (29 U.S.C. 657(c)(3)) requires employers to notify promptly any employee who is exposed to levels in excess of the PEL. The final EtO standard requires the employer to notify each employee in writing of that employee's measurement within 15 working days after receipt of the results of any measurements required under paragraph (d) of the standard, whether exposure measurements were above or below the PEL.

The final standard, like the proposal, does not require a specific monitoring procedure to be used but does include a performance requirement for the method chosen. OSHA recognizes that the accuracy of monitoring and measurement will decrease as EtO concentration levels decrease below 1 ppm and that breathing zone (BZ) samples provide the most representative indication of an employee's exposure. The final standard, therefore, requires

BZ samples to be taken to determine exposures for comparison with the PEL. Additionally, the final standard requires an accuracy of plus or minus 35% for measurements of employee exposures at the action level, and plus or minus 25% for measurements of exposures at the 1 ppm TWA.

These accuracy requirements are feasible, as shown in the Summary of the Regulatory Impact and Regulatory Flexibility Analysis section of the preamble, and are intended to provide the employer with a degree of confidence in his or her sampling results. As noted earlier, monitoring is carried out for the purpose of determining what measures are necessary to ensure employee protection in a given operation. OSHA anticipates that the standard's flexible criteria for sampling methodology will enable employers to perform the required monitoring without difficulties. The monitoring requirements in this standard are similar to those found in other toxic substance standards promulgated by OSHA (see vinyl chloride, acrylonitrile, coke oven emissions, asbestos, arsenic) and the Agency believes that these standards have been met without difficulty, thus indicating that compliance with the EtO rule should also be feasible.

Finally, several commenters requested clarification of the meaning of the phrase "representative monitoring" as used in paragraph (d)(1)(ii) of the proposed standard (Exs. 11–57, 11–133, 11–137). For example, the EOIC stated:

> In the preamble * * * to the proposed regulation, OSHA makes clear that it intends to allow companies to use representative monitoring for groups of employees where their work exposures to EO are similar. The proposed regulation itself is somewhat ambiguous in this regard. OSHA should make clear in the text of the final regulation that representative monitoring is appropriate and that terms such as "each employee" or "each such employee" refer to each employee or to a representative of a group of employees (Ex. 11–57).

The exposure monitoring provisions require the employer to determine the exposure for each employee exposed to EtO. This does not require separate measurements for each employee. If a number of employees perform essentially the same job under the same conditions, it may be sufficient to monitor a fraction of such employees to obtain data that are representative of the remaining employees. Representative personal sampling for employees engaged in similar work and exposed to similar EtO levels can be achieved by measuring that member of the exposed group who can reasonably be expected to have the highest exposure. This result would then be attributed to the remaining employees of the group.

In many specific work situations, the representative monitoring approach can be more cost-effective in identifying the exposures of affected employees. However, employers may use any monitoring strategy that correctly identifies the extent to which their employees are exposed.

OSHA has rewritten paragraph (d)(1)(ii) of the proposal to clarify, as discussed above, the requirement for representative monitoring. However, the intent of the provision is identical to that of the proposal.

Paragraph (d)(2)(ii) contains a provision designed to eliminate unnecessary and redundant exposure monitoring. It permits employers who have monitored employee exposures to EtO within the one-year period immediately preceding publication of this final rule in the **Federal Register** to forego the initial monitoring required by paragraph (d)(2)(i) if the results of monitoring within this period have shown that their employees are not exposed to EtO levels at or above the action level. OSHA is aware that most workplaces in many EtO-using industries have already monitored employee exposures. For example, OSHA estimated that all facilities in the EtO producer sector had already performed initial monitoring, and that 87 percent of all hospitals had also done so (Ex. 6–22).

The (d)(2)(ii) provision simply makes clear that OSHA does not intend employers who have voluntarily performed employee monitoring to be required to repeat such monitoring if they have reliable and objective data showing that their employees are not exposed to EtO at the action level, which triggers several of the standard's provisions, e.g., medical surveillance, periodic monitoring, training. Thus, OSHA believes that paragraph (d)(2)(ii) will enhance the cost effectiveness of the standard's monitoring requirements without compromising employee protection.

Paragraph (e) Regulated Areas

This paragraph of the final standard requires employers to identify as regulated areas any locations in their workplaces where there may be occupational exposures to airborne concentrations of EtO above the PEL. In addition, only authorized persons may enter regulated areas, which are required to be clearly marked to ensure that employees are aware of these locations. Taken together, these provisions are intended to increase the standard's effectiveness by limiting the number of employees exposed above the PEL.

Rulemaking participants commented on two aspects of the regulated areas paragraph of the proposal: the language used to describe the conditions that would trigger designation of an area as regulated and the degree of specification versus performance language embodied in the requirements in this paragraph. These issues are discussed below.

Several representatives of industry objected to the wording of the proposal's regulated area requirement (Exs. 11–48, 11–74, 11–125, 142), which specified that employers must establish regulated areas "wherever the airborne concentration of EtO is above 1 ppm." They argued that, as written, the proposed language could be interpreted to mean that a regulated area was required to be established in "an area of a facility where the ambient level of EtO is greater than 1 ppm but which, if the employees were personally monitored, would result in an eight-hour TWA which is likely to be far below even the action level" (Ex. 142).

In a similar vein, the Health Industry Manufacturers Association stated:

> The proposal is ambiguous because it might be said to require regulated areas wherever [the] ambient EtO concentration exceeds 1 ppm (TWA) rather than where actual employee exposures are above 1 ppm (Ex. 11–74).

Some of these commenters (Exs. 11–48, 11–74) also inquired whether the standard would require area monitoring to establish the location of regulated areas.

In response to these commenters, OSHA has changed this provision to clarify its intent. The final rule requires employers to establish regulated areas "whenever there may be occupational exposures" in excess of the PEL. This language better communicates OSHA's purpose—to enhance employee protection by alerting employees about the location of workplace areas that might increase their exposures to levels above the PEL. The final standard therefore requires establishment of regulated areas only where potential occupational exposures above the PEL may occur, thus clarifying the link between employee exposures and regulated areas. This change will also eliminate any confusion about ara monitoring to establish the location of regulated areas. The final rule's identification of employee exposures rather than area EtO concentrations as the basis for establishing a regulated

area makes it clear that employee rather than area monitoring is required.

The second issue raised by commenters in relation to this paragraph of the proposal concerned the degree of specification that should be included in the requirements of the final standard's regulated areas provision. The proposal specifically stated that employers could demarcate regulated areas in any manner that would serve to limit the number of employees entering such areas. Permitting employers to choose how best to identify and limit access to regulated areas is consonant with OSHA's belief that employers are in the best position to make such a determination based on the physical configuration and other aspects of their particular workplaces.

Some rulemaking participants, however, commented that the standard should specifically identify the workplace locations to be designated as regulated areas (Exs. 4–25, 44). For example, the testimony of the American Federation of State, County and Municipal Employees (AFSCME) states

> Regulated areas should be established *wherever* EtO storage, EtO sterilization or aeration expose workers to any amount of EtO, or could expose them in the event of a malfunction, leak or other mishap (Ex. 44).

In contrast to AFSCME's views were those of several commenters who argued that the language of the proposed provision was too specification-oriented (Exs. 4–15, 4–47, 4–51, 4–55). For example, R. Parlante, Director of Lederle Laboratories' Safety and Environmental Services Division, stated

> It is not necessary to establish provisions * * * as part of the EtO standard for * * * regulated areas * * * Once an EtO performance standard is established, the methodology used [by the employer] to achieve compliance should be flexible * * * (Ex. 4–55).

OSHA believes that, as written, the requirements of paragraph (e) strike the right balance between specification and performance language. If, as AFSCME suggested. OSHA required employers to establish regulated areas wherever workers could be exposed to EtO in the event of a leak or malfunction, many areas of the plant that actually have low or non-existent EtO concentrations under normal operating conditions would have to be designated as regulated. OSHA believes that the final rule clearly sets forth the employer's obligation to maximize employee protection by informing employees of the location of workplace areas having EtO concentrations that will increase their exposures above the PEL. At the same time, this paragraph permits employers to determine where employees might be overexposed in any particular workplace.

At the same time, employers are free to choose whether to use, for example, ropes, markings, temporary barricades, gates, or more permanent enclosures to demarcate and limit access to these areas. Factors that employers might consider in determining the type of identification system used to demarcate regulated areas include the configuration of the area in question, whether the regulated area is permanent, the airborne EtO concentration, the number of employees in areas adjacent to the regulated area, and the period of time the area is expected to have exposure levels above the PEL.

Paragraph (f) Methods of Compliance

The final standard, like the proposed standard, requires employees to institute engineering and work practice controls to reduce the exposures of employees to or below the permissible exposure limit, to the extent feasible. If engineering and work practice controls have been implemented but have not been sufficient to reduce exposures to the permissible limit, respirators selected in accordance with paragraph (g) shall be used to suppplement the engineering and work practice controls.

OSHA has identified several operations where engineering controls generally are not feasible and has listed them in paragraph (f)(1)(iii). In addition, in situations where engineering controls and work practices are demonstrated as not being feasible, respirators appropriate for the airborne EtO concentration and selected in accordance with Table 1 of paragraph (g) must be used to reduce employee exposures.

These requirements are consistent with OSHA's traditional policy regarding the hierarchy of controls. This hierarchy specifies that engineering and work practice controls be used in preference to personal protective equipment; personal protective equipment may only be used in emergencies or where other methods are not feasible, not adequate, or have not yet been installed. Engineering controls involve the installation of equipment, such as forced ventilation, or the modification of a process, for example by enclosing it. Work practice controls reduce worker exposures by altering the manner in which a task is performed. An example of a work practice control would be to train a tank car loader to stand up-wind rather than down-wind of the tank car's hatch when loading a hazardous substance.

Respirators have traditionally been accorded the least preferred position in the hierarchy of controls because of the many problems associated with their use. For example, the effective use of respirators requires that they be individually selected and fitted, conscientiously worn, carefully maintained, and replaced when necessary; these conditions may be difficult to achieve and to maintain consistently in many workplace environments.

At present, the Agency is reviewing the health benefits, appropriateness, and cost-effectiveness of the hierarchy of controls concept, and has recently published two Advance Notices of Proposed Rulemaking relevant to this subject (47 FR 20803, May 14, 1982, Respirators; 48 FR 7473, February 22, 1983, Methods of Compliance). Because OSHA is interested in determining whether and in what situations greater reliance might be placed on the use of respirators, the EtO proposal requested comments on the use of respirators for EtO exposure. Many participants in the EtO rulemaking submitted information to the record on the general subject of control strategy and on the appropriate use of respirators in the handling, storage, and use of EtO in the workplace. The record evidence on these issues is summarized below.

Many commenters reported that they preferred to rely on engineering and work practice controls to reduce employee exposure to EtO (Exs. 11–38, 11–40, 11–45, 11–70, 11–87). For example, Donna Swenson, Central Service Supervisor and Chairman of the EtO Committee of Rockford Memorial Hospital (RMH), stated:

> At RMH we feel that it is possible with the use of appropriate engineering and workplace controls to comply with the proposed standard. Respirators should not be needed except during emergency situations, such as leakage of a tank or canister (Ex. 11–81).

Similarly, Brian J. Kuske, Assistant Administrator of St. Mark's Hospital in Salt Lake City, commented:

> After review of the exposure levels recommended by OSHA (in the proposal), St. Mark's Hospital has concluded that * * * respirators are not essential (to meet the 1 ppm requirement) (Ex. 11–38).

The views of these and other commenters generally provided support for the determination made by OSHA at the time of the proposal:

> The (control) methods that can be used to reduce employee exposure to EtO are conventional technology such as * * * exhaust ventilation, double mechanical seals, leak detection and use of respiratory

protection for intermittent exposures (48 FR 17298).

Evidence submitted at the hearing and in post-hearing comments has identified a number of intermittent exposure situations in EtO-using facilities where respiratory protection may be needed to protect workers from hazardous exposures. For example, in the EtO production sectors, several commenters stated that respirators would be needed for maintenance and repair activities and during the loading/unloading of tank cars (Exs. 11-110, 11-131, 11-133, Tr. 863).

Edward J. Kerfoot, Director, Toxicology and Industrial Hygiene for BASF Wyandotte Corporation, stated that, "Respirators should be allowed in other operations in addition to maintenance and repair. In industry, examples would be bulk loading and unloading operations" (Ex. 11-131). Two ethoxylator firms, Nalco Chemical Company and PPG Industries, Inc., also stated that in loading/unloading operations respirators would be required to achieve compliance with the standard (Exs. 11-69, 11-105).

The EOIC also indicated that the use of respirators would be necessary during maintenance, repair, and tank car loading/unloading activities (Ex. 11-57). In addition, the EOIC suggested that "* * * companies may need to use respirators during start-up and shut-down and during certain laboratory operations" (Ex. 11-57). OSHA also recognizes that unexpected release of EtO might occur during shut-down and start-up because processes are not operating in steady-state conditions, and the use of respirators may be appropriate in such situations.

OSHA agrees that some EtO operations do not lend themselves to control through engineering means. Respirators are permitted for the operations cited by commenters above, if other methods of control are demonstrated by the employer to be infeasible.

A number of commenters addressed the need for the limited use of respirators in the industry sectors that use EtO for sterilization (Exs. 11-47, 11-54, 11-57, 11-74, 11-94, 11-109, 11-112, 11-113, 11-136, 11-139, Tr. 873). Deborah M. Badger, Senior Counsel for the American Hospital Supply Corporation, proposed a list of activities where respirators might have to be worn during the sterilization of medical products:

> * * * employees using EtO as a sterilant are primarily exposed in an intermittent or episodic fashion. Thus, critical work tasks can be identified which, although short in duration, constitute the critical opportunity, for exposures to levels higher than a reasonable PEL. American [Hospital Supply Corporation] proposes that OSHA permit the limited use of respiratory protection equipment during the following work tasks:
>
> • Opening sterilization chamber doors.
> • Unloading sterilization chamber contents.
> • Delivering freshly sterilized goods to the outgassing area.
> • Entering outgassing areas to collect quality control samples.
> • Performing maintenance and repair work on sterilization equipment
> • Changing EtO cylinders (Ex. 11-47).

OSHA agrees that, depending on workplace conditions, respirators may be necessary when employees enter a sterilization chamber for unloading and when they enter heated off-gassing rooms to collect quality control samples. However, as discussed previously in the section dealing with feasibility, evidence indicates that most EtO sterilizing operations can be controlled by currently available engineering controls. Thus, OSHA does not feel that it is appropriate to provide a general allowance for the use of respirators for all short-term EtO operations.

Based upon evidence in the rulemaking record and the Regulatory Analyses, OSHA has found that the use of engineering and work practice controls will reduce employee exposure to or below the PEL for practically all situations. OSHA recognizes that there are some situations where engineering controls are not generally feasible. Rather than continuing to enforce the engineering control provisions in these cases, OSHA has indicated in the regulatory text, paragraph (f)(1)(iii), those operations where engineering controls are generally not feasible. For these situations, OSHA will have to bear the burden of proof, in the enforcement context, to show that engineering and work practice controls are feasible for that specific condition. In addition, OSHA recognizes that there will be other situations where engineering controls may not be feasible due to a unique feature or condition. For example, work involving repair of leaks may not lend itself to engineering controls. These situations are recognized in paragraph (f)(1) of the final rule, which permits the use of approved respiratory protection where employers can demonstrate that engineering and work practice controls are not feasible. In such situations, the burden of proof of infeasibility is appropriately placed on the employer, because the employer is familiar with operations in the workplace and is therefore in the best position to evaluate various types of controls as they apply to that particular workplace. It is noted here, however, that employers may raise the issue of feasibility in an enforcement action. As noted in a decision on OSHA's lead standard, the court in United Steelworkers of America v. Marshall, 647 F. 2d 1189 (D.C. Cir. 1980):

> * * * An employer who is cited for failing to meet the standard in a particular operation, and who believes the standard has proved technologically infeasible for that operation, can claim this "specific" infeasibility as a defense in an enforcement proceeding * * * Thus an OSHA standard remains subject to a * * * test of feasibility with respect to special difficulties in certain operations.

However, in the great majority of workplaces affected by the final standard, OSHA believes that engineering and work practice controls will limit worker exposures to levels below the PEL. The technology needed to control employee exposures to these levels represents generally available and traditional technology, such as general and local ventilation, pump seals, and aeration chambers. This technology is discussed in detail in the Technological Feasibility section of this preamble.

The requirements contained in paragraph (f)(2) of the permanent standard describe the employer's written compliance program. The requirement for a written compliance program to reduce exposure by means of engineering and work practice controls, contained in paragraph (f)(2)(i), applies where employee exposures are at or above the PEL.

Few commenters objected to the provisions of the proposed standard requiring employers to develop a written compliance program. One commenter, Thomas F. Evans, Director of Regulatory Management-OSHA for the Monsanto Company, objected to the inclusion of a schedule of leak detection in the required compliance program, as required by paragraph (f)(2)(ii) (Ex. 11-98). Mr. Evans objected that "Such a requirement is not performance oriented" (Ex. 11-98). Although the final rule does not mandate a frequency for leak detection, OSHA believes that leak detection should be included in any effective program for controlling employee exposures to EtO because early and prompt leak detection helps to eliminate emissions of EtO at their source. This is particularly true where fugitive emissions are a potential source of exposure.

Many commenters endorsed the idea of including a compliance program provision in the standard (Exs. 11-68, 21-8, 44). For example, Howard L.

Kusnetz, Manager of Safety and Industrial Hygiene for Shell Oil Company, stated:

> Shell Oil Company endorses the concept of written control programs prepared by the employer if employee exposure exceeds the PEL. A requirement for a written control program ensures affirmative action by the employer and communication with employees (Ex. 11-68).

Peter Roy described some of the reasons for and elements of a compliance program:

> I endorse the necessity for employers to develop written compliance plans * * *. Written programs and procedures should be established regardless of the number of exposed employees. The development of documented programs and procedures is already a well established and common practice in both hospitals and the medical device industry. These policies and procedures are important for the employee communication and training programs necessary to ensure the "human element" of the EtO exposure control system. Written plans should be reviewed annually, and might vary from fairly simple to quite complicated depending on the size and scope of the EtO process, and number of employees in a given facility (Ex. 21-8).

OSHA believes that the written plan is an essential element of the compliance program since it will encourage employers to implement the necessary controls to reduce employee exposure. It also provides the information to allow OSHA, the employer and employees to examine the control methods chosen and to evaluate the extent to which these planned controls are being implemented in the workplace. As with other OSHA rulemakings, the written compliance plan is to be accessible to the individuals designated in paragraph (f)(2)(iii) for inspection and copying. This implements section 8(c)(3) of the OSH Act, which provides for the employer to inform employees of correction actions being taken to lower exposure to the PEL.

Paragraph (f)(2)(iv) prohibits the use of employee rotation as a method of reducing exposure to EtO. On the other hand administrative controls, which utilize methods such as scheduling to reduce a particular employee's total exposure, is an acceptable compliance strategy. An example of acceptable use of scheduling is performing an operation where EtO exposure occurs on the work shift with the fewest employees present. Worker rotation, however, has been determined by OSHA to be inappropriate in workplaces involving exposures to potential human carcinogens. Although administrative controls may reduce the cumulative risk of cancer among a particular group of workers, their use places a larger total number of workers at risk. Paragraph (f)(2)(iv) specifically prohibits the use of worker rotation in situations involving exposure to EtO. As noted in the preamble to OSHA's proposed rule for ethylene dibromide (48 FR 45984):

> Administrative controls * * * are not permitted in lieu of engineering controls or limited respirator usage. The use of this control practice (worker rotation) increases the population of employees at risk from exposure * * *.

Industry representatives generally condemned the practice of employee rotation as a method of reducing exposure to EtO (Tr. 971, 1041). For example, G. Briggs Phillips, HIMA's Senior Vice President for Scientific Affairs, stated, "* * * HIMA does not support and our companies do not intend to use, worker rotation practices" (Tr. 1041). Although Duane Amato, the Corporate Manager of Occupational Health Services and Safety at Travenol Laboratories, testified that worker rotation is an acceptable method of reducing 8-hour TWA exposures (Ex. 75, Tr. 871), Lawrence Rampy, testifying on behalf of the EOIC, strongly disagreed:

> Structuring jobs simply to reduce exposure and to avoid other means of controlling exposure is simply not acceptable. In other words, the exposure of each job must be evaluated and structured to achieve acceptable exposure by a variety of means but not by rotation of different people through a high exposure task in order to achieve a net average exposure below some limit. (Tr. 971).

The prohibition against worker scheduling or rotation contained in the final standard for EtO is, therefore, consistent with OSHA's view that this control strategy is not appropriate in occupational environments involving exposure to potential carcinogens.

Paragraph (g) Respiratory Protection

The final standard provides that respirators be used to limit employee exposure to EtO in the following circumstances:

(i) During the interval necessary to install or implement feasible engineering and work practice controls;

(ii) In work operations such as maintenance and repair activities or vessel cleaning or other activities for which the employer establishes that engineering and work practice controls are not feasible;

(iii) In work situations where feasible engineering and work practice controls are not yet sufficient to reduce exposure to or below the TWA or STEL; and

(iv) In emergencies.

The final standard also requires that the employer provide respirators at no cost to employees and ensure that employees use them.

Comments regarding the appropriate use of respirators were addressed above in Section 6, Paragraph (f) *Method of Compliance*, and will not be discussed further in this section. However, numerous commenters addressed the issue of appropriate respirator selection (Exs. 4-15, 4-19, 4-22, 4-25, 2-40, 4-45, 4-55, 11-57, 11-74, 11-76, 11-94, 11-99, 11-111, 11-113, 11-133, 11-136, 11-152, Tr. 857, 893). These commenters provided information on two types of respirators that were specified in Table 1 of the proposed EtO standard:

- Full-facepiece respirators with organic vapor gas mask canisters.
- Positive-pressure, supplied-air respirators with full-facepieces.

Addressing OSHA's specification for organic vapor canister respirators for EtO concentrations of 50 ppm or less, most commenters argued that this type of respirator provided inadequate protection against EtO exposure (Exs. 4-25, 11-57, 11-74, 11-99, 11-111, 11-136, 11-152, Tr. 857). The inadequacies of chemical cartridge respirators were documented by Matthew Gillen, representing the Amalgamated Clothing and Textile Workers Union (ACTWU):

> * * * The chemical cartridge respirator has not been certified (for EtO) by NIOSH * * * because EtO lacks adequate warning properties and is not generally detectable by smell until levels of 250-700 ppm are reached * * *. The other major problem with chemical cartridge respirators is migration. In testing performed on the canister, it was demonstrated that the cartridge could withstand several hours of exposure without penetration. However, after setting several hours, the EtO "migrated" within the canister, so that penetration was observed upon re-use (Ex. 4-25).

Frederick G. Giel, Senior Attorney for Miles Laboratories, Inc., agreed:

> The standard specifies that NIOSH/MSHA full facepiece respirators approved for organic vapors can be used in certain instances where EtO vapors remain below 50 ppm. Miles (Laboratories) understands that studies exist which show that these respirators purify breathing air for only a matter of minutes before significant EtO breakthrough occurs (Ex. 11-111).

Anthony J. Vetrano, Attorney for Abbott Laboratories, stated:

> * * * Because various companies have tested full facepiece respirators with organic vapor gas mask canisters and found them unsuitable for use with EO, Abbott believes that Table 1 (of the EtO standard) should specify only canisters with specially impregnated charcoal that are designed for use with EO (Ex. 11-136).

A number of companies, including Dow Chemical Company (Ex. 4–31), A.E. Staley Manufacturing Company (Ex. 4–22), De Soto, Inc. (Ex. 4–15), and others (Exs. 4–45, 11–94, 11–113,), stated that they use air-supplied respirators rather than air-purifying respirators in operations that require respiratory protection.

Based on this evidence, OSHA has revised Table 1, referenced in paragraph (g)(2), to permit the use of NIOSH/MSHA-approved air-purifying respirators with canisters containing sorbents especially designed for EtO removal if such equipment is approved in the future. OSHA is aware that no air-purifying respirators for EtO have been approved by NIOSH or MSHA. However, one respirator manufacturer has applied to NIOSH for certification of an EtO-specific canister respirator (Exs. 6–27, 11–112, Tr. 891). This provision of the final rule is intended to allow the use of this or similar products when and if they are granted NIOSH/MSHA approval.

A number of commenters requested that half-mask respirators be allowed in lieu of the full-facepiece respirators that were proposed for airborne EtO levels of 2,000 ppm or lower (Exs. 11–57, 11–133, 11–98, 11–136, 76). The following comments were submitted by the EOIC:

> The EOIC industrial hygiene task force believes that the respiratory protection table contained in the proposed standard should be revised so as to allow the use of half-face supplied air respirators at or below 1,000 ppm. At those levels, a half-face positive pressure respirator will provide adequate protection. Contact with EO at that level would not cause eye irritation, so there is no reason to prohibit such respirators (Ex. 11–57).

However, these commenters provided no objective data to show that EtO is not an eye irritant at concentrations of 1,000 ppm or less. OSHA has identified two references that note that EtO is an eye irritant. For example, a 1977 publication by NIOSH, entitled *Occupational Diseases: A Guide to Their Recognition*, states: "Exposure to the (EtO) vapor in high concentrations leads to irritation of the eyes." An article in *Industrial Hygiene and Toxicology*, Volume 3, edited by Frank A. Patty (1981), states that:

> Vapors of ethylene oxide in high concentrations are known to be irritating to the eyes of animals and man * * * the eyes should therefore be protected from ethylene oxide and its solutions.

This reference also states that the "threshold for vapor irritation (to eyes) is 500 ppm" (Patty, 1981). The information in these references was confirmed by Peter Roy (Ex. 21–8, Tr. 215), who stated that he had observed irritation resulting from exposures to concentrations of EtO below the current PEL of 50 ppm.

James T. Marrinan, Director, Federal Agency Affairs for the American Hospital Association, stated:

> EtO acts as a tissue irritant, having effects similar to those of ammonia gas. Exposure can cause inflammation of mucous membranes, especially those of the eyes and respiratory passages, possibly resulting in conjunctivitis, scleritis, or bronchitis (Ex. 104).

The record reflects that high exposures to EtO have been shown to cause eye irritation and that such effects may occur at exposures that may be reached for short periods. Therefore, OSHA has chosen to retain the requirement for full-facepiece respirators in the final rule.

Some commenters (Exs. 11–131, 11–137) suggested that no respirator protection provision was needed because requirements for respirator use are contained in 29 CFR 1910.134, *Respiratory Protection*. For example, Edward J. Kerfoot, Director of Toxicology and Industrial Hygiene for BASF Wyandotte Corporation, stated:

> Regarding the selection of the type of respirator used, the requirement that companies provide adequate respiratory protection is already specified in 29 CFR 1910.134. Therefore, proposing detailed requirements in the EO standard is unnecessary. In keeping with the need for a performance based standard, 29 CFR 1910.134 should be referenced as the guide for respiratory protection, and companies should be allowed to choose the respirators that are adequate for individual circumstances, rather than be limited to the choices in Table 1, as referenced in 1910.1047 paragraph (g)(2)(i) (Ex. 11–131).

Table 1 is OSHA's application of the requirements for respirator selection contained in 29 CFR 1910.134, as they relate to EtO and its characteristics. In addition, these requirements are consistent with those in the American National Standards Institute's Z88.2–1969 standard.

From past experience, OSHA is aware of the problems of respirator use as the primary means of exposure control. Proper facial fit is essential, but variations in individual facial dimensions, as well as facial hair, scars or growths, make it difficult to maintain this facial fit. Fatigue and reduced efficiency may occur because of increased breathing resistance when negative-pressure respirators are used. Thus, a medical examination requirement that the physician's written opinion include recommended limitations on the employee's use of respirators was proposed and is maintained in the final standard. Additionally, heat stress, reduced vision, and other safety problems presented by respirators should be considered by the employer. Visual impairment could pose a significant problem where physical hazards exist and the ability to see is important. Speech is also limited by respirator use. Voice transmission through a respirator can be difficult, annoying, and fatiguing, and communication may make the difference between a safe and efficient operation and a hazardous operation, especially in dangerous jobs. Entanglement of air respirator hoses as well as limited mobility due to hose length is a problem in heavy industrial environments where airline respirators are used. Air hoses can also present serious safety hazards if used in restrictive work environments, such as a sterilization room in a health care facility. A self-contained breathing apparatus is burdensome and limits freedom of movement.

OSHA does not presently believe that respirators should be considered the primary means of employee health protection against exposure to EtO for activities where engineering controls are feasible. However, despite these problems OSHA has concluded that if the permissible exposure levels for EtO are exceeded, employers must provide respirators as a secondary means of protection. However, the goal of the standard is the control of emissions at the source, which will minimize the need for routine use of respirators.

The employee must be properly trained to wear the respirator, to know why the respirator is needed, and to understand the limitations of the respirator. An understanding of the hazards involved is necessary to enable the employee to take steps for his or her own protection. The respiratory protection program implemented by the employer must conform to that set forth in 29 CFR 1910.134. That section contains basic requirements for proper selection, fit, use, cleaning, and maintenance of respirators.

Emergencies are situations where respirators must be used to protect employees. Since it is unrealistic to expect accurate prediction of the expected contaminant concentrations to which an employee might be exposed in all emergencies, OSHA requires the use of respirators of the type approved for protection against unknown concentrations. If an employee is working in an area and using an approved respirator of the type appropriate for the existing concentration, and an emergency

occurs, the employee should continue using the respirator during his or her escape. Paragraph (g)(1)(iv) is designed to provide proper protection for emergency personnel assigned to enter vessels or workplaces containing an unknown concentration to rescue workers or to control the release of the contaminant or perform any necessary repairs. In addition, this paragraph will ensure that employers identify operations in which emergencies are apt to occur and make appropriate respirators available to employees in these operations.

Paragraph (g)(3) references § 1910.134 (b), (d), (e), and (f), which stipulate the minimum acceptable respirator program, the air quality required for air-supplied respirators, standard respirator use procedures, and maintenance and care procedures for respiratory protection, respectively. For example, paragraph (e)(5)(i) of § 1910.134 states: * * * "To assure proper protection, the facepiece fit shall be checked by the wearer each time he puts on the respirator * * *." Section 1910.134(e)(5) further requires that the respirator be worn in a "test atmosphere," i.e. an irritant smoke or isoamyl acetate atmosphere, as part of the training for respirator wearers. A requirement to comply with § 1910.134(e) is contained in paragraph (g)(3) of the final rule.

Several commenters requested that a requirement for quantitative fit testing be included in the final rule (Exs. 44, 100, 103). OSHA does not believe that such a requirement is warranted at this time, in part because the only approved respirators currently available for EtO are positive-pressure respirators. Such respirators do not allow contaminated air to leak into the respirator facepiece since it is pressurized when compared to the ambient environment. Thus, leakage is restricted to clean air escaping from the inside of the facepiece rather than contaminated air leaking into the respirator. Moreover, issues of quantitative fit testing will be dealt with generically in the respiratory protection standard revision discussion above.

Finally, the standard requires that respirators required for protection from exposure to EtO shall be provided at no cost to the employee. OSHA views this allocation of costs to control employee exposure to EtO as being necessary to effectuate the purposes of the Act. The requirement makes explicit an Agency position which has long been implicit in health standards proceedings under section 6(b) of the Act.

Protective Clothing

The final standard for EtO explicitly references general provisions in sections 1910.132 and 1910.133 pertaining to protective clothing and devices. This cross-reference highlights for the employer the need to comply with all applicable standards to prevent employee exposure through contact with liquid EtO.

In the proposal, OSHA made no reference to provisions for protective clothing for EtO workers. However, the following questions were raised for general discussion: "Is reliance on these two general provisions (sections 1910.132 and 1910.133) sufficient for protecting against potential dermal and eye hazards for liquid EtO? If not, explain and specify what additional provisions are necessary." Based on information submitted to the docket, OSHA now believes that these two sections do provide adequate regulation to prevent employees from having eye and skin contact with liquid EtO or EtO solutions, and separate provisions specific to EtO are unnecessary.

A number of commenters replied, either in written comment or testimony, to the proposal's questions about personal protective equipment and clothing. Several commenters agreed with OSHA's assessment that reliance on the requirements of sections 1910.132 and 1910.133 was adequate (Exs. 11–25, 11–47, 11–57, 11–67, 11–69, 11–74, 11–110, 11–133, 21–8).

For example, HIMA stated:

> The general provisions in 29 CFR 1910.132 and 1910.133 are adequate to provide employee protection for skin and eyes against contact with liquid EtO. The protective equipment and other provisions of these requirements would apply to EtO. Because they have proved satisfactory with other hazardous liquids, they will provide adequate protection in this case. HIMA is not aware of any specific provisions that would provide greater employee protection than is already required by OSHA's general regulations. (Ex. 11–74).

In contrast to these views, several commenters raised questions regarding the acute effects of skin and eye contact with liquid EtO and concluded that reliance on the general provisions contained in sections 1910.132 and 1910.133 would not provide adequate protection (Exs. 11–46, 11–88, 11–99, 42, 44, 100, 103, 152, Tr. 1200, 1253, 1589).

In explaining the Institute's position that general requirements for skin and eye protection will not provide the necessary protection to EtO-exposed workers, NIOSH commented that:

> The standards concerning protective equipment * * * and eye and face protection * * * provide only general guidelines and do not address substance specific issues particularly as they relate to the serious hazards presented by liquid ethylene oxide or EtO solutions. Therefore sections 132 and 133 cannot be viewed as prescribing "* * * suitable protective equipment * * *" because they do not consider the particular hazards presented by liquid ethylene oxide or EtO solutions, spills and splashes. Neither sections 132 nor 133 specify how the equipment is to be used nor how it is to be selected to protect the worker from exposure to (ethylene oxide) (Ex. 11–146).

Several respondents pointed out that EtO readily penetrates rubber where, as in leather, it is retained for long periods of time and cannot be washed out (Exs. 11–99, 11–146; Tr. 1200, 1253). This raised the issue, as expressed by William Borwegen of the Food and Beverage Trade Department, AFL–CIO (Tr. 1253), that some employers whose workplaces contain EtO would be unaware of the inadequacies of rubber and other common materials used for personal protective clothing (Tr. 1589).

To prevent the use of materials readily penetrated by EtO, several commenters felt that specific recommendations or statements on the types of materials that can be used were needed within the EtO standard (Exs. 11–88, 11–99, 11–146, 11–152, Tr. 1200). Several individuals or groups made specific material recommendations such as cloth or PVC coated materials (Tr. 1200) or polymer-coated cotton gloves (Tr. 391). However, of all the respondents, only NIOSH developed an in-depth assessment of the effectiveness of personal protective clothing in preventing contact with liquid EtO.

In a 1977 report, *Special Occupational Hazard Review with Control Recommendations for the Use of Ethylene Oxide as a Sterilant in Medical Facilities*, NIOSH stated that:

> Due to the extreme penetrating ability of EtO, and the consequent ineffectiveness of many types of clothing materials to prevent skin contact, the use of conventional 'impervious' clothing is not suggested. There are, however, certain special types of protective clothing which are effective when working with EtO. For example, one of the large manufacturers provides its workers with knitted gloves which have been coated with certain polymers, including polyvinyl chloride. (Ex. 2–4).

NIOSH went on to comment, however, that information now available indicates materials made of other substances will afford a greater measure of protection than that afforded by polyvinyl chloride.

> Permeation studies have shown that garments made of chlorinated polyethylene provide the greatest protection against pure, liquid EtO; breakthrough did not occur for at least one hour. Degradation studies have shown that garments made with nitrile and butyl rubber also have a lifetime of about 1 hour. (Guidelines for the Selection of

Chemical Protection Clothing, Vol. I Field Guide. U.S. EPA Contract No. C-87611, January 19, 1983. (Ex. 11-146).)

Even with proper selection of materials, NIOSH reported (Ex. 11-146), exposure can still occur "* * * by (1) bulk penetration through pinholes, rips, zippers, seams, etc., (2) material failure through chemical degradation, or (3) permeation through the material." Even where test data are available, NIOSH commented that the differences in use and manufacturing conditions are sufficiently great to necessitate actual field evaluations "under typical use conditions of mixtures, temperatures, and physical abuse." NIOSH recommended that methods such as those being summarized by the ASTM F23.20 Committee be used to determine suitable garment materials for use with EtO.

The NIOSH testimony provides OSHA with convincing evidence that it would be premature on the part of OSHA to mandate the use of only specific types of materials for personal protective clothing in the EtO standard. Too few materials have been tested for EtO breakthrough time or degradation, and even these results may have only partial applicability under actual field conditions. The alternative is to require a specific testing protocol within the standard before any clothing is considered "approved" for personal protection. This would trigger additional recordkeeping, and adequate permeation testing is likely to be well beyond the capabilities of the many EtO-using facilities where only a few employees are potentially exposed to EtO. In addition, the handling of materials for testing presents a hazard to a different group of employees.

After a thorough review of the expert testimony and other evidence in the record, OSHA has chosen not to add a specific requirement for protective clothing in the final standard for EtO. However, the final rule does contain, in paragraph (g), a cross-reference to §§ 1910.132 and 1910.133 that is intended to remind employers of their obligations under these provisions to provide appropriate clothing to protect against eye and dermal contact.

Showers and Changerooms

OSHA received three comments on the need for a provision requiring showers and changerooms. The American Federation of State, County, and Municipal Employees (AFSCME) stated:

> No provisions for chemical showers, eye wash stations, protective clothing, or lockers and change rooms have been incorporated into this [proposed] standard. These are all essential for a minimally effective standard, and as such should be incorporated into the EtO standard (Ex. 7-6)

In a post-hearing submittal, AFSCME reiterated:

> Because of the danger of any permeable clothing—including shoes—absorbing EtO and off-gassing, such clothing exposed to EtO must be removed upon cessation of exposure (Ex. 44)

In addition, William B. Dennis of Duke University Medical Center commented as follows:

> I think (emergency showers and eye wash stations) * * * should be in close proximity * * * in case there is a liquid spill (Tr. 1367).

OSHA shares the concern of these participants that employees should be protected from contact with EtO in liquid form. Hazardous exposures to liquid EtO or EtO-containing solutions will most likely occur only accidentally in the industry sectors covered by this final rule, because exposures in these sectors will usually be from the gaseous form of EtO. Section 1910.151(c) of the General Industry standards, however, specifically requires employers to provide changerooms and emergency showers "* * * where the eyes or body of any person may be exposed to injurious corrosive materials * * *." As discussed in the health effects section liquid EtO does pose a hazard to the skin upon contact. Therefore, employers who use EtO in liquid form that may come in contact with employees' eyes or bodies, must provide changerooms and emergency showers in accordance with § 1910.151(c).

Paragraph (h) Emergency Situations

Paragraph (h) of OSHA's final rule for EtO requires that employers develop written plans for emergency situations (see discussion of definition of "emergency") and that they develop methods of alerting employees of these situations and evacuating workers when necessary. The plan must contain a requirement that employees engaged in correcting an emergency situation be provided with appropriate respiratory protection. Employers must also be prepared to alert employees to evacuate the workplace in the event of an emergency. The performance language of the emergency situation paragraph of the final standard will give employers the flexibility to choose any effective method of alerting employees, including communications systems, voice communication, or a bell or other alarm.

These requirements are identical to the emergency situation requirements included in the EtO proposal (48 FR 17284, April 21, 1983). The purpose of this provision is to protect workers from unexpected significant releases of EtO that pose an acute or other health risk.

There is considerable evidence in the record that the use of written emergency plans is widespread throughout industry (Exs. 21-8, 6-22), and many commenters supported the inclusion of such a requirement in the final rule (Exs. 4-26, 11-81, 21-8, 104, Tr. 1349). In addition, other OSHA health standards (Vinyl Chloride, 43 FR 45762, October 3, 1978; DBCP, 43 FR 11514, March 17, 1978) contain such a provision.

Several commenters suggested specific procedures to be followed in the event of an emergency (Ex. 11-125, 104). For example, Merry K. Hollhof, Central Service Supervisor of the Grand Rapids Osteopathic Hospital, suggested that the emergency provision of the standard require: (1) That local fire departments be provided with a copy of the standard in order to better respond to EtO emergencies, and (2) that hospitals require a practice emergency drill (for EtO) at least once a year (Ex. 11-125). Although OSHA agrees that these are good suggestions, it believes that the measures necessary to control emergency situations should be specific to particular workplaces. The Agency is not convinced that local fire departments, in general, will be able to respond adequately to EtO emergencies in the majority of workplace settings. Further, although practice emergency drills might be an effective means of teaching employees how to respond to emergency situations in many hospitals, such drills might be unnecessary for some facilities, such as small hospitals with only one EtO sterilizer. The Agency will therefore not require such specific measures in the emergency situations paragraph of the final EtO standard.

The proposed rule required the development of a written plan for each workplace where there is a possibility of an emergency and required that employees be informed of the emergency procedures at the time of initial assignment (or upon institution of the program), and at least annually thereafter.

There was general agreement by participants that effective emergency plans are essential and being in a standard for EtO (Exs. 11-17, 11-45, 11-77, 11-125, 17, 18-17, 103, 104, 142, Tr. 357, 364, 1305, 1349). For example, William Dennis, Director of Sterile Processing at Duke University Medical Center, testified that:

> * * * a plan in the event of a leak or spill is of absolute importance. With any type of mechanical equipment * * *, accidents are going to occur. We need to make sure that if a spill does occur, that our employees * * *

know that they need to evaluate the area immediately. They need to notify the appropriate health and safety personnel (Tr. 1349).

Gerald McEntee, International President of the American Federation of State, County and Municipal Employees (AFSCME) stated that "because of the constant potential for leaks or high EtO exposure due to equipment failure, a clearly drawn requirement for emergency procedures will be an essential fact of a new EtO standard" (Tr. 364).

Few respondents specifically addressed the issue of whether the requirement should be limited in coverage. However, these respondents expressed clearly the opinion that a written plan should be required for all employers regardless of their firm's size or the number of their employees potentially exposed (Exs. 11–17, 11–45). One comment noted that OSHA has already adopted general language for emergency plans in section 29 CFR 1910.38(a). Employee emergency plans and fire prevention plans. A cross-reference to the general language has been added to paragraph (h)(1)(iii) to highlight the employer's obligation to comply with all applicable standards.

Several respondents observed that any emergency plan for EtO should be incorporated into the facility's overall disaster plan (Exs. 104, 125). There are considerable advantages to such an approach and, as suggested by the commenters, this practice would encourage periodic drills for EtO emergencies as well as inservice training programs. However, it should be noted that OSHA is not requiring employers to develop general disaster plan under this final EtO standard. One respondent (Ex. 125) commented that many health care facilities' emergency plans require notification of the local fire department, and that fire department personnel are often uninformed of the hazards of EtO. OSHA expects that employees will provide non-employees such as fire department staff with a copy of the written emergency plan as well as this standard (including Appendices A, B, and C) when arranging for such non-employees to assist in an emergency.

Several respondents felt that the term "emergency" was inadequately defined (Exs. 7–1, 11–145, 103, 142), and some proposed alternative definitions for "emergency." For example, McEntee of AFSCME and Hill of the International Union of Operating Engineers (IUOE) testified that an emergency should be defined as any situation that might result in worker exposure to concentrations of EtO that are immediately dangerous to life or health (IDLH) (Tr. 103, 364.) Although OSHA agrees that such situations would certainly constitute an emergency, the Agency does not believe that the information on human health effects is adequate to define a precise numerical IDLH (Hill recommends 800 ppm). In addition, the health effects data suggest that evacuation based on an IDLH level alone would not provide adequate employee protection against such effects as irritation and sensitization. McEntee and Hill also suggested evacuation of the work area immediately if employees smelled EtO (Tr. 364). Since EtO's odor warning the threshold is about 700 ppm, and since this level is substantially above levels identified as having adverse health impacts, OSHA has chosen not to use odor threshold to define an EtO-related emergency. In addition, as Hill points out, many employees may not be particularly sensitive to the smell of EtO (Tr. 103). As defined in the final rule (see definitions section of summary and explanation above), the term emergency covers those unexpected occurrences, such as a failure of control equipment, that might produce a release of EtO of sufficient size to produce significant acute effects, including eye or respiratory irritation.

Paragraph (i) Medical Surveillance

The final standard requires each employer to institute a medical surveillance program to be performed by or under the supervision of a licensed physician. Employees would be offered medical examinations upon initial assignment and annually thereafter where EtO exposure is known or is likely to be at or above the action level for a total of at least 30 days in a year. Medical surveillance is provided also to employees exposed in an emergency situation and to those who are terminating employment in the EtO area. Consultations and appropriate examinations are to be made available to employees who believe they are experiencing signs or symptoms of overexposure to EtO or who are concerned about the effects of EtO on their ability to conceive a healthy child.

The physician is given broad discretion in selecting appropriate tests for medical surveillance. This is necessary to provide flexibility to the physician should new procedures become available that would help to identify situations where an employee has been placed at risk of chronic EtO-related disease while the effects are still reversible. Certain elements of medical surveillance, including comprehensive medical and work histories, a comprehensive physical examination, and a complete blood count may be useful to detect otherwise unrecognized overexposure, and these procedures are therefore required under the standard. Additional elements of the medical surveillance section ensure adequate communication among the employer, the employee, and the physician. These elements and the rationale for their inclusions remain as stated in the proposal.

Two substantial changes in medical surveillance requirements were made as the result of OSHA's review of extensive public comment and testimony. First, the suggested test for chromosome damage, included in proposed Appendix C, was deleted because the results of such tests, as applied to an individual rather than a group, cannot be interpreted. Second, to ensure uniformity of medical surveillance for all EtO workers, the standard mandates certain elements for all examinations. In the proposal, OSHA had not specified the type of surveillance to be made available to EtO-exposed employees. Instead, the physician was referred to a nonmandatory appendix, Medical Surveillance Guidelines for Ethylene Oxide. OSHA's analysis of comments received on medical surveillance, including responses to the supplemental questions raised in the proposal, is given below.

Medical surveillance programs are considered by OSHA to be a proper means of monitoring the adequacy of the permissible exposure limits. To that end, OSHA requested specific comment from the public on the adequacy of the proposed medical surveillance requirements. Two important elements to be considered were whether a proper balance had been struck between requirements and nonmandatory guidelines and whether the tests specified were appropriate.

Among the respondents, there was little agreement on a proper medical surveillance program. A few concurred with the proposed plan (Exs. 11–45, 11–61, 11–73, 11–76, 85) and some felt that medical surveillance, as provided, was irrelevant to employee health concerns (Exs. 11–64, 11–90, 11–92, 11–123, Tr. 316, Tr. 1537). Many commenters stated that a specific medical surveillance plan should be mandatory and a part of the standard language (Exs. 11–34, 11–42, 11–50, 11–81, 11–91, 11–125, Tr. 1253, Tr. 1284, Tr. 1586). Those supporting this view generally felt that without mandatory tests, no uniformity of results could be ensured. They considered this to be a more important factor than the

current lack of knowledge about what constitutes adequate medical surveillance for EtO-exposed individuals. Others felt that medical surveillance requirements should be left to the discretion of the physician. These groups argued that test recommendations should not be mandatory (Exs. 11-56, 11-71, 11-74, 11-105, 11-110, 11-124, 11-133, 11-137, 11-138, 118, 141-H, 142, Tr. 993, Tr. 997). In general, larger companies with existing comprehensive surveillance plans favored a performance-oriented standard permitting broad latitude to the examining physician. Smaller facilities, with few affected workers and no existing program in occupational medicine, tended to prefer mandatory requirements.

The preamble to the proposed standard indicated that information then available to OSHA was insufficient to justify specification of the precise tests to be administered. The belief was expressed that the examining physician is best qualified to make this judgment. The advantage to this approach is that it permits the examining physician flexibility to modify the medical surveillance program as new methodology and new information on the toxic effects of EtO become available. The disadvantage to this approach is the potential for failure to provide meaningful surveillance to EtO-exposed workers. For example, one Regional Administrator for OSHA commented that "If the agency, with all these resources available, is unable to recommend a specific medical protocol, how is an ordinary practicing physician going to do any better? * * * If the employers provide unfocused medical examinations and have no guidance on interpreting or using the results, then the employees concerned will gain no health benefit" (Ex. 11-145).

In comments (Ex. 11-146) and testimony (Tr. 320), NIOSH stated its belief that the proposed medical surveillance would not provide additional protection to EtO-exposed workers. They commented that:

> * * * the phrase "protective medical monitoring of affected employees" implies that we understand the mechanism of the disease process and that as long as physiological changes are detected at an early stage they may possibly be reversed. Unfortunately, the mechanism of the disease process is not completely understood * * * Specifically, the medical history solicits information concerning symptoms related to the eyes, blood forming organs, lungs, nervous system, reproductive system and skin. Knowledge obtained by acquisition of this information will not contribute to an understanding of the long-term effects of EtO exposure, nor is such information likely to contribute to the protection of the individual worker.

In response to questioning at the OSHA hearings, Phillip Landrigan, a NIOSH physician, stated:

> * * * we are certainly not opposed in general to the principle that physical examinations are good for workers and probably convey general benefits to the improvement of worker health. However, in the case of specific examinations in order to protect against disease or against hazardous health effects which result from exposure to a particular toxic agent, it's our considered opinion that the tests that are done to screen for adverse effects have to be worthwhile to us or they shouldn't be here (Tr. 319-321).
>
> Now, we have reviewed the proposals that OSHA has put forth, including the latest revision by Dr. Yodaikan for the medical screening of workers exposed to EtO, and it's our opinion that none of those tests are worthwhile. None of those tests are likely to detect the presence of cancer. None of those tests are likely to detect the presence of adverse reproductive effects in workers at some early stage in which medical intervention would be worthwhile. And consequently, we cannot support the inclusion of hematological tests, tests of the immune function, tests of liver function in the proposed standard.

This testimony represents a shift from NIOSH's stated position in 1981. In a Current Intelligence Bulletin sent to OSHA by NIOSH as an attachment to the Institute's comments (Ex. 11-146), the following position was taken on medical surveillance for EtO workers.

> A medical surveillance program should * * * be made available that can evaluate both the acute and chronic effects of EtO exposure. Effects such as upper respiratory irritation, dermatitis, or other forms of sensitization and irritation should alert management that unacceptable acute exposure to EtO may be occurring. A careful history with emphasis on the reproductive history should be done initially and updated yearly. In addition, an evaluation of chronic effects would require that an examination give particular attention to the hematological, neurological, and reproductive systems. Unusual findings for a worker should prompt medical personnel to consider specific test (eg. cytogenetic analysis) for the individual.

Comments that specific medical tests now available are not adequate to identify potential long-term effects of exposure to EtO must be given serious consideration. For example, the increased incidence of cancer in animals exposed to EtO, coupled with several reports of cases of leukemia in workers exposed to EtO, is sufficient to conclude that humans exposed to excessive concentrations of EtO are at risk of developing cancer, in particular leukemia. This information alone is inadequate to give any assurance that humans are at risk only with respect to leukemia or even to leukemia plus the other types of cancer seen in animals. Even if all cancer sites were known, clinical tests now available would be inadequate screening tools for cancer. As NIOSH stated:

> * * * these findings (from medical monitoring) could not be used * * * to predict the likelihood of development of cancer or adverse reproductive effects or to protect the worker from the development of those effects. On the other hand, in the event of an exposure to a high concentration of EtO, the immediate exam might include the elements described by OSHA (Ex. 11-146).

However, based on the entire record, OSHA is convinced that, to the extent possible, medical surveillance requirements for EtO should be mandatory. This will ensure that EtO workers exposed for 30 or more days a year at or above the action level receive reasonably uniform protection. Thus, the medical surveillance requirements described below focus not on cancer, but on treatment of EtO emergencies and identification of persons who appear, medically, to have been overexposed to EtO.

Although views were divided on whether specific exams should be mandatory elements of the standard or be included in the appendices, several groups presented written testimony on what they considered appropriate testing for EtO workers. For example, the American Hospital Association, while in favor of nonmandatory tests (Ex. 154), stated that annual medical exams should be available and should include a complete physical, blood cell counts, and urinalysis. Chest X-rays every 5 years were recommended and the essential nature of a medical exam for EtO workers if they received accidential excess exposure was stressed (Ex. 104). John Venable, testifying for the Ethylene Oxide Industry Council, recommended biannual health histories and blood chemistries and annual hematology in establishing an EtO medical surveillance program (Tr. 997-998). The 3-M Corporation also stated a preference for a performance-oriented medical surveillance program, but felt that appropriate testing should include a general history, physical exam, and routine hematology and blood chemistry (Ex. 146).

In testimony for the Ethylene Oxide Industry Council, Lawayne Stromberg made recommendations based on a Canadian Task Force report (Ex. 85, Tr. 985-995). He concluded that annual exams would be inappropriate for monitoring illnesses with a long latent period in persons early in their work

history. For younger workers he recommended exams every 5 years. Exams for EtO workers would include a history oriented to the exposure situation, follow-up with appropriate tests if the physician discovered any problems, and a complete blood count (CBC) based on the risk of the particular occupation.

Several groups recommended that mandatory testing be made part of the standard. Among the several recommendations were those of the Amalgamated Clothing and Textile Workers Union (ACTWU) and the American Federation of State, County and Municipal Employees (AFSCME) which testified that hematologic exams should be patterned after those in the benzene standard and that employees exposed to EtO in the past should continue to be offered medical surveillance (Exs. 44, 101, Tr. 1285). Jeanne Stellman, a physician from the Women's Occupational Health Center, testified in favor of making a complete physical and blood cell counts mandatory and leaving additional clinical procedures to the discretion of the physician (Ex. 117).

The AFL–CIO requested that specific and uniform medical requirements include a complete medical and work history with specific emphasis directed to symptoms relating to the eyes, the blood-forming organs, the lungs, the neurological and reproductive systems, and the skin; a reproductive history; a physical exam emphasizing the same elements as the history; and a CBC with white cell count, differential, hemoglobin and hematocrit (Ex. 112). Although Dr. Landrigan of NIOSH opposed most testing for EtO on the grounds that it would not detect adverse effects at an early stage permitting medical intervention, he testified in favor of including examination of the neurological system on the basis that diseases of this system are only slowly progressive (Tr. 321). The AFSCME believed that Appendix C should include not only information on neurotoxicity but on delayed effects, sensitization, and cataractogenesis as well (Ex. 44).

OSHA's Office of Occupational Medicine also testified at the hearings in support of mandatory medical surveillance. Dr. Ralph Yodaiken, the physician who heads that office, stated that EtO-related exams should include a CBC, an annual comprehensive medical and occupational history, and an annual comprehensive physical examination. He also asked that other elements relating to respirator use be included (Tr. 801).

Although they did not provide testimony supporting mandatory testing for EtO workers in general, the American Hospital Supply Corporation conducts an extensive medical surveillance program for its employees who work with EtO (Ex. 145). Their recommendations involve medical evaluation, including elicitation of a careful family history, reproductive history and past medical events and laboratory assessment of possible documentable effects on health, including possible effects on the blood, liver, reproductive organs, respiratory tract and basic cellular structure. They have also considered conducting a cytogenetic monitoring program and have on occasion medically removed employees from further EtO exposure on the basis of such tests (Ex. 145).

Based on a review of the total record, OSHA concludes that specific tests should be mandated as part of the standard's medical surveillance program. These tests are designed to detect and consequently to prevent inadvertent or otherwise unrecognized excessive exposure to EtO. Alone, the tests will not prevent or even detect all potential adverse consequences of EtO overexposure. However, coupled with employer action to eliminate exposure situations identified through the medical examinations, they will, despite these limitations, greatly reduce the risk of chronic effects.

One basic element of any medical surveillance plan for EtO workers is a medical and work history. These histories should focus on the collection of information that would indicate the worker is being overexposed to EtO. Episodes of nausea, vomiting and headaches, or a "peculiar taste" may suggest that acute exposure has occurred. Delayed effects might include pulmonary edema, drowsiness, weakness and incoordination. A history of burns or blistering of the skin, brown pigmentation, or irritation of the eye may also be an indication of overexposure to EtO (Ex. 2–5). A thorough reproductive history for employees of childbearing age, updated regularly, is essential given the data on EtO's adverse effects on both male and female reproduction. This history should elicit information on stillbirths, miscarriages, past attempts at conception, and present reproductive status.

To complement the medical and work histories the attending physician must perform a comprehensive physical with special emphasis on the same organ systems. To accomplish this task, the physician must be knowledgeable of the signs and symptoms of EtO overexposure. In addition, the physician must be capable of counselling employees who wish to conceive on the risks of exposure to EtO. For reasons discussed in a later section, the physician must make available tests for fertility and pregnancy, as needed, if requested by a potentially affected employee. The advantages to offering these tests if the employee is sufficiently concerned far outweigh the criticisms of these tests received by OSHA.

Review of the record indicates several reasons for inclusion of a complete blood count (CBC) as a routine requirement for EtO-exposed workers. The study of Ehrenberg and Hallstrom (Ex. 2–38) shows a number of hematologic changes in active employees exposed to EtO. It also gives evidence to suggest that these effects may occur even when exposure is brief but intense. Inclusion of the CBC as a requirement is virtually noncontroversial. As stated by Stromberg of the Ethylene Oxide Industry Council, "a CBC is clearly justified by the risk of the particular occupation" (Ex. 85).

Some employees not ordinarily exposed to EtO may briefly encounter exposure to EtO unrelated to their assigned work. A cut-off point is needed for the required medical surveillance program, since it would not be practical to require medical surveillance for every employee regardless of duration of exposure. The surveillance period selected must be sufficiently inclusive but not administratively impractical. From OSHA's experience in the inorganic arsenic and coke oven proceedings and from testimony and public comment on the EtO proposal, the Agency has determined that 30 exposure days per year is an appropriate point for including employees in the medical surveillance program. However, worker rotation shall not be used as an administrative convenience to deprive workers of medical surveillance or of the protection afforded by any other provisions of the standard.

The standard requires the employer to provide examinations to any employee exposed to high EtO concentrations under emergency conditions. Although there is little uncertainty about the long-term effects of high short-term exposures, it appears prudent to monitor such affected employees in light of existing health data.

On the basis of OSHA's evaluation of public response to specific questions raised in the proposal, medical surveillance is also being made available to employees when they

terminate their employment or transfer to another job assignment not involving EtO exposure. The scope of this examination is determined by the physician. For the same reason, employees who believe they are suffering from signs or symptoms of overexposure to EtO may request an interim evaluation by a physician.

The final standard requires that a medical surveillance program provide each covered employee with an opportunity for a medical examination. All examinations and procedures are to be performed by or under the supervision of a licensed physician and be provided without cost to the employee. Clearly, a licensed physician is the appropriate person to be supervising and evaluating a medical examination. However, certain parts of the required examination do not necessarily require the physician's expertise and may be conducted by another person under the supervision of the physician.

Several commenters raised questions concerning the adequacy of the coverage of medical surveillance. AFSCME, in noting that medical surveillance ignores past exposure, recommended changes in the language to provide for continued medical surveillance if workers have been exposed in the past but become reassigned to other work by the same employer (Ex. 44). Cited as precedence were § 1910.1018(1)(i)(B) of the arsenic standard and § 1910.1029(j)(3)(iii) of the coke ovens emissions final rule. In arguing for extended coverage for medical surveillance, the ACTWU pointed out that at one plant only 24 of its members were currently exposed to EtO but that 84 union members and 24 management personnel had received previous EtO exposure (Ex. 101, Tr. 1284). The AFL–CIO also expressed the opinion that specific medical surveillance should be provided to all formerly exposed as well as presently exposed employees (Ex. 112).

Although the concerns expressed by these commenters are realistic, the present state of knowledge about EtO's long-term effects on humans is insufficient to warrant a requirement for medical surveillance of previously exposed employees. The evidence suggests that EtO may cause leukemia, as well as cancer in other organs. However, present knowledge is inadequate to identify an EtO-related preleukemic state in employees and former employees. Thus, medical intervention would occur at a late stage in the development of the disease. In addition, cancer in animals was not limited to leukemia, and available information at this time does not even begin to address whether other tumors seen in animals or even unrelated tumors are also likely outcomes of EtO exposure in humans. Thus, a meaningful medical surveillance program directed at detecting chronic effects, as would be needed for formerly exposed employees, cannot be devised at this time.

The employer is required, in paragraph (i)(3), to provide the physician with the following information: a copy of this standard and its appendices; a description of the affected employee's duties as they relate to the employee's exposure level; the employee's representative exposure level or anticipated exposure level; a description of any personal protective equipment and respiratory equipment used or to be used; and information from the employee's previous medical examinations which is not readily available to the examining physician. Making this information available to the physician will aid in the evaluation of the employee's health in relation to his or her assigned duties and fitness to wear personal protective equipment when required.

The employer is required to obtain a written opinion from the examining physician containing the results of the medical examinations; the physician's opinion as to whether the employee has any detected medical conditions which would place the employee at increased risk of material health impairment from exposure to EtO; any recommended restrictions upon the employee's exposure to EtO or upon the use of protective clothing or equipment such as respirators; and a statement that the employee has been informed by the physician of the results of the medical examination and of any medical conditions which require further explanation or treatment. This written opinion must not reveal specific findings or diagnoses unrelated to occupational exposure to EtO, and a copy of the opinion must be provided to the affected employee.

The purpose in requiring the examining physician to supply the employer with a written opinion is to provide the employer with a medical basis to aid in the initial placement of employees and to assess the employee's ability to use protective clothing and equipment. The requirement that an employee be provided with a copy of the physician's written opinion will ensure that the employee is informed of the results of the medical examination. The purpose in requiring that specific findings or diagnoses unrelated to occupational exposure to EtO not be included in the written opinion is to encourage employees to take the medical examination by removing any concern that the employer will obtain information about their physical condition that is unrelated to present occupational exposures.

In addition to raising the question about the adequacy of the medical surveillance requirements, OSHA requested public response on a number of related issues. Specifically, OSHA asked for comment on the appropriateness of the inclusion of genetic screening, chromosome analysis, male fertility testing and pregnancy testing for some employees. The possibility of providing medical removal protection for employees wishing to procreate was also raised. OSHA also sought public comment on whether the coverage of employees under medical surveillance should be expanded to include exams following emergencies, at termination of employment, and for employees who believe they are suffering from symptoms associated with EtO overexposure. In view of OSHA's uncertainty as to what constitutes an appropriate physical examination, the possibility of including a multiphysician review mechanism in the EtO standard was also addressed in the questions to the public.

As part of the proposed nonmandatory Appendix C—Medical Surveillance Guidelines for Ethylene Oxide, OSHA recommended screening for chromosomal damage. Almost all public comments including those from trade associations, unions, manufacturers, suppliers, users, and government agencies agreed that routine chromosome screening is inappropriate and should not be mandated by the standard (Exs. 11–19, 11–48, 11–54, 11–56, 11–64, 11–67, 11–68, 11–74, 11–76, 11–88, 11–93, 11–102, 11–105, 11–110, 11–111, 11–128, 11–131, 11–133, 11–136 to 11–139, 11–142, 11–143, 11–146, 11–157, 85, 90, 101, 112, 135, 152, Tr. 1285, 1049, 453, 464, 998, 1586). The Office of Occupational Medicine at OSHA also testified against the use of chromosomal screening in the medical surveillance programs for EtO (Tr. 801).

In a review of the EtO proposal submitted to OSHA, NIOSH stated:

Exposure to EtO can result in chromosomal abnormalities and increased frequencies of sister chromatid exchanges; however, as of yet NIOSH knows of no data that correlates these effects to the manifestation of cancer or adverse reproductive effects in an individual. The chromosome studies of an individual suggested by OSHA are not likely to provided this information. Ability to detect such damage is limited and the disease can be manifested in the absence of detectable

chromosomal damage. Conversely, the presence of detectable chormosomal damage does not appear to provide a firm basis for predicting the likelihood of an individual demonstrating a tumorigenic response. Despite this uncertainty we believe that the identification of such changes in groups of workers is cause for concern about their continued well being, but is not appropriate for inclusion in a standard for EtO (Ex. 11-146).

In a letter to R.C. Barnard of the Ethylene Oxide Industry Council (Ex. 49), J.W. Grisham of the University of North Carolina stated that:

* * * information from chromosomal analysis on a population of workers exposed to ethylene oxide could not be used to predict future risk of chronic disease. Chromosomal aberrations are not now a scientifically valid, cost effective means to screen populations of workers for extent of exposure to EtO or for assessment of risk of future development of chronic disease. Evaluation of SCE technically is less demanding and cheaper to perform but not correlated with any disease outcome.

Patterson, in testimony for the Health Industry Manufacturers Association (Ex. 90) and Stromberg for the Ethylene Oxide Industry Council (Ex. 85, Tr. 993) stressed the still experimental nature of cytogenetic testing. Patterson stated, "Cytogenetic testing is a complex research tool. In its present state of development, it is not an accepted clinical test for evaluating individual EtO exposures" (Ex. 90). Stromberg stated that there is "no basis for assuming that cytogenetic testing could assist us in identifying workers who as individuals would have predilection for developing malignant disease. Cytologic testing would not allow us to classify or segregate workers in this way and therefore would serve no useful purpose" (Ex. 85).

Although the Health Industry Manufacturers Association stressed that the foremost reason for rejecting cytogenetic screening is that the findings cannot be used to predict individual risk of adverse health effects, the Association gave several other reasons to support its position (Ex. 152). These included the need carefully to control cytogenecity studies with large and well-matched populations, the expense of the test, and the limited number of laboratories presently capable of doing acceptable work.

The AFL-CIO concurred in not recommending chromosomal tests for routine surveillance. They commented that "from our understanding of genetic monitoring for chromosomal abnormalities, it does not appear that such test conditions and analyses on an individual basis provide any information on the effects of exposure that can be meaningfully interpreted" (Ex. 112). The United Steelworkers of America (USWA) without taking a direct position on chromosomal screening suggested that such testing might be used to screen out workers at preemployment and periodic surveillance examinations (Ex. 11-46).

On the basis of the complete record, OSHA finds that exposure to EtO has caused an increase in chromosome damage in groups of workers exposed to this substance. However, there is no quantitative basis to compare chromosome damage with exposure, so that such measurements would not provide an index of exposure for the individual worker. Furthermore, it is presently not possible to determine on the basis of preemployment examination of chromosomes those employees who will be at highest risk of subsequent health effects if exposed to EtO. Finally, it is not possible to determine in an individual the increased risk of developing cancer or reproductive problems on the basis of a series of test results of chromosomal screening taken over a period of time. Therefore, OSHA has imposed no requirement for cytogenetic testing and has deleted reference to testing for chromosomal damage from the nonmandatory Appendix C. The possible usefulness of this test as followup to an emergency exposure was not explored in the rulemaking and consequently no position is taken in the standard on this issue.

In the general questions supplementary to the proposed rule, OSHA asked for comments on whether medical removal protection (MRP) including maintenance of earnings, seniority, and other benefits and employment rights should be provided for employees removed from exposure to EtO because they wish to procreate and, if so, under what circumstances. This question received considerable public response, with employee representatives supporting MRP, generally in the broadest sense (Exs. 11-152, 44, 101, 112, Tr. 1254, 1588). With some exceptions (Exs. 11-34, 11-88, 11-102, 11-107), employers and industry associations were opposed to mandating any form of MRP (Exs. 11-25, 11-47, 11-57, 11-108, 11-110, 11-131, 11-133, 90, 142, 152, 154, Tr. 452).

The most far reaching position taken in support of MRP was that of AFSCME, which recommended up to 15 months of medical removal every three years for men and women wishing to procreate and additional removal benefits for pregnancy. AFSCME based its position on an evaluation of adverse effects, which caused this union to take the position that EtO levels as low as 0.5 ppm present a probable reproductive danger for both men and women. AFSCME also noted that emergency exposures would remain possible under any standard (Ex. 44). AFSCME did not address the potential economic consequences associated with implementation of its recommendations.

The AFL-CIO did not support a 1 ppm TWA, and consequently took the position that "there are situations when temporary removal of workers will be advisable to protect against reproductive risk, particularly if the final standard sets a 1 ppm PEL" (Ex. 112). However, the AFL-CIO also observed that at present no clear-cut determination can be made as to which situations warrant removal from exposure, and the union recommended that MRP be based on a medical determination. Although the AFL-CIO provided no detailed analyses, it stated that, based on experience with the much broader removal requirements under the lead standard, a limited voluntary removal program for EtO-exposed workers would be feasible (Ex. 112).

The public responses received do not provide OSHA with arguments sufficient either to support or refute the need for MRP in an EtO standard. There is no evidence in the EtO record that a wage guarantee requirement for EtO would be reasonably necessary for the achievement of a safe and healthful work environment. Furthermore, the effects of exposure to EtO are not highly reversible, as evidenced by the persistence of chromosomal aberrations after the cessation of exposure, and the record contains insufficient evidence to indicate that temporary removal would provide long-term employee health benefits. For these reasons, OSHA is not including mandatory MRP in the final standard.

In view of the uncertainty as to what constitutes an appropriate physical examination, OSHA requested public comment on whether a multiphysician review should be required. In the lead standard, where a three-stage review process is mandated, multiphysician review was justified on the basis of the increased probability that such a review would facilitate the correct diagnosis of lead-related disease. This was so because the inherent biological variability of lead disease meant that no one medical specialty was uniquely suited to diagnose it and that many company physicians had difficulty recognizing it.

OSHA received comment that multiphysician review is essential to ensure employee cooperation and

confidence, but evidence given to support this position was testimony from the record of the lead standard, where an extremely different picture emerged in the record as compared to that for EtO (Ex. 101, Tr. 285). In the EtO rulemaking, employers and their associations overwhelmingly considered multiphysician review inappropriate (Exs. 11-25, 11-47, 11-48, 11-57, 11-67, 11-68, 11-71, 11-88, 11-105, 11-110, 11-131, 11-133, 11-148, 152, 154). For example, the American Hospital Association stated that "there is no evidence to support a finding that company physicians lack medical sophistication to detect the subtle and illusive signs of diseases in health impairments associated with exposure to EtO" (Ex. 154). However, NIOSH presents the most convincing argument against mandatory multiphysician review: "NIOSH does not believe that the uncertainty described by OSHA can be resolved by a multiphysician review since the uncertainty arises from the interpretation and not the performance of such tests" (Ex. 11-146). OSHA agrees that multiphysician review cannot compensate for the underlying problem, i.e., the lack of medical tests that give an early warning of most EtO-related chronic diseases, and multiphysician review is not included in the final standard.

Two questions raised by OSHA proved to be noncontroversial. One question addressed the issue of offering interim medical examinations to employees who believe they are suffering from symptoms associated with EtO exposure. The other question asked if it would be appropriate for the standard to require that employers offer medical examinations at the termination of employment. Of the few responses received, support for the provision of exams at termination greatly outweighed any negative replies (Exs. 11-25, 11-28, 11-34, 11-47, 11-48, 11-68, 11-102, 85, Tr. 999). Several respondents affirmatively addressed the question of providing interim exams upon employee request (Exs. 11-34, 11-67, 11-68, 11-102, 11-146). NIOSH, however, also stated that:

> * * * the employee should be informed that such an examination cannot with any certainty predict the likelihood of a carcinogenic or adverse reproductive response and that workers should also be informed that the results will not provide a basis for medical intervention that will protect the worker's health (Ex. 11-146).

However, OSHA believes that the interim examination will serve purposes other than that noted by NIOSH. For example, an examination may be needed to assess and alleviate the acute effects of EtO exposure. This may, in turn, indicate that a leak or some other source of high transient EtO levels needs to be repaired or corrected.

In the final standard, OSHA has incorporated provisions for interim medical exams and for examinations at termination of employment. After the employee has terminated his or her job in an EtO exposure area, the employer has no further obligation under this standard to provide medical surveillance.

Interim exams are required to ensure that employees have access to a physician if a hazardous situation has been recognized. This obligation parallels the requirement that employers provide medical services for employees potentially overexposed in an emergency. Through training required in other sections of the standard, employees should become competent in recognizing the signs and symptoms associated with overexposure to EtO. Thus, medical intervention may be needed when the employee believes that a problem is occurring. The cost-effectiveness of the standard's approach is ensured because the physician performs only those tests he or she deems necessary based on the employee's complaints.

OSHA asked for public comment on whether fertility testing and pregnancy testing should be provided as a part of routine physical examination for employees exposed in emergency situations, and for persons wishing to procreate. Evidence available from both human and animal studies gave strong indication of both male and female reproductive effects. Despite this evidence, many commenters were opposed to providing fertility tests or pregnancy tests particularly as part of the routine physical examination (Exs. 11-25, 11-64, 11-71, 11-88, 11-110, 11-124, 11-128, 11-131, 11-133, 152). Reasons for rejecting these two tests generally fell into two categories. Some participants contended that evidence of EtO's effects on reproduction, at least at the proposed PEL, was inadequate, making medical surveillance meaningless. Others found the proposed tests i.e., for male fertility, to be too unreliable. In rejecting the inclusion of these tests in the standard, NIOSH stated "we do not believe that sperm or pregnancy test results obtained from individual workers will provide meaningful diagnostic information. As with genetic screening, we believe that sperm test results are currently only of value for interpreting effects of EtO exposure on an entire population" (Ex. 11-146).

Consideration of the interests of the individual employee leads OSHA to disagree with NIOSH's position, at least in part. Certainly, pregnancy test results are not unreliable. For a female employee, knowledge of her pregnancy can lead to careful medical maintenance and precautions on the part of the employee and management to minimize exposure throughout her pregnancy. For men and women, results of fertility tests may not be conclusive and even indication of a problem would not necessarily implicate EtO as the sole cause. However, repeated reproductive failure coupled, for example, with a low sperm count, sperm morphology and sperm motility in the male might serve as indicators to decrease exposure to EtO as much as possible, especially if other signs or symptoms of overexposure to EtO are evident. Thus, to be consistent with the Agency's position in the lead standard (§ 1910.1025), and in response to the record evidence in support of this option, OSHA is requiring that fertility tests and pregnancy tests be made available to potentially affected employees who specifically request them when the physician concurs in the need for the testing. Abusive of frivolous application of this section will be avoided by requiring the physician to approve requests for fertility and pregnancy tests.

Paragraph (j) Communication of EtO Hazards to Employees

OSHA has combined the requirements from several proposed paragraphs into a new paragraph (j) in the final rule entitled "Communication of EtO Hazards to Employees." These requirements ensure that information about the hazards of EtO will be transmitted to employees through the use of: (1) Signs and labels, (2) material safety data sheets, and (3) information and training. The proposed standard for EtO included requirements addressing signs and labels and information and training in two separate paragraphs.

Since OSHA's proposed rule for EtO was published on April 21, 1983, OSHA promulgated a final rule on Hazard Communication (48 FR 53280, November 25, 1983) (29 CFR 1910.1200). That standard requires that chemical manufacturers and importers assess the hazards of the chemicals they produce or import. Employers having workplaces in the manufacturing industry sectors (Standard Industrial Classification (SIC) codes 20 through 39) are required to provide information to their employees concerning the hazards of chemicals used in the workplace. Chemical hazard

information is to be transmitted to employees "* * * by means of comprehensive hazard communication programs, which are to include container labeling and other forms of warning, material safety data sheets and employee training" (§ 1910.1200(a)(1)).

The purpose of reformatting paragraph (j) in this final EtO standard is to avoid repeating the requirement in § 1910.1200 and to ensure consistency with that standard. OSHA wishes to point out, however, that the Hazard Communication standard only applies to employers with workplaces in the manufacturing industry sectors (SIC codes 20 through 39). For these and other sectors, however, paragraph (j) of OSHA's final rule for EtO provides that EtO labels must meet the criteria set forth in § 1910.1200 all facilities covered by the EtO standard.

Signs and Labels. The final rule for EtO requires that regulated areas be demarcated by posting legible signs that bear the following legend:

DANGER
ETHYLENE OXIDE
CANCER HAZARD AND REPRODUCTIVE HAZARD
AUTHORIZED PERSONNEL ONLY
RESPIRATORS AND PROTECTIVE CLOTHING MAY BE
REQUIRED TO BE WORN IN THIS AREA

OSHA intends the posting of these signs to serve as a warning to employees who may otherwise not know they are entering a regulated area. Such warning signs are required to be posted whenever a regulated area exists, that is, whenever occupational exposures are likely to exceed the PEL. For some work sites, regulated areas are permanent, for example, in areas where engineering controls cannot reduce exposures to or below the PEL. In such situations, signs are necessary to warn employees not to enter the area without adequate respiratory protection and unless authorized to do so.

Warning signs are also required to designate temporary regulated areas, e.g., when maintenance or repair activities create a situation where occupational exposures could exceed the PEL. Warning signs are important in this situation because they will help to prevent the unnecessary exposure of employees who may not be aware that an area temporarily contains high levels of EtO.

The standard also requires that containers of EtO be labeled with the legend:

CAUTION
CONTAINS ETHYLENE OXIDE
CANCER AND REPRODUCTIVE HAZARD

and with a statement warning against breathing airborne concentrations of EtO.

The signs and labels requirements discussed above are consistent both with Section 6(b)(7) of the OSH Act, which prescribes the use of labels or other appropriate forms of warning to apprise employees of the hazards to which they are exposed, and with the requirements of OSHA's Hazard Communication rule, 1910.1200(f).

Employee representatives supported the inclusion of a requirement in OSHA's final EtO rule mandating that signs and labels warn workers of the health hazards of EtO (Exs. 4–19, 4–26, 4–52). Although industry representatives generally agreed that employees should be warned about the hazards of EtO, several commenters objected to including information about the reproductive hazards of EtO exposure on the signs and labels (Exs. 11–25, 11–57, 11–74, 11–101, 11–136). These participants also believed that the words "cancer and reproductive hazard" were alarming and inaccurate (Exs. 11–25, 11–57, 11–74, 11–101, 11–136).

The EOIC contended that "there is no sufficient basis upon which to require that signs and labels bear a warning regarding reproductive hazards and only a warning of potential cancer hazard should be required" (Ex. 11–57). The EOIC explained that "the only human study * * * that has linked exposure to EO with reproductive effects is the Hemminki study * * * that study has methodological shortcomings and does not establish that EO is in fact a reproductive hazard. At best, it suggests that further research may be warranted" (Ex. 11–57). The EOIC stated also that the animal studies submitted to OSHA's rulemaking docket for EtO are "* * * insufficient (evidence) to support the requirement of a reproductive effects warning" (Ex. 11–57). On the subject of EtO's carcinogenicity, the EOIC concluded that the evidence in man is uncertain and therefore "* * * the use of the word 'potential' provides a more accurate description of the scientific knowledge regarding the possible carcinogenic hazard posed by EO" (Ex. 11–57).

The purpose of signs demarcating regulated areas and of labels on containers warning employees of the hazards of chemicals is to alert workers, in clear and concise language, to the possible adverse effects of exposure to chemicals. Signs and labels are not meant to be judgments on the quality of the scientific evidence pertaining to the health effects of hazardous chemicals. OSHA believes that the scientific evidence discussed above in the Health Effects section of the preamble is sufficient to warrant a clear and strong warning on signs and labels designed to alert workers to EtO's reproductive and carcinogenic effects. In addition, the language on the signs and labels required by this standard is consistent with that used by the Agency in several other rulemakings involving carcinogens (Acrylonitrile, 29 CFR 1910.1045; Inorganic Arsenic, 29 CFR 1910.1018; Coke Oven Emissions, 29 CFR 1910.1029; Ethylene Dibromide, 48 FR 45956, October 7, 1983).

The proposal's labeling requirement did not apply "where EtO is used as a pesticide, as such term is defined in the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) (7 U.S.C. 136 et seq.) when * * * (EtO) is labeled pursuant to that Act and regulations issued under that Act by the Environmental Protection Agency" (48 FR 17312, April 21, 1983). At the time the proposal was published, there was concern that OSHA's labels might conflict with information required on labels of pesticide products regulated by the Environmental Protection Agency under FIFRA. OSHA has since determined that the label required by the final EtO standard does not conflict with EPA labels under FIFRA. OSHA and EPA will continue to coordinate their activities when regulating hazardous chemicals in an effort to avoid conflicts.

The EOIC (Ex. 11–57) requested that OSHA clarify whether or not tank cars are exempt from the container labeling requirement. The EOIC suggested that "if the word 'container' is construed to include tank cars, the OSHA requirements may conflict with regulations imposed by Department of Transportation" (Ex. 1–57).

Tank cars are not exempt from the final standard's container labeling

requirement. OSHA believes it is important that employees involved in the loading and unloading of tank cars are aware of the health hazards associated with EtO exposure to ensure that they take precautionary and protective measures. OSHA has examined its labeling requirements for EtO and has determined that they do not conflict with Department of Transportation regulations under the Hazardous Materials Transportation Act, 49 U.S.C. 1801 *et seq.*

Material Safety Data Sheets. Paragraph (j) of the final rule for EtO also requires that manufacturers or importers of EtO obtain or develop material safety sheets (MSDS's) for EtO and make them available to their employees, in accordance with OSHA's Hazard Communication standard (29 CFR 1910.1200(g)). The Hazard Communication rule establishes "uniform requirements for hazard communication in one segment of industry, the manufacturing division" (48 FR 53281, Nov. 25, 1983). Paragraph (g) of the Hazard Communication rule specifies what information must be included in MSDS's.

Although the Hazard Communication standard applies to most facilities that will be affected by the EtO standard (SIC's 20–39), many EtO-using workplaces (e.g., hospitals, museums, libraries) are not included in the scope of the Hazard Communication standard as it applies to the MSDS. However, most of the information contained in a MSDS is also included in the appendices to the EtO standard. Since paragraph (j) of the final rule for EtO requires all affected employers to provide copies of the EtO standard and its appendices to their employees, OSHA believes that all employees potentially exposed to EtO will, in fact, be adequately apprised of the hazard associated with EtO. Thus, OSHA does not explicitly require manufacturers to send MSDS's to downstream users outside SIC's 20–39.

Information and Training. The final EtO standard requires affected employers to provide a training program for all employees expected to be exposed to airborne EtO at or above the action level of 0.5 ppm. The training requirement in the standard is patterned after OSHA's Hazard Communication standard (29 CFR 1910.1200(h) (1) and (2)).

Information and training are to be provided at least annually to employees when they are initially assigned to a work station where there is a potential for exposure to EtO to be at or above the action level. Information required to be provided to potentially exposed employees includes an explanation of the requirements of the EtO standard; identification of operations in the work area that contain EtO; and the location and availability the EtO final rule. The required elements of the training program, as specified in 29 CFR 1910.1200(h)(2), include: methods and observations that may be used to detect the presence or release of EtO; the physical and health hazards of EtO; the measures employers must take to protect employees from EtO hazards; and the details of the hazard communication program developed by the employer. Employers covered by the scope of the final EtO standard must also provide their EtO-exposed employees with an explanation of the contents of the EtO standard and its appendices. In addition, the medical surveillance program required by the EtO standard must be described to affected employees.

Training and information requirements are routine components of OSHA health standards and are required by section 6(b)(7) of the Act, and their inclusion reflects the Agency's conviction that informed employees are essential to the operation of any effective occupational health program. OSHA believes that informing and training employees about the chemical hazards to which they are exposed will contribute substantially to reducing the incidence of occupational diseases caused by current exposure conditions. In addition, training serves to reinforce information presented to employees through the written media of labels and material safety data sheets required by the other communication provisions of this paragraph.

Many commenters strongly endorsed the inclusion of information and training provisions in the final rule (Exs. 4–32, 4–33a, 4–52, 4–54, 11–33, 11–34, 11–36, 11–38, 11–77, 104). Commenters representing hospitals particularly stressed the importance of training for sterilizer operators (Exs. 4–32, 11–36, 11–33, 11–34, 11–38, 11–77, 104). For example, Neil Danielson, Central Service Manager of the Wesley Medical Center, stated that:

> Part of our * * * education programs includes informing our personnel that EO is a toxic substance and that it has mutagenic effects * * * Training requirements for operators of sterilization equipment * * * includes competency in performance evaluation and review by the supervisor with the operators prior to assignment * * * to sterilization procedures (Ex. 11–36).

The American Hospital Association (AHA), a trade association representing several hundred hospitals, also reported that it has conducted an extensive educational program on the hazards of EtO in the hospital setting (Ex. 4–32). For example, the AHA held three training seminars in 1982 and developed training manuals for EtO users entitled, *Ethylene Oxide Use in Hospitals: A Manual for Health Care Personnel* (Ex. 4–32).

One commenter expressed concern about confidential information being disseminated via the training program mandated by the standard (Ex. 11–48). Michele Malloy, Attorney for Conoco, Inc., stated:

> The proposed standard does not address the issue of confidential information contained in training materials. * * * Training material may include information that describes plant processes, information considered confidential and proprietary. The proposed rule should contain a mechanism to maintain the confidentiality of this information (Ex. 11–48).

OSHA shares Conoco's concern but does not believe that the final standard will create problems concerning confidentiality. Employees are routinely in a position to have access to information about materials in use in their workplace and to observe production processes at first hand in the course of their work assignments. OSHA believes that training information is not likely to be sufficiently detailed to divulge trade secrets. In addition, as discussed in the preamble to the Hazard Communication standard (48 FR 53280, November 25, 1983), employers may take steps to protect the specific chemical identities of materials used in their production processes (see the discussion at 48 FR 53312 *et seq.*).

Considerable evidence was submitted to the record demonstrating that training and information programs are also common in EtO-using facilities in the non-hospital sectors of industry. For example, the Ethylene Oxide Industry Council (EOIC) conducted a survey among 18 of its non-producer ethoxylator members (Ex. 4–33a). Fifteen of the 18 companies responding stated that they had already established "formal training program[s] for employees, * * * both supervisors and workers potentially exposed to ethylene oxide" (Ex. 4–33a). In addition, a study prepared under contract to OSHA by JRB Associates (Ex. 6–22) reported that the overwhelming majority of EtO-using firms in the EtO producer, ethoxylator, and medical equipment manufacturing sectors have training programs in place.

In sum, the record evidence in regard to information and training reinforces OSHA's own convictions as to the importance of informed employees to the successful implementation of occupational health programs, and provides strong support for the inclusion of these requirements in the final rule.

Paragraph (k) Recordkeeping

Section 8(c)(3) of the Act provides for the promulgation of regulations requiring employers to maintain accurate records of employee exposures to potentially toxic or harmful physical agents which are required to be monitored or measured.

As proposed, the final standard requires that employers who rely on objective data to be exempted from the standard (paragraph (a)(2) and (d)(2)(ii)) shall maintain records of such information to demonstrate that their employees are not exposed to airborne EtO concentrations at or above the action level. In this respect, the objective data substitute for the initial monitoring requirements.

The final rule provides that records be kept to identify the employee monitored and to reflect the employee's exposure accurately. Specifically, records must include the following information: (a) The names and social security numbers of the employees sampled; (b) the number, duration, and results of each of the samples taken, including a description of the representative sampling procedure and equipment used to determine employee exposure where applicable; (c) a description of the operation involving exposure to EtO which is being monitored and the date on which monitoring is performed; (d) the type of respiratory protective devices, if any, worn by the employee; and (e) a description of the sampling and analytical methods used, and evidence of their accuracy.

The final standard also requires that the employer keep an accurate medical record for each employee subject to medical surveillance. Section 8(c) of the Act authorizes the promulgation of regulations requiring any employer to keep such records regarding the employer's activities relating to the Act as are necessary or appropriate for the enforcement of the Act or for developing information regarding the causes and prevention of occupational illnesses. OSHA believes that medical records, like exposure monitoring records, are necessary and appropriate both to the enforcement of the standard and the development of information regarding the causes and prevention of illness. In addition, medical records are necessary for the proper evaluation of the employee's health.

The final standard requires that all records required to be kept shall be made available upon request to the Assistant Secretary and the Director of NIOSH for examination and copying. Access to these records is necessary for the agencies to monitor compliance with the standard. These records may also contain essential information which is necessary for the agencies to carry out their other statutory responsibilities.

The final rule provides for employees, former employees, and their designated representatives to have access to mandated records upon request. Section 8(c)(3) of the Act explicitly provides that "employees or their representatives shall be provided with an opportunity to observe monitoring and to have access to the records of monitoring and exposures to toxic substances"; and several other provisions of the Act contemplate that employees and their representatives are entitled to have an active role in the enforcement of the Act. Employees and their representatives need to know relevant information concerning employee exposures to toxic substances and their health consequences if they are to benefit fully from these statutorily created rights.

In addition, the final rule specifies that access to exposure and medical records by employees, designated representatives, and OSHA shall be provided in accordance with 29 CFR 1910.20. Section 1910.20 is OSHA's recently promulgated generic rule for access to employee exposure and medical records (45 FR 35212). By its terms, it applies to records required by specific standards, such as this EtO standard, as well as records which are voluntarily created by employers. In general, it provides for unrestricted employee and designated representative access to exposure records. Access to medical records is also provided for employees and, if the employee has given specific written consent, for the employee's designated representatives. OSHA retains unrestricted access to both kinds of records, but its access to personally identifiable records is subject to rules of Agency practice and procedure concerning OSHA access to employee medical records, which have been published at 29 CFR 1913.10. An extensive discussion of the provisions and the rationale for § 1920.20 may be found at 45 FR 35312; the discussion of § 1913.10 may be found at 45 FR 35384. It is noted that revisions to the access to records standard are being developed in an ongoing rulemaking proceeding. The EtO standard may be affected by any changes which result from that rulemaking effort.

It is necessary to keep records for extended periods because of the long latency periods commonly observed for the induction of cancer caused by exposure to carcinogens. Cancer often cannot be detected until 20 or more years after onset of exposure. The extended record retention period is therefore needed for two purposes. First, diagnosis of disease in employees is assisted by having present and past exposure data as well as the results of the medical exams. In addition, retaining records for extended periods also makes it possible at some future date to review effectiveness and the adequacy of the standard.

The time periods required for retention of exposure records and medical records are thirty years, and period of employment plus thirty years, respectively. These retention periods are consistent with those in the OSHA records access standard.

The final standard requires employers to notify the Director of NIOSH in writing at least 3 months prior to the disposal of the records. Section 1910.20(h) also contains requirements regarding the transfer of records. The employer is required to comply with that provision and any other applicable requirements set forth in that standard.

Paragraph (l) Observation of Monitoring

Section 8(c) of the Act requires that employers provide employees and their representatives with the opportunity to observe monitoring of employee exposures to toxic substances or harmful physical agents. In accordance with this section, as proposed, the final rule contains provisions for such observation of monitoring of EtO exposures.

The observer, whether an employee or a designated representative, must be provided with, and is required to use, any personal protective equipment required to be worn by employees working in the area that is being monitored, and must comply with all other applicable safety and health procedures.

The record contains little objection to the requirements addressing observation of monitoring. One commenter did object, however, as noted below:

> * * * It is necessary that OSHA define "designated representative", and second, there must be clarification as to when an employer must provide affected employees an opportunity to observe monitoring. Clearly, an employer should not be obligated to let employees observe monitoring at any time the employee desires. The disruption this would cause in a working environment could be substantial. (Ex. 142.)

Experience gained from previous health standards containing these same observation provisions has indicated that the concerns expressed above are not warranted and that compliance with

this requirement has not been unduly burdensome.

This commenter's concern over the potential "substantial" disruption in the working environment caused by employees' observation of monitoring is also unsubstantiated by the record or OSHA's experience. Therefore, OSHA has determined that the final requirements for employee observation of monitoring are appropriate.

Paragraph (m) Dates

Effective Date

In the NPRM, OSHA proposed an effective date of thirty (30) days following publication in the **Federal Register** and invited comment on whether additional time should be provided. In addition, the Agency solicited information and supporting data on delayed implementation dates for compliance with various provisions of the standard.

After careful review of comments in response to the proposal, the hearing testimony, and post-hearing comments, the final rule shall become effective sixty (60) days following publication in the **Federal Register**. Providing a 60 day rather than 30 day effective date is believed by OSHA to be necessary for affected parties to familiarize themselves with this rather comprehensive document. In addition, because of the considerable range of estimates for time to come into compliance with the PEL among the affected industries, the Agency has decided to establish startup dates for specific provisions of the standard based on the affected industry. This is based on the record and on OSHA's experience with other standards as to the time required for employers to complete air monitoring and medical surveillance, to obtain necessary equipment, respirators, and protective clothing, to produce written compliance plans, and to design, procure, and install engineering controls. OSHA believes that the dates set in this standard should be adequate in all but unusual circumstances. If the time period for meeting any of these startup dates cannot be met because of technical difficulties, any employer is entitled to petition the Assistant Secretary for a temporary variance under § 6(b)(6)(A) of the Act. Based on its evaluation of the feasibility of the standard, however, OSHA does not anticipate that many employers will need to use this variance mechanism.

Startup Dates

Among producers/ethoxylators, comments on the estimated time to institute any necessary engineering controls and/or work practice controls ranged from companies whose facilities were already reported to be in compliance to those who suggested that up to two years were needed to install engineering controls. For example, U.V. Henderson, Associate Director of Environmental Affairs at Texaco, stated that while his company's manufacturing plant is currently achieving fairly close to 1 ppm, additional engineering controls are now planned or being placed in service to permit consistent compliance with the PEL (Ex. 11–71). In responding to the question OSHA raised in the proposal regarding time to compliance, Mr. Henderson stated:

> At our manufacturing plant, compliance with a 1 ppm PEL is already achievable. At other locations where to EtO is used, a 12 month period would probably be adequate to institute any necessary engineering and/or work practice controls.

Similarly, Howard Kusnetz, Manager of Safety and Industrial Hygiene at Shell Oil Co., stated that Shell had successfully reduced employee exposures through a combination of engineering controls, work practices, and respiratory protection (TR. 815). Moreover, he stated that "with few exceptions, employee exposures today are below 1 ppm as a work-shift time-weighted average without regard to the use of respirators" (Tr. 815). During cross-examination at the hearings, he indicated that while two job categories in the production section required the use of air-supplied respirators, compliance with the proposed PEL of 1 ppm had already been achieved in the ethoxylator section without regard to the use of respirators (Tr. 816, 829).

Among producers/ethoxylators not already in compliance with the PEL, PPG Industries, Inc. estimated several months to two years to meet the PEL (Ex. 11–105). SunOlin Chemical Company, the smallest of the EtO producing companies, stated that it would need 18–24 months to meet the PEL through engineering and work practice controls (Ex. 11–25), as did A.E. Staley Manufacturing Company (Ex. 11–124), and Dow Chemical Company (Ex. 11–110). Union Carbide Corporation, the largest producer/consumer of EtO, recommended a biphasic compliance plan, Phase I requiring 6 months to develop and design engineering controls, and Phase II requiring an additional 18 to 24 months to implement those engineering controls defined in Phase I (Ex. 11–133). During the hearings, Donald E. Rapp of Dow indicated that his company would need 12 or 18 months to comply with 1 ppm (Tr. 839), thereby decreasing his company's earlier estimate of time to compliance (Ex. 11–110) by six months. Eastman Kodak requested a minimum of two years (Ex. 11–67). Finally, BASP Wyandotte Corporation requested 12–36 months to install engineering controls.

Arlin G. Voress, Chairman of the EOIC, and Geraldine V. Cox, Vice President and Technical Director of the Chemical Manufacturers Association, stated that the PEL is generally achievable by industry if the use of respirators is permitted in certain operations as part of an integrated control strategy and if appropriate phase-in periods are provided (Ex. 11–57). They estimated that producers and ethoxylators would neet up to two years to install engineering controls.

OSHA has determined that the record supports the adequacy of a twelve-month period for producers and ethoxylators to institute any necessary engineering and/or work practice controls. In this regard it is particularly notable that Shell Oil Company already has achieved compliance with the TWA in its ethoxylator section without regard to respirator usage, that only two job categories in Shell's producer section required periodic use of respirators, and that at Texaco, compliance with the PEL is already achievable. Therefore, producers and ethoxylators have one year from the effective date to achieve compliance with the PEL by means of engineering and work practice controls.

Among medical products manufacturers, including sterilizers, the estimated time to compliance using engineering and/or work practice controls ranged from 7 to 24 months. For example, in response to the proposed effective date, Harold O. Buzzell of HIMA stated that since nearly 60 percent of HIMA members using EtO are small entities, a 1 ppm TWA could not be widely met in any reasonable length of time using only engineering and work practice controls. He indicated that "allowing respiratory protective devices for limited specific and defined work tasks would result in compliance in approximately 7 months at significant savings" (Ex. 11–74). Testimony by G. Briggs Phillips, Senior Vice President for Scientific Affairs of HIMA, indicated his organization's support of a 1 ppm TWA and that compliance in 7 to 12 months would be possible with the limited use of respirators for short periods (Ex. 89). Frank P. Wilton, President of Ethox Corporation, testified on behalf of HIMA that his Corporation will need 7 to 12 months to achieve the PEL with respirator usage. Post-hearing comments by Phillips reiterated HIMA's

recommended time to compliance of 7 to 12 months (Ex. 135). Futhermore, in a post-hearing brief (Ex. 152), Phillips and Wilton indicated that Lawrence Hecker's statement at the hearings was representative of the position of HIMA members on the time needed for compliance.

Sterilant user members of the EOIC believe that it will take about 7 months to achieve compliance with the PEL if respirators can be used as part of an integrated program (Tr. 451).

In summary, HIMA, a trade organization representing 285 medical device and diagnostic product manufacturers, proposed a phase-in time of 7 to 12 months with considerable respirator usage thereafter.

However, OSHA witness Peter A. Roy testified that in the vast majority of cases in health care facilities and industrial sterilizers of medical devices, a 12-month period would provide sufficient time for compliance by means of engineering and work practice controls (Ex. 21-8). More specifically, he stated:

I base this opinion on the following facts: many industrial and hospital users of EtO have already taken significant steps in work practice and engineering controls to reduce exposures; the ACGIH TLV Committee has already adopted a 5 ppm TWA and has proposed 1 ppm to be effective in 1984; many industrial sterilization facilities and medical device manufacturers have gone on record as adopting in house levels at 10 or less ppm TWA and the feasibility and effectiveness of control measures has been proven.

* * * * *

In instances where individual facilities or institutions may be unable to comply within the 12 month period, I believe that employees may be adequtely protected in the interim through the use of proper respiratory protection. A 12 month lead time should be sufficient for the development or application of ventilation equipment work process controls for hospital and industrial sterilization facilities. Again, EtO control is merely the application, in most cases, of well established control technology and does not require the development of any new technology or new methods of control. Nevertheless, new methods of control, if proven effective, may of course be used. These could include new sterilizer designs, combination sterilizer aerators, and other technological advancements in equipment design and function. However even where existing equipment and facilities must be modified, a 12 month lead time should provide an ample period for the planning, development, design, implementation and testing of control measures.

Other comments regarding time to compliance in medical products firms and sterilizers ranged from 1 to 4 years. Sterile Products Technology conducted a survey of four small medical products manufacturers and indicated that one would use an alternate sterilization process, two would need 12 months to implement engineering controls, and the fourth would need two years (Ex. 11-126). Howmedica, Inc. (Ex. 11-54) and American Hospital Supply Corp. (Ex. 11-47) indicated that compliance could be achieved within 12-18 months allowing respiratory protection for limited specific and defined work tasks. In posthearing comments, John Kuchta, Vice President and General Counsel for Kendall Co., advocated a 24-month phase-in period to implement the PEL (Ex. 142) as did AAMI (Ex. 11-127) and Warner-Lambert Co. (Ex. 11-76). S. Richard Nusbaum felt that both hospital and industrial sterilizers needed 3 years to meet a 1 ppm TWA (Ex. 11-64). Midwest Sterilizing Corp., a small contract sterilizer, contended that 3 to 4 years were needed to implement the PEL.

In summary, there is a considerable range of estimates of the necessary time to compliance among medical products manufacturers and sterilizers. Based on the Agency's feasibility analysis and expert testimony, OSHA believes that one year after the effective date will provide sufficient time for the vast majority of medical products manufacturers and sterilizers to implement engineering controls and work practices which will meet the PEL. As mentioned above, if because of technical difficulties the startup date cannot be met, any employer may request a temporary variance under § 6(b)(6)(A) of the Act.

Among spice manufacturers, McCormick and Co. and R.T. French Co. submitted comments on the time frame needed to meet the PEL. Richard L. Hall, Vice President of Science and Technology at McCormick, stated that the use of respirators was necessary to achieve the 1 ppm TWA during maintenance and emergency operations as well as during re-engineering of facilities. Hall believes that a phase-in is needed and recommended a minimum of 18 months to compliance (Ex. 11-138). A.R. Hatfield, Vice President and Secretary at R.T. French, was in favor of a two-year evaluation and modification period. The first year would be spent developing analytical methodology and validation for monitoring, the second for emplementing engineering controls (Ex. 11-141). The above commenters provided no substantive evidence on engineering or economic problems which would support the need to extend the date of compliance to 2 years. In addition, as noted in the monitoring section of the preamble, OSHA believes that adequate exposure monitoring methods are presently available to all segments of the industry, including spice manufacturers. Because the equipment and methods for spice sterilization are very similar to those used for the sterilization of other items with EtO, OSHA is confident that spice manufacturers can comply with the EtO standard within the same time period as the other industry segments. Consequently, the spice manufacturing industry has one year to meet the PEL through engineering and work practice controls.

The great majority of comments regarding the effective date to compliance with the PEL were received from the health care industry. Estimated effective dates ranged from compliance within 24 hours to within 4 to 5 years. For example, Sara Beddow, Central Supply Supervisor at Memorial Hospital (Colorado Springs) stated that 24 hours were needed to reduce exposure to the PEL through engineering and work practice controls (Ex. 11-34). Brian J. Kuske, Assistant Administrator, and DeLoa Pitt, Central Processing, of St. Mark's Hospital (Salt Lake City) stated that while their present equipment can meet the 1 ppm TWA, a one year maximum compliance date for other hospitals was recommended (Ex. 11-38). Donna Swenson, Central Service Supervisor at Rockford Memorial Hospital (Illinois), stated that a relatively short period of time was needed to reduce employee exposures to the PEL, and that engineering controls for her facility would be completed by June 1, 1984 (Ex. 11-81).

Malcolm G. Ridgway *et al.* of Council Shared Services, an engineering consulting firm serving 230 hospitals in six Southern California counties, stated that engineering controls were usually installed within three months after that company's recommendations (Ex. 11-122). Ridgway reported the results of 148 EtO environmental safety site surveys performed during March 1982 through March 1983 at 95 sites in 86 member hospitals in which 95.3% of the surveys indicated EtO levels less than 5.0 ppm.

Mesa Luthern Hospital (Arizona) requested a minimum of 6 months for implementation of engineering controls (Ex. 11-31), as did St. Joseph Hospital Health Center (Syracuse) (Ex. 11-119). St. John's Regional Medical Center (Joplin, Missouri) and Petaluma Valley Hospital (California) requested 6 to 12 months to reduce exposures to the PEL (Exs. 11-17, 11-43). Michael L. Schneier, Director of Research, Development and Engineering of Castle Co., a manufacturer of EtO sterilizers used in hospitals, indicated that it would take

more than 30 days for sites not in compliance to obtain and install equipment. Schneier stated that 9 to 12 months is a more realistic time to compliance (Ex. 11-53).

A majority of hospitals and health care facilities indicated that one year was needed to reduce exposure to the PEL by means of engineering controls. Commenters included the Missouri Association for Hospital Central Service Personnel, Sid Peterson Memorial Hospital (Kerrville, Texas), Michigan Hospital Association, International Association for Hospital Central Service Management, Samaritan Health Service (Phoenix), University of Washington Hospital (Seattle), Missouri Hospital Association, Arizona Hospital Association Service Corporation, St. Mary's Hospital (Rochester, Minnesota), Grand Rapids Osteopathic Hospital, and University of Virginia Hospitals (Charlottesville) (Exs. 11-12, 11-16, 11-26, 11-44, 11-70, 11-85, 11-86, 11-103, 11-116, 125, 129).

In addition, there appeared to be a consensus among unions representing health care employees (AFGE, AFSCME, and SEIU) that while engineering controls should be installed as soon as possible, installation should occur no later than one year following the effective date (Exs. 11-99, 11-152, 44, Tr. 357, 365, 1201). For example, AFSCME recognized that a PEL that requires extensive retrofit of equipment to comply will necessarily require time to procure needed equipment from manufacturers.

> In the health care industry, we believe that a reasonable end point can be established that is less than one year from the effective date of this standard. (Ex. 44)

Furthermore, Neil Davis of AFGE testified:

> In terms of deadlines, we believe that adequate engineering controls should be installed as soon as possible. But no later than one year. (Tr. 1201).

Other estimates of time to compliance were for longer periods. For example, Harrison Memorial Hospital (Washington) and Great Plains Society Hospital Central Services personnel recommended one to two years depending upon the type of modifications needed. South Community Hospital (Oklahoma City) recommended an effective date for compliance within two years, Health Central System (Minneapolis) one to three years, Munson Medical Center (Traverse City, Michigan) one and one-half to three years, Methodist Hospital (Houston) two years, Department of the Army two to five years, and Henrietta D. Hoodall Hospital (Maine) and University of Minnesota Hospitals and Clinics (Minneapolis) three years (Exs. 11-107, 11-128, 29, 45, 51, 88, 90, 92, 143). Tacoma General Hospital (Washington) was in favor of the longest time to implement engineering controls, requesting four to five years (Ex. 11-73).

The remaining commenters among health care facilities were in favor of a realistic phased compliance schedule to afford hospitals time to implement the standard in a way that will protect both patients and employees. In response to OSHA's request for an estimate of time to compliance through engineering and work practice controls, the AHA recommended adoption of the following schedule for full implementation of the standard's provisions:

> Where needed—
>
> Major construction must be initiated within 23 months, and completed within 30 months of publication of the final standard.
>
> Within 18 months of publication—
>
> Other engineering controls and departmental modifications must be completed.
>
> Respirator training, fit testing, and maintenance programs must be developed and implemented.
>
> Within 12 months of publication—
>
> New equipment must be purchased.
>
> Within 6 months of publication—
>
> Work practice modifications must be made.
>
> Employee training programs must be in place.
>
> Medical surveillance programs (exclusive of cytogenetic testing) must be initiated.
>
> Within 3 months of publication—
>
> Monitoring protocols must be developed and implemented. Emergency procedures must be developed and disseminated within sterilizer areas.
>
> Recordkeeping, signs, and regulated area requirements must be implemented. [Ex. 11-115].

Other recommending "phase-in" periods of varying lengths included the Association of Operating Room Nurses, Wesley Medical Center (Wichita, Kansas), Harper Grace Hospitals (Detroit), and Medical Instrumentation Systems-Hospital Shared Services (Exs. 11-32, 11-36, 11-106, 77).

The information provided to OSHA clearly indicates that, with few exceptions, affected employers can be reasonably expected to be able to install engineering controls that would bring their workplaces into compliance with the final standard's PELs within one year from the effective date of this standard. Available engineering controls combined with good work practices, such as simply vacating the sterilizer area for 10-15 minutes after opening the sterilizer door after cycle completion, provide a readily available means for employers to comply with this standard in the time-frame specified.

Compliance with the other requirements of the standard within one-hundred and eighty (180) days of the effective date also is believed by OSHA to be appropriate. As discussed elsewhere in this document, many EtO employers have already instituted or are developing programs regarding training, compliance plans, respirators, medical surveillance, exposure monitoring and work practice. In addition, commenters specifically indicated that work practice modifications, training and medical surveillance programs, monitoring protocols, emergency procedures, recordkeeping, signs, and regulated areas requirements should be implemented within 6 months of the effective date of the final standard (Exs. 11-33, 11-115).

Paragraph (n) Appendices

Four appendices have been included in this final standard. These appendices have been included primarily for purposes of information. None of the statements contained herein should be construed as establishing a mandatory requirement not otherwise imposed by the standards or as detracting from an obligation which the standard does impose.

The information contained in Appendices A and B is designed to aid the employer in complying with requirements of the standard. Appendix A also contains workplace design and work practice recommended by EPA for hospital and health care facilities using EtO as a sterilant. The material in Appendix C primarily provides information needed by the physician to evaluate the results of the medical examination. It should be noted that paragraph (i) of the standard specifically requires that the information obtained in Appendix A and B be provided to employees as part of their information and training program.

Appendix D gives details of the OSHA sampling method for use in monitoring employee exposures to EtO, as well as information on other available methods.

Minor changes have been made in the Appendices in the final standard to reflect changes from the proposed rule, and in response to suggestions from commenters.

IX. State Plan Applicability

Twenty-four states and U.S. territories have their own OSHA-approved occupational safety and health plans. These states and territories are: Alaska, Arizona, California, Connecticut (for

state and local government employees only), Hawaii, Indiana, Iowa, Kentucky, Maryland, Michigan, Minnesota, Nevada, New Mexico, North Carolina, Oregon, Puerto Rico, South Carolina, Tennessee, Utah, Vermont, Virginia, Virgin Islands, Washington, and Wyoming. These states and territories are to adopt a standard comparable to that of OSHA's within 6 months of the effective date of the Federal rule.

X. Authority

This document was prepared under the direction of Patrick R. Tyson, Deputy Assistant Secretary of Labor for Occupational Safety and Health, 200 Constitution Ave., N.W., Washington, D.C. 20210.

Accordingly, pursuant to sections 4(b), 6(b) and 8(c) of the Occupational Safety and Health Act of 1970 (84 Stat. 1592, 1593, 1599; 29 U.S.C. 653, 655, 657), Secretary of Labor's Order No. 8–76 (41 FR 25059) and 29 CFR Part 1911, Part 1910 of Title 29, Code of Federal Regulations is hereby amended as set forth below.

List of Subjects in 29 CFR Part 1910

Ethylene oxide, Occupational safety and health, Chemicals, Cancer, Health, Risk assessment.

(Secs. 4, 6, and 8 of the Occupational Safety and Health Act of 1970, 84 Stat. 1593, 1597, 1599 (29 U.S.C. 653, 655, 657); Secretary of Labor's Order 9–83 (48 FR 35736); 29 CFR Part 1911)

Signed at Washington, D.C., this 15th day of June 1984.

Patrick R. Tyson,

Deputy Assistant Secretary of Labor.

PART 1910—[AMENDED]

Part 1910 of Title 29 of the Code of Federal Regulations is amended as follows:

1. By adding a new paragraph (h) to § 1910.19 to read as follows:

§ 1910.19 Special provisions for air contaminants.

* * * * *

(h) *Ethylene oxide.* Section 1910.1047 shall apply to the exposure of every employee to ethylene oxide in every employment and place of employment covered by section 1910.12, 1910.13, 1910.14, 1910.15, or 1910.16, in lieu of any different standard on exposure to ethylene oxide which would otherwise be applicable by virtue of those sections.

§ 1910.1000 [Amended]

2. By deleting the entry "Ethylene oxide * * * 50 ppm * * * 90 mg/m³" from Table Z–1 of Section 1910.1000.

3. By adding a new section 1910.1047 to read as follows:

§ 1910.1047 Ethylene oxide.

(a) *Scope and application.* (1) This section applies to all occupational exposures to ethylene oxide (EtO), Chemical Abstracts Service Registry No. 75–21–8, except as provided in paragraph (a)(2) of this section.

(2) This section does not apply to the processing, use, or handling of products containing EtO where objective data are reasonably relied upon that demonstrate that the product is not capable of releasing EtO in airborne concentrations at or above the action level under the expected conditions of processing, use, or handling that will cause the greatest possible release.

(3) Where products containing EtO are exempted under paragraph (a)(2) of this section, the employer shall maintain records of the objective data supporting that exemption and the basis for the employer's reliance on the data, as provided in paragraph (k)(1) of this section.

(b) *Definitions:* For the purpose of this section, the following definitions shall apply:

"Action level" means a concentration of airborne EtO of 0.5 ppm calculated as an eight (8)-hour time-weighted average.

"Assistant Secretary" means the Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, or designee.

"Authorized person" means any person specifically authorized by the employer whose duties require the person to enter a regulated area, or any person entering such an area as a designated representative of employees for the purpose of exercising the right to observe monitoring and measuring procedures under paragraph (l) of this section, or any other person authorized by the Act or regulations issued under the Act.

"Director" means the Director of the National Institute for Occupational Safety and Health, U.S. Department of Health and Human Services, or designee.

"Emergency" means any occurrence such as, but not limited to, equipment failure, rupture of containers, or failure of control equipment that is likely to or does result in an unexpected significant release of EtO.

"Employee exposure" means exposure to airborne EtO which would occur if the employee were not using respiratory protective equipment.

"Ethylene oxide" or *"EtO"* means the three-membered ring organic compound with chemical formula C_2H_4O.

(c) *Permissible exposure limits (PEL). 8-hour time-weighted average (TWA).* The employer shall ensure that no employee is exposed to an airborne concentration of EtO in excess of one (1) part EtO per million parts of air (1 ppm) as an eight (8)-hour time-weighted average (8-hour TWA).

(d) *Exposure monitoring.* (1) *General.* (i) Determinations of employee exposure shall be made from breathing zone air samples that are representative of the 8-hour TWA of each employee.

(ii) Representative 8-hour TWA employee exposure shall be determined on the basis of one or more samples representing full-shift exposure for each shift for each job classification in each work area.

(iii) Where the employer can document that exposure levels are equivalent for similar operations in different work shifts, the employer need only determine representative employee exposure for that operation during one shift.

(2) *Initial monitoring.* (i) Each employer who has a workplace or work operation covered by this standard, except as provided for in paragraph (a)(2) or (d)(2)(ii) of this section, shall perform initial monitoring to determine accurately the airborne concentrations of EtO to which employees may be exposed.

(ii) Where the employer has monitored after June 15, 1983 and the monitoring satisfies all other requirements of this section, the employer may rely on such earlier monitoring results to satisfy the requirements of paragraph (d)(2)(i) of this section.

(3) *Monitoring frequency (periodic monitoring).* (i) If the monitoring required by paragraph (d)(2) of this section reveals employee exposure at or above the action level but at or below the 8-hour TWA, the employer shall repeat such monitoring for each such employee at least every 6 months.

(ii) If the monitoring required by paragraph (d)(2)(i) of this section reveals employee exposure above the 8-hour TWA, the employer shall repeat such monitoring for each such employee at least every 3 months.

(iii) The employer may alter the monitoring schedule from quarterly to semiannually for any employee for whom two consecutive measurements taken at least 7 days apart indicate that the employee's exposure has decreased to or below the 8-hour TWA.

(4) *Termination of monitoring.* (i) If the initial monitoring required by paragraph (d)(2)(i) of this section reveals employee exposure to be below the

action level, the employer may discontinue the monitoring for those employees whose exposures are represented by the initial monitoring.

(ii) If the periodic monitoring required by paragraph (d)(3) of this section reveals that employee exposures, as indicated by at least two consecutive measurements taken at least 7 days apart, are below the action level, the employer may discontinue the monitoring for those employees whose exposures are represented by such monitoring.

(5) *Additional monitoring.* Notwithstanding the provisions of paragraph (d)(4) of this section, the employer shall institute the exposure monitoring required under paragraphs (d)(2)(i) and (d)(3) of this section whenever there has been a change in the production, process, control equipment, personnel or work practices that may result in new or additional exposures to EtO or when the employer has any reason to suspect that a change may result in new or additional exposures.

(6) *Accuracy of monitoring.* Monitoring shall be accurate, to a confidence level of 95 percent, to within plus or minus 25 percent for airborne concentrations of EtO at the 1 ppm TWA and to within plus or minus 35 percent for airborne concentrations of EtO at the action level of 0.5 ppm.

(7) *Employee notification of monitoring results.* (i) The employer shall, within 15 working days after the receipt of the results of any monitoring performed under this standard, notify the affected employee of these results in writing either individually or by posting of results in an appropriate location that is accessible to affected employees.

(ii) The written notification required by paragraph (d)(7)(i) of this section shall contain the corrective action being taken by the employer to reduce employee exposure to or below the PEL, wherever monitoring results indicated that the PEL has been exceeded.

(e) *Regulated Areas.* (1) The employer shall establish a regulated area wherever occupational exposures to airborne concentrations of EtO may exceed the TWA.

(2) Access to regulated areas shall be limited to authorized persons.

(3) Regulated areas shall be demarcated in any manner that minimizes the number of employees within the regulated area.

(f) *Methods of compliance.* (1) *Engineering controls and work practices.* (i) The employer shall institute engineering controls and work practices to reduce and maintain employee exposure to or below the TWA, except to the extent that such controls are not feasible.

(ii) Wherever the feasible engineering controls and work practices that can be instituted are not sufficient to reduce employee exposure to or below the TWA, the employer shall use them to reduce employee exposure to the lowest levels achievable by these controls and shall supplement them by the use of respiratory protection that complies with the requirements of paragraph (g) of this section.

(iii) Engineering controls are generally infeasible for the following operations: collection of quality assurance sampling from sterilized materials removal of biological indicators from sterilized materials: loading and unloading of tank cars; changing of ethylene oxide tanks on sterilizers; and vessel cleaning. For these operations, engineering controls are required only where the Assistant Secretary demonstrates that such controls are feasible.

(2) *Compliance program.* (i) Where the TWA is exceeded, the employer shall establish and implement a written program to reduce employee exposure to or below the TWA by means of engineering and work practice controls, as required by paragraph (f)(1) of this section, and by the use of respiratory protection where required or permitted under this section.

(ii) The compliance program shall include a schedule for periodic leak detection surveys and a written plan for emergency situations, as specified in paragraph (h)(i) of this section.

(iii) Written plans for a program required in paragraph (f)(2) shall be developed and furnished upon request for examination and copying to the Assistant Secretary, the Director, affected employees and designated employee representatives. Such plans shall be reviewed at least every 12 months, and shall be updated as necessary to reflect significant changes in the status of the employer's compliance program.

(iv) The employer shall not implement a schedule of employee rotation as a means of compliance with the TWA.

(g) *Respiratory protection and personal protective equipment.* (1) *General.* The employer shall provide respirators, and ensure that they are used, where required by this section. Respirators shall be used in the following circumstances.

(i) During the interval necessary to install or implement feasible engineering and work practice controls;

(ii) In work operations, such as maintenance and repair activities, vessel cleaning, or other activities for which engineering and work practice controls are not feasible;

(iii) In work situations where feasible engineering and work practice controls are not yet sufficient to reduce exposure to or below the TWA; and

(iv) In emergencies.

(2) *Respirator selection.* (i) Where respirators are required under this section, the employer shall select and provide, at no cost to the employee, the appropriate respirator as specified in Table 1, and shall ensure that the employee uses the respirator provided.

(ii) The employer shall select respirators from among those jointly approved as being acceptable for protection against EtO by the Mine Safety and Health Administration (MSHA) and by the National Institute for Occupational Safety and Health (NIOSH) under the provisions of 30 CFR Part 11.

(3) *Respirator program.* Where respiratory protection is required by this section, the employer shall institute a respirator program in accordance with 29 CFR 1910.134 (b), (d), (e), and (f).

(4) *Protective clothing and equipment.* Where eye or skin contact with liquid EtO or EtO solutions may occur, the employer shall select and provide, at no cost to the employee, appropriate protective clothing or other equipment in accordance with 29 CFR 1901.132 and 1910.133 to protect any area of the body that may come in contact with liquid EtO or EtO in solution, and shall ensure that the employee wears the protective clothing and equipment provided.

(h) *Emergency situations.* (1) *Written plan.* (i) A written plan for emergency situations shall be developed for each workplace where there is a possibility of an emergency. Appropriate portions of the plan shall be implemented in the event of an emergency.

(ii) The plan shall specifically provide that employees engaged in correcting emergency conditions shall be equipped with respiratory protection as required by paragraph (g) of this section until the emergency is abated.

(iii) The plan shall include the elements prescribed in 29 CFR 1910.38, "Employee emergency plans and fire prevention plans."

(2) *Alerting employees.* Where there is the possibility of employee exposure to EtO due to an emergency, means shall be developed to alert potentially affected employees of such occurrences promptly. Affected employees shall be immediately evacuated from the area in the event that an emergency occurs.

TABLE 1.—MINIMUM REQUIREMENTS FOR RESPIRATORY PROTECTION FOR AIRBORNE ETO

Condition of use or concentration of airborne EtO (ppm)	Minimum required respirator
Equal to or less than 50.	(a) Full facepiece respirator with EtO approved canister, front-or back-mounted.
Equal to or less than 2,000.	(a) Positive-pressure supplied air respirator, equipped with full facepiece, hood, or helmet, or (b) Continuous-flow supplied air respirator (positive pressure) equipped with hood, helmet or suit.
Concentration above 2,000 or unknown concentration (such as in emergencies).	(a) Positive-pressure self-contained breathing apparatus (SCBA), equipped with full facepiece, or (b) Positive-pressure full facepiece supplied air respirator equipped with an auxiliary positive-pressure self-contained breathing apparatus.
Firefighting	(a) Positive pressure self-contained breathing apparatus equipped with full facepiece.
Escape	(a) Any respirator described above.

Note.—Respirators approved for use in higher concentrations are permitted to be used in lower concentrations.

(i) *Medical Surveillance.* (1) *General.* (i) *Employees covered.* (A) The employer shall institute a medical surveillance program for all employees who are or may be exposed to EtO at or above the action level, without regard to the use of respirators, for at least 30 days a year.

(B) The employer shall make available medical examinations and consultations to all employees who have been exposed to EtO in an emergency situation.

(ii) *Examination by a physician.* The employer shall ensure that all medical examinations and procedures are performed by or under the supervision of a licensed physician, and are provided without cost to the employee, without loss of pay, and at a reasonable time and place.

(2) *Medical examinations and consultations.* (i) Frequency. The employer shall make available medical examinations and consultations to each employee covered under paragraph (i)(1)(i) of this section on the following schedules:

(A) Prior to assignment of the employee to an area where exposure may be at or above the action level for at least 30 days a year.

(B) At least annually each employee exposed at or above the action level for at least 30 days in the past year.

(C) At termination of employment or reassignment to an area where exposure to EtO is not at or above the action level for at least 30 days a year.

(D) As medically appropriate for any employee exposed during an emergency.

(E) As soon as possible, upon notification by an employee either (1) that the employee has developed signs or symptoms indicating possible overexposure to EtO, or (2) that the employee desires medical advice concerning the effects of current or past exposure to EtO on the employee's ability to produce a healthy child.

(F) If the examining physician determines that any of the examinations should be provided more frequently than specified, the employer shall provide such examinations to affected employees at the frequencies recommended by the physician.

(ii) *Content.* (A) Medical examinations made available pursuant to paragraphs (i)(2)(i)(A)–(D) of this section shall include:

(*1*) A medical and work history with special emphasis directed to symptoms related to the pulmonary, hematologic, neurologic, and reproductive systems and to the eyes and skin.

(*2*) A physical examination with particular emphasis given to the pulmonary, hematologic, neurologic, and reproductive systems and to the eyes and skin.

(*3*) A complete blood count to include at least a white cell count (including differential cell count), red cell count, hematocrit, and hemoglobin.

(*4*) Any laboratory or other test which the examining physician deems necessary by sound medical practice.

(B) The content of medical examinations or consultation made available pursuant to paragraph (i)(2)(i)(E) of this section shall be determined by the examining physician, and shall include pregnancy testing or laboratory evaluation of fertility, if requested by the employee and deemed appropriate by the physician.

(3) *Information provided to the physician.* The employer shall provide the following information to the examining physician:

(i) A copy of this standard and Appendices A, B, and C.

(ii) A description of the affected employee's duties as they relate to the employee's exposure.

(iii) The employee's representative exposure level or anticipated exposure level.

(iv) A description of any personal protective and respiratory equipment used or to be used.

(v) Information from previous medical examinations of the affected employee that is not otherwise available to the examining physician.

(4) *Physician's written opinion.* (i) The employer shall obtain a written opinion from the examining physician. This written opinion shall contain the results of the medical examination and shall include:

(A) The physician's opinion as to whether the employee has any detected medical conditions that would place the employee at an increased risk of material health impairment from exposure to EtO;

(B) Any recommended limitations on the employee or upon the use of personal protective equipment such as clothing or respirators; and

(C) A statement that the employee has been informed by the physician of the results of the medical examination and of any medical conditions resulting from EtO exposure that require further explanation or treatment.

(ii) The employer shall instruct the physician not to reveal in the written opinion given to the employer specific findings or diagnoses unrelated to occupational exposure to EtO.

(iii) The employer shall provide a copy of the physician's written opinion to the affected employee within 15 days from its receipt.

(j) *Communication of EtO hazards to employees.* (1) *Signs and labels.* (i) The employer shall post and maintain legible signs demarcating regulated areas and entrances or accessways to regulated areas that bear the following legend:

DANGER
ETHYLENE OXIDE
CANCER HAZARD AND REPRODUCTIVE HAZARD
AUTHORIZED PERSONNEL ONLY
RESPIRATORS AND PROTECTIVE CLOTHING MAY BE REQUIRED TO BE WORN IN THIS AREA

(ii) The employer shall ensure that precautionary labels are affixed to all containers of EtO whose contents are capable of causing employee exposure at or above the action level, and that the labels remain affixed when the containers of EtO leave the workplace. For the purposes of this paragraph, reaction vessels, storage tanks, and pipes or piping systems are not considered to be containers. The labels shall comply with the requirements of 29 CFR 1910.1200(f) of OSHA's Hazard Communication standard, and shall include the following legend:

(A) CAUTION
CONTAINS ETHYLENE OXIDE
CANCER AND REPRODUCTIVE HAZARD;

and

(B) A warning statement against breathing airborne concentrations of EtO.

(2) *Material safety data sheets.* Employers who are manufacturers or importers of EtO shall comply with the requirements regarding development of material safety data sheets as specified in 29 CFR 1910.1200(g) of OSHA's Hazard Communication standard.

(3) *Information and training.* (i) The employer shall provide employees who are potentially exposed to EtO at or above the action level with information and training on EtO at the time of initial assignment and at least annually thereafter.

(ii) Employees shall be informed of the following:

(A) The requirements of this section with an explanation of its contents, including Appendices A and B;

(B) Any operations in their work area where EtO is present;

(C) The location and availability of the written EtO final rule; and

(D) The medical surveillance program required by paragraph (i) of this section with an explanation of the information in Appendix C.

(iii) Employee training shall include at least:

(A) Methods and observations that may be used to detect the presence or release of EtO in the work area (such as monitoring conducted by the employer, continuous monitoring devices, etc.);

(B) The physical and health hazards of EtO;

(C) The measures employees can take to protect themselves from hazards associated with EtO exposure, including specific procedures the employer has implemented to protect employees from exposure to EtO, such as work practices, emergency procedures, and personal protective equipment to be used; and

(D) The details of the hazard communication program developed by the employer, including an explanation of the labeling system and how employees can obtain and use the appropriate hazard information.

(k) *Recordkeeping.* (1) *Objective data for exempted operations.*

(i) Where the processing, use, or handling of products made from or containing EtO are exempted from other requirements of this section under paragraph (a)(2) of this section, or where objective data have been relied on in lieu of initial monitoring under paragraph (d)(2)(ii) of this section, the employer shall establish and maintain an accurate record of objective data reasonably relied upon in support of the exemption.

(ii) This record shall include at least the following information:

(A) The product qualifying for exemption;

(B) The source of the objective data;

(C) The testing protocol, results of testing, and/or analysis of the material for the release of EtO;

(D) A description of the operation exempted and how the data support the exemption; and

(E) Other data relevant to the operations, materials, processing, or employee exposures covered by the exemption.

(iii) The employer shall maintain this record for the duration of the employer's reliance upon such objective data.

(2) *Exposure measurements.* (i) The employer shall keep an accurate record of all measurements taken to monitor employee exposure to EtO as prescribed in paragraph (d) of this section.

(ii) This record shall include at least the following information:

(A) The date of measurement;

(B) The operation involving exposure to EtO which is being monitored;

(C) Sampling and analytical methods used and evidence of their accuracy;

(D) Number, duration, and results of samples taken;

(E) Type of protective devices worn, if any; and

(F) Name, social security number and exposure of the employees whose exposures are represented.

(iii) The employer shall maintain this record for at least thirty (30) years, in accordance with 29 CFR 1910.20.

(3) *Medical surveillance.* (i) The employer shall establish and maintain an accurate record for each employee subject to medical surveillance by paragraph (i)(1)(i) of this section, in accordance with 29 CFR 1910.20.

(ii) The record shall include at least the following information:

(A) The name and social security number of the employee;

(B) Physicians' written opinions;

(C) Any employee medical complaints related to exposure to EtO; and

(D) A copy of the information provided to the physician as required by paragraph (i)(3) of this section.

(iii) The employer shall ensure that this record is maintained for the duration of employment plus thirty (30) years, in accordance with 29 CFR 1910.20.

(4) *Availability.* (i) The employer, upon written request, shall make all records required to be maintained by this section available to the Assistant Secretary and the Director for examination and copying.

(ii) The employer, upon request, shall make any exemption and exposure records required by paragraphs (1)(1) and (1)(2) of this section available for examination and copying to affected employees, former employees, designated representatives and the Assistant Secretary, in accordance with 29 CFR 1910.20 (a)–(e) and (g)–(i).

(iii) The employer, upon request, shall make employee medical records required by paragraph (k)(3) of this section available for examination and copying to the subject employee, anyone having the specific written consent of the subject employee, and the Assistant Secretary, in accordance with 29 CFR 1910.20.

(5) *Transfer of records.* (i) The employer shall comply with the requirements concerning transfer of records set forth in 29 CFR 1910.20(h).

(ii) Whenever the employer ceases to do business and there is no successor employer to receive and retain the records for the prescribed period, the employer shall notify the Director at least 90 days prior to disposal and transmit them to the Director.

(l) *Observation of monitoring.* (1) *Employee observation.*

The employer shall provide affected employees or their designated representatives an opportunity to observe any monitoring of employee exposure to EtO conducted in accordance with paragraph (d) of this section.

(2) *Observation procedures.* When observation of the monitoring of employee exposure to EtO requires entry into an area where the use of protective clothing or equipment is required, the observer shall be provided with and be required to use such clothing and equipment and shall comply with all other applicable safety and health procedures.

(m) *Dates* (1) *Effective date.* This section shall become effective August 21, 1984.

(2) *Start-up dates.* (i) The requirements of paragraphs (c) through (l) of this section, including feasible work practice controls but not including engineering controls specified in paragraph (f)(1), shall be complied with within one-hundred and eighty (180) days after the effective date of this section.

(ii) Engineering controls specified by paragraph (f)(1) of this section shall be implemented within one (1) year after the effective date of this section.

(n) *Appendices.* The information contained in the appendices is not intended by itself to create any additional obligations not otherwise imposed or to detract from any existing obligation.

Appendix A—Substance Safety Data Sheet for Ethylene Oxide

I. Substance Identification

A. Substance: Ethylene oxide (C_2H_4O).

B. Synonyms: dihydrooxirene, dimethylene oxide, EO, 1,2-epoxyethane, EtO, ETO, oxacyclopropane, oxane, oxidoethane, alpha/beta-oxidoethane, oxiran, oxirane.

C. Ethylene oxide can be found as a liquid or vapor.

D. EtO is used in the manufacture of ethylene glycol, surfactants, ethanolamines, glycol ethers, and other organic chemicals. EtO is also used as a sterilant and fumigant.

E. Appearance and odor: Colorless liquid below 10.7 °C (51.3 °F) or colorless gas with ether-like odor detected at approximately 700 parts EtO per million parts of air (700 ppm).

F. Permissible exposure: Exposure may not exceed 1 part EtO per million parts of air averaged over the 8-hour work day, nor may short-term exposure exceed 10 parts of EtO per million parts of air averaged over a 15 minute period.

II. Health Hazard Data

A. Ethylene oxide can cause bodily harm if you inhale the vapor, if it comes into contact with your eyes or skin, or if you swallow it.

B. Effects of overexposure:

1. Ethylene oxide in liquid form can cause eye irritation and injury to the cornea, frostbite, and severe irritation and blistering of the skin upon prolonged or confined contact. Ingestion of EtO can cause gastric irritation and liver injury. Acute effects from inhalation of EtO vapors include respiratory irritation and lung injury, headache, nausea, vomiting, diarrhea, shortness of breath, and cyaonosis (blue or purple coloring of skin). Exposure has also been associated with the occurrence of cancer, reproductive effects, mutagenic changes, neurotoxicity, and sensitization.

1. EtO has been shown to cause cancer in laboratory animals and has been associated with higher incidences of cancer in humans. Adverse reproductive effects and chromosome damage may also occur from EtO exposure.

a. Reporting signs and symptoms: You should inform your employer if you develop any signs or symptoms and suspect that they are caused by exposure to EtO.

III. Emergency First Aid Procedures

A. Eye exposure: If EtO gets into your eyes, wash your eyes immediately with large amounts of water, lifting the lower and upper eyelids. Get medical attention immediately. Contact lenses should not be worn when working with this chemical.

B. Skin exposure: If EtO gets on your skin, immediately wash the contaminated skin with water. If EtO soaks through your clothing, especially your shoes, remove the clothing immediately and wash the skin with water using an emergency deluge shower. Get medical attention immediately. Thoroughly wash contaminated clothing before reusing. Contaminated leather shoes or other leather articles should not be reused and should be discarded.

C. Inhalation: If large amounts of EtO are inhaled, the exposed person must be moved to fresh air at once. If breathing has stopped, perform cardiopulmonary resuscitation. Keep the affected person warm and at rest. Get medical attention immediately.

D. Swallowing: When EtO has been swallowed, give the person large quantities of water immediately. After the water has been swallowed, try to get the person to vomit by having him or her touch the back of the throat with his or her finger. Do not make an unconscious person vomit. Get medical attention immediately.

E. Rescue: Move the affected person from the hazardous exposure. If the exposed person has been overcome, attempt rescue only after notifying at least one other person of the emergency and putting into effect established emergency procedures. Do not become a casualty yourself. Understand your emergency rescue procedures and know the location of the emergency equipment before the need arises.

IV. Respirators and Protective Clothing

A. Respirators: You may be required to wear a respirator for nonroutine activities, in emergencies, while your employer is in the process of reducing EtO exposures through engineering controls, and where engineering controls are not feasible. As of the effective date of the standard, only air supplied positive-pressure, full-facepiece respirators are approved for protection against EtO. If air-purifying respirators are worn in the future, they must have a joint Mine Safety and Health Administration (MSHA) and National Institute for Occupational Safety and Health (NIOSH) label of approval for use with ethylene oxide. For effective protection, respirators must fit your face and head snugly. Respirators should not be loosened or removed in work situations where their use is required.

EtO does not have a detectable odor except at levels well above the permissible exposure limits. If you can smell EtO while wearing a respirator, proceed immediately to fresh air. If you experience difficulty breathing while wearing a respirator, tell your employer.

B. Protective clothing: You may be required to wear impermeable clothing, gloves, a face shield, or other appropriate protective clothing to prevent skin contact with liquid EtO or EtO-containing solutions. Where protective clothing is required, your employer must provide clean garments to you as necessary to assure that the clothing protects you adequately.

Replace or repair protective clothing that has become torn or otherwise damaged.

EtO must never be allowed to remain on the skin. Clothing and shoes which are not impermeable to EtO should not be allowed to become contaminated with EtO, and if they do, the clothing should be promptly removed and decontaminated. Contaminated leather shoes should be discarded. Once EtO penetrates shoes or other leather articles, they should not be worn again.

C. Eye protection: You must wear splashproof safety goggles in areas where liquid EtO or EtO-containing solutions may contact your eyes. In addition, contact lenses should not be worn in areas where eye contact with EtO can occur.

V. Precautions for Safe Use, Handling, and Storage

A. EtO is a flammable liquid, and its vapors can easily form explosive mixtures in air.

B. EtO must be stored in tighly closed containers in a cool, well-ventilated area, away from heat, sparks, flames, strong oxidizers, alkalines, and acids, strong bases, acetylide-forming metals such as cooper, silver, mercury and their alloys.

C. Sources of ignition such as smoking material, open flames and some electrical devices are prohibited wherever EtO is handled, used, or stored in a manner that could create a potential fire or explosion hazard.

D. You should use non-sparking tools when opening or closing metal containers of EtO, and containers must be bonded and grounded in the rare

instances in which liquid EtO is poured or transferred.

E. Impermeable clothing wet with liquid EtO or EtO-containing solutions may be easily ignited. If your are wearing impermeable clothing and are splashed with liquid EtO or EtO-containing solution, you should immediately remove the clothing while under an emergency deluge shower.

F. If your skin comes into contact with liquid EtO or EtO-containing solutions, you should immediately remove the EtO using an emergency deluge shower.

G. You should not keep food, beverages, or smoking materials in regulated areas where employee exposures are above the permissible exposure limits.

H. Fire extinguishers and emergency deluge showers for quick drenching should be readily available, and you should know where they are and how to operate them.

I. Ask your supervisor where EtO is used in your work area and for any additional plant safety and health rules.

VI. Access to Information

A. Each year, your employer is required to inform you of the information contained in this standard and appendices for EtO. In addition, your employer must instruct you in the proper work practices for using EtO emergency procedures, and the correct use of protective equipment.

B. Your employer is required to determine whether you are being exposed to EtO. You or your representative has the right to observe employee measurements and to record the results obtained. Your employer is required to inform you of your exposure. If your employer determine that you are being overexposed, he or she is required to inform you of the actions which are being taken to reduce your exposure to within permissible exposure limits.

C. Your employer is required to keep records of your exposures and medical examinations. These exposure records must be kept by the employer for at least thirty (30) years. Medical records must be kept for the period of your employment plus thirty (30) years.

D. Your employer is required to release your exposure and medical records to your physician or designated representative upon your written request.

VII. Sterilant Use of EtO in Hospitals and Health Care Facilities

This section of Appendix A, for informational purposes, sets forth EPA's recommendations for modifications in workplace design and practice in hospitals and health care facilities for which the Environmental Protection Agency has registered EtO for uses as a sterilant or fumigant under the Federal Insecticide, Funigicide, and Rodenticide Act, 7 U.S.C. 136 *et seq.* These new recommendations, published in the **Federal Register** by EPA at 49 FR 15268, as modified in today's **Register**, are intended to help reduce the exposure of hospital and health care workers to EtO to 1 ppm. EPA's recommended workplace design and workplace practice are as follows:

1. Workplace Design

a. *Installation of gas line hand valves.* Hand valves must be installed on the gas supply line at the connection to the supply cylinders to minimize leakage during cylinder change.

b. *Installation of capture boxes.* Sterilizer operations result in a gas/water discharge at the completion of the process. This discharge is routinely piped to a floor drain which is generally located in an equipment or an adjacent room. When the floor drain is not in the same room as the sterilizer and workers are not normally present, all that is necessary is that the room be well ventilated.

The installation of a "capture box" will be required for those work place layouts where the floor drain is located in the same room as the sterilizer or in a room where workers are normally present. A "capture box" is a piece of equipment that totally encloses the floor drain where the discharge from the sterilizer is pumped. The "capture box" is to be vented directly to a non-recirculating or dedicated ventilation system. Sufficient air intake should be allowed at the bottom of the box to handle the volume of air that is ventilated from the top of the box. The "capture box" can be made of metal, plastic, wood or other equivalent material. The box is intended to reduce levels of EtO discharged into the work room atmosphere. The use of a "capture box" is not required if: (1) The vacuum pump discharge floor drain is located in a well ventilated equipment or other room where workers are not normally present or (2) the water sealed vacuum pump discharges directly to a closed sealed sewer line (check local plumbing codes).

If it is impractical to install a vented "capture box" and a well ventilated equipment or other room is not feasible, a box that can be sealed over the floor drain may be used if: (1) The floor drain is located in a room where workers are not normally present and EtO cannot leak into an occupied area, and (2) the sterilizer in use is less than 12 cubic feet in capacity (check local plumbing codes).

c. *Ventilation of aeration units* i. *Existing aeration units.* Existing units must be vented to a non-recirculating or dedicated system or vented to an equipment or other room where workers are not normally present and which is well ventilated. Aerator units must be positioned as close as possible to the sterilizer to minimize the exposure from the off-gassing of sterilized items.

ii. *Installation of new aerator units (where none exist).* New aerator units must be vented as described above for existing aerators. Aerators must be in place by July 1, 1986.

d. *Ventilation during cylinder change.* Workers may be exposed to short but relatively high levels of EtO during the change of gas cylinders. To reduce exposure from this route, users must select one of three alternatives designed to draw off gas that may be released when the line from the sterilizer to the cylinder is disconnected:

i. Location of cylinders in a well ventilated equipment room or other room where workers are not normally present.

ii. Installation of a flexible hose (at least 4" in diameter) to a non-recirculating or dedicated ventilation system and located in the area of cylinder change in such a way that the hose can be positioned at the point where the sterilizer gas line is disconnected from the cylinder.

iii. Installation of a hood that is part of a non-recirculating or dedicated system and positioned no more than one foot above the point where the change of cylinders takes place.

e. *Ventilation of sterilizer door area.* One of the major sources of exposure to EtO occurs when the sterilizer door is opened following the completion of the sterilization process. In order to reduce this avenue of exposure, a hood or metal canopy closed on each end must be installed over the sterilizer door. The hood or metal canopy must be connected to a non-recirculating or dedicated ventilation system or one that exhausts gases to a well ventilated equipment or other room where workers are not normally present. A hood or canopy over the sterilizer door is required for use even with those sterilizers that have a purge cycle and must be in place by July 1, 1986.

f. *Ventilation of sterilizer relief valve.* Sterilizers are typically equipped with a safety relief device to release gas in case of increased pressure in the sterilizer. Generally, such relief devices are used on pressure vessels. Although these pressure relief devices are rarely

opened for hospital and health care sterilizers, it is suggested that they be designed to exhaust vapor from the sterilizer by one of the following methods:

i. Through a pipe connected to the outlet of the relief valve ventilated directly outdoors at a point high enough to be away from passers by, and not near any windows that open, or near any air conditioning or ventilation air intakes.

ii. Through a connection to an existing or new non-recirculating or dedicated ventilation system.

iii. Through a connection to a well ventilated equipment or other room where workers are not normally present.

g. *Ventilation systems.* Each hospital and health care facility affected by this notice that uses EtO for the sterilization of equipment and supplies must have a ventilation system which enables compliance with the requirements of section (b) through (f) in the manner described in these sections and within the timeframes allowed. Thus, each affected hospital and health care facility must have or install a non-recirculating or dedicated ventilation equipment or other room where workers are not normally present in which to vent EtO.

h. *Installation of alarm systems.* An audible and visual indicator alarm system must be installed to alert personnel of ventilation system failures, i.e., when the ventilation fan motor is not working.

2. Workplace Practices

All the workplace practices discussed in this unit must be permanently posted near the door of each sterilizer prior to use by any operator.

a. *Changing of supply line filters.* Filters in the sterilizer liquid line must be changed when necessary, by the following procedure:

i. Close the cylinder valve and the hose valve.

ii. Disconnect the cylinder hose (piping) from the cylinder.

iii. Open the hose valve and bleed slowly into a proper ventilating system at or near the in-use supply cylinders.

iv. Vacate the area until the line is empty.

v. Change the filter.

vi. Reconnect the lines and reverse the value position.

vii. Check hoses, filters, and valves for leaks with a fluorocarbon leak detector (for those sterilizers using the 88 percent chlorofluorocarbon, 12 percent ethylene oxide mixture (12/88)).

b. *Restricted access area.* i. Areas involving use of EtO must be designated as restricted access areas. They must be identified with signs or floor marks near the sterilizer door, aerator, vacuum pump floor drain discharge, and in-use cylinder storage.

ii. All personnel must be excluded from the restricted area when certain operations are in progress, such as discharging a vacuum pump, emptying a sterilizer liquid line, or venting a non-purge sterilizer with the door ajar or other operations where EtO might be released directly into the face of workers.

c. *Door opening procedures.* i. *Sterilizers with purge cycles.* A load treated in a sterilizer equipped with a purge cycle should be removed immediately upon completion of the cycle (provided no time is lost opening the door after cycle is completed). If this is not done, the purge cycle should be repeated before opening door.

ii. *Sterilizers without purge cycles.* For a load treated in a sterilizer not equipped with a purge cycle, the sterilizer door must be ajar 6" for 15 minutes, and then fully opened for at least another 15 minutes before removing the treated load. The length of time of the second period should be established by peak monitoring for one hour after the two 15-minute periods suggested. If the level is above 10 ppm time-weighted average for 8 hours, more time should be added to the second waiting period (door wide open). However, in no case may the second period be shortened to less than 15 minutes.

d. *Chamber unloading procedures.* i. Procedures for unloading the chamber must include the use of baskets or rolling carts, or baskets and rolling tables to transfer treated loads quickly, thus avoiding excessive contact with treated articles, and reducing the duration of exposures.

ii. If rolling carts are used, they should be pulled not pushed by the sterilizer operators to avoid offgassing exposure.

e. *Maintenance.* A written log should be instituted and maintained documenting the date of each leak detection and any maintenance procedures undertaken. This is a suggested use practice and is not required.

i. *Leak detection.* Sterilizer door gaskets, cylinder and vacuum piping, hoses, filters, and valves must be checked for leaks under full pressure with a Fluorocarbon leak detector (for 12/88 systems only) every two weeks by maintenance personnel. Also, the cylinder piping connections must be checked after changing cylinders. Particular attention in leak detection should be given to the automatic solenoid valves that control the flow of EtO to the sterilizer. Specifically, a check should be made at the EtO gasline entrance port to the sterilizer, while the sterilizer door is open and the solenoid valves are in a closed position.

ii. *Maintenance procedures.* Sterilizer/areator door gaskets, valves, and fittings must be replaced when necessary as determined by maintenance personnel in their bi-weekly checks; in addition, visual inspection of the door gaskets for cracks, debris, and other foreign substances should be conducted daily by the operator.

Appendix B—Substance Technical Guidelines for Ethylene Oxide

I. Physical and Chemical Data

A. Substance identification:

1. Synonyms: dihydrooxirene, dimethylene oxide, EO, 1,2-epoxyethane, EtO ETO oxacyclopropane, oxane, oxidoethane, alpha/beta-oxidoethane, oxiran, oxirane.

2. Formula: (C_2H_4O).

3. Molecular weight: 44.06

B. Physical data:

1. Boiling point (760 mm Hg): 10.70°C (51.3°F);

2. Specific gravity (water = 1): 0.87 (at 20°C or 68°F)

3. Vapor density (air = 1): 1.49;

4. Vapor pressure (at 20°C): 1,095 mm Hg;

5. Solubility in water: complete;

6. Appearance and odor: colorless liquid; gas at temperature above 10.7°F or 51.3°C with ether-like odor above 700 ppm.

II. Fire, Explosion, and Reactivity Hazard Data

A. Fire:

1. Flash point: less than O°F (open cup);

2. Stability: decomposes violently at temperatures above 800°F;

3. Flammable limits in air, percent by volume: Lower: 3, Upper: 100;

4. Extinguishing media: Carbon dioxide for small fires, polymer or alcohol foams for large fires;

5. Special fire fighting procedures: Dilution of ethylene oxide with 23 volumes of water renders it non-flammable;

6. Unusual fire and explosion hazards: Vapors of EtO will burn without the presence of air or other oxidizers. EtO vapors are heavier than air and may travel along the ground and be ignited by open flames or sparks at locations remote from the site at which EtO is being used.

7. For purposes of compliance with the requirements of 29 CFR 1910.106, EtO is classified as a flammable gas. For

example, 7,500 ppm, approximately one-fourth of the lower flammable limit, would be considered to pose a potential fire and explosion hazard.

8. For purposes of compliance with 29 CFR 1910.155, EtO is classified as a Class B fire hazard.

9. For purpose of compliance with 29 CFR 1919.307, locations classified as hazardous due to the presence of EtO shall be Class I.

B. Reactivity:

1. Conditions contributing to instability: EtO will polymerize violently if contaminated with aqueous alkalies, amines, mineral acids, metal chlorides, or metal oxides. Violent decomposition will also occur at temperatures above 800 °F;

2. Incompatabilities: Alkalines and acids;

3. Hazardous decomposition products: Carbon monoxide and carbon dioxide.

III. Spill, Leak, and Disposal Procedures

A. If EtO is spilled or leaked, the following steps should be taken:

1. Remove all ignition sources.

2. The area should be evacuated at once and re-entered only after the area has been thoroughly ventilated and washed down with water.

B. Persons not wearing appropriate protective equipment must be restricted from areas of spills or leaks until cleanup has been completed.

C. Waste disposal methods: Waste material shall be disposed of in a manner that is not hazardous to employees or to the general population. In selecting the method of waste disposal, applicable local, State, and Federal regulations should be consulted.

IV. Monitoring and Measurement Procedures

A. Exposure above the Permissible Exposure Limit:

1. Eight-hour exposure evaluation: Measurements taken for the purpose of determining employee exposure under this section are best taken with consecutive samples covering the full shift. Air samples must be taken in the employee's breathing zone (air that would most nearly represent that inhaled by the employee.)

2. Monitoring techniques: The sampling and analysis under this section may be performed by collection of the EtO vapor on charcoal adsorption tubes or other composition adsorption tubes, with subsequent chemical analysis. Sampling and analysis may also be performed by instruments such as real-time continuous monitoring systems, portable direct reading instruments, or passive dosimeters as long as measurements taken using these methods accurately evaluate the concentration of EtO in employees' breathing zones.

Appendix D describes the validated method of sampling and analysis which has been tested by OSHA for use with EtO. Other available methods are also described in Appendix D. The employer has the obligation of selecting a monitoring method which meets the accuracy and precision requirements of the standard under his unique field conditions. The standard requires that the method of monitoring must be accurate, to a 95 percent confidence level, to plus or minus 25 percent for concentrations of EtO at 1 ppm, and to plus or minus 35 percent for concentrations at 0.5 ppm. In addition to the method described in Appendix D, there are numerous other methods available for monitoring for EtO in the workplace. Details on these other methods have been submitted by various companies to the rulemaking record, and are available at the OSHA Docket Office.

B. Since many of the duties relating to employee exposure are dependent on the results of measurement procedures, employers must assure that the evaluation of employee exposures is performed by a technically qualified person.

V. Protective Clothing and Equipment

Employees shall be provided with and be required to wear appropriate protective clothing wherever there is significant potential for skin contact with liquid EtO or EtO-containing solutions. Protective clothing shall include impermeable coveralls or similar full-body work clothing, gloves, and head coverings, as appropriate to protect areas of the body which may come in contact with liquid EtO or EtO-containing solutions.

Employers must ascertain that the protective garments are impermeable to EtO. Permeable clothing, including items made of rubber, and leather shoes should not be allowed to become contaminated with liquid EtO. If permeable clothing does become contaminated, it should be immediately removed, while the employer is under an emergency deluge shower. If leather footwear or other leather garments become wet from EtO they should be discarded and not be worn again, because leather absorbs EtO and holds it against the skin.

Any protective clothing that has been damaged or is otherwise found to be defective should be repaired or replaced. Clean protective clothing should be provided to the employee as necessary to assure employee protection. Whenever impermeable clothing becomes wet with liquid EtO, it should be washed down with water before being removed by the employee. Employees are also required to wear splash-proof safety goggles where there is any possibility of EtO contacting the eyes.

VI. Miscellaneous Precautions

A. Store EtO in tightly closed containers in a cool, well-ventilated area and take all necessary precautions to avoid any explosion hazard.

B. Non-sparking tools must be used to open and close metal containers. These containers must be effectively grounded and bonded.

C. Do not incinerate EtO cartridges, tanks or other containers.

D. Employers shall advise employees of all areas and operations where exposure to EtO occur.

VII. Common Operations

Common operations in which exposure to EtO is likely to occur include the following: Manufacture of EtO, surfactants, ethanolamines, glycol ethers, and specialty chemicals, and use as a sterilant in the hospital, health product and spice industries.

Appendix C-Medical Surveillance Guidelines for Ethylene Oxide

I. Route of Entry

Inhalation.

II. Toxicology

Clinical evidence of adverse effects associated with the exposure to EtO is present in the form of increased incidence of cancer in laboratory animals (leukemia, stomach, brain), mutation in offspring in animals, and resorptions and spontaneous abortions in animals and human populations respectively. Findings in humans and experimental animals exposed to airborne concentrations of EtO also indicate damage to the genetic material (DNA). These include hemoglobin alkylation, unsecheduled DNA synthesis, sister chromatid exchange chromosomal aberration, and functional sperm abnormalities.

Ethylene oxide in liquid form can cause eye irritation and injury to the cornea, frostbite, severe irritation, and blistering of the skin upon prolonged or confined contact. Ingestion of EtO can cause gastric irritation and liver injury. Other effects from inhalation of EtO vapors include respiratory irritation and lung injury, headache, nausea, vomiting, diarrhea, dyspnea and cyanosis.

III. Signs and Symptoms of Acute Overexposure

The early effects of acute overexposure to EtO are nausea and vomiting, headache, and irritation of the eyes and respiratory passages. The patient may notice a "peculiar taste" in the mouth. Delayed effects can include pulmonary edema, drowsiness, weakness, and incoordination. Studies suggest that blood cell changes, an increase in chromosomal aberrations, and spontaneous abortion may also be causally related to acute overexposure to EtO.

Skin contact with liquid or gaseous EtO causes characteristic burns and possibly even an allergic-type sensitization. The edema and erythema occurring from skin contact with EtO progress to vesiculation with a tendency to coalesce into blebs with desquamation. Healing occurs within three weeks, but there may be a residual brown pigmentation. A 40–80% solution is extremely dangerous, causing extensive blistering after only brief contact. Pure liquid EtO causes frostbite because of rapid evaporation. In contrast, the eye is relatively insensitive to EtO, but there may be some irritation of the cornea.

Most reported acute effects of occupational exposure to EtO are due to contact with EtO in liquid phase. The liquid readily penetrates rubber and leather, and will produce blistering if clothing or footwear contaminated with EtO are not removed.

IV. Surveillance and Preventive Considerations

As noted above, exposure to EtO has been linked to an increased risk of cancer and reproductive effects including decreased male fertility, fetotoxicity, and spontaneous abortion. EtO workers are more likely to have chromosomal damage than similar groups not exposed to EtO. At the present, limited studies of chronic effects in humans resulting from exposure to EtO suggest a causal association with leukemia. Animal studies indicate leukemia and cancers at other sites (brain, stomach) as well. The physician should be aware of the findings of these studies in evaluating the health of employees exposed to EtO.

Adequate screening tests to determine an employee's potential for developing serious chronic diseases, such as cancer, from exposure to EtO do not presently exist. Laboratory tests may, however, give evidence to suggest that an employee is potentially overexposed to EtO. It is important for the physician to become familiar with the operating conditions in which exposure to EtO is likely to occur. The physician also must become familiar with the signs and symptoms that indicate a worker is receiving otherwise unrecognized and unacceptable exposure to EtO. These elements are especially important in evaluating the medical and work histories and in conducting the physical exam. When an unacceptable exposure in an active employee is identified by the physician, measures taken by the employer to lower exposure should also lower the risk of serious long-term consequences.

The employer is required to institute a medical surveillance program for all employees who are or will be exposed to EtO at or above the action level (0.5 ppm) for at least 30 days per year, without regard to respirator use. All examinations and procedures must be performed by or under the supervision of a licensed physician at a reasonable time and place for the employee and at no cost to the employee.

Although broad latitude in prescribing specific tests to be included in the medical surveillance program is extended to the examining physician, OSHA requires inclusion of the following elements in the routine examination:

(i) Medical and work histories with special emphasis directed to symptoms related to the pulmonary, hematologic, neurologic, and reproductive systems and to the eyes and skin.

(ii) Physical examination with particular emphasis given to the pulmonary, hematologic, neurologic, and reproductive systems and to the eyes and skin.

(iii) Complete blood count to include at least a white cell count (including differential cell count), red cell count, hematocrit, and hemoglobin.

(iv) Any laboratory or other test which the examining physician deems necessary by sound medical practice.

If requested by the employee, the medical examinations shall include pregnancy testing or laboratory evaluation of fertility as deemed appropriate by the physician.

In certain cases, to provide sound medical advice to the employer and the employee, the physician must evaluate situations not directly related to EtO. For example, employees with skin diseases may be unable to tolerate wearing protective clothing. In addition those with chronic respiratory diseases may not tolerate the wearing of negative pressure (air purifying) respirators. Additional tests and procedures that will help the physician determine which employees are medically unable to wear such respirators should include: An evaluation of cardiovascular function, a baseline chest x-ray to be repeated at five year intervals, and a pulmonary function test to be repeated every three years. The pulmonary function test should include measurement of the employee's forced vital capacity (FVC), forced expiratory volume at one second (FEV1), as well as calculation of the ratios of FEV1 to FVC, and measured FVC and measured FEV1 to expected values corrected for variation due to age, sex, race, and height.

The employer is required to make the prescribed tests available at least annually to employees who are or will be exposed at or above the action level, for 30 or more days per year; more often than specified if recommended by the examining physician; and upon the employee's termination of employment or reassignment to another work area. While little is known about the long term consequences of high short-term exposures, it appears prudent to monitor such affected employees closely in light of existing health data. The employer shall provide physician recommended examinations to any employee exposed to EtO in emergency conditions. Likewise, the employer shall make available medical consultations including physician recommended exams to employees who believe they are suffering signs or symptoms of exposure to EtO.

The employer is required to provide the physician with the following informatin: a copy of this standard and its appendices; a description of the affected employee's duties as they relate to the employee exposure level; and information from the employee's previous medical examinations which is not readily available to the examining physician. Making this information available to the physician will aid in the evaluation of the employee's health in relation to assigned duties and fitness to wear personal protective equipment, when required.

The employer is required to obtain a written opinion from the examining physician containing the results of the medical examinations; the physician's opinion as to whether the employee has any detected medical conditions which would place the employee at increased risk of material impairment of his or her health from exposure to EtO; any recommended restrictions upon the employee's exposure to EtO, or upon the use of protective clothing or equipment such as respirators; and a statement that the employee has been informed by the physician of the results of the medical examination and of any medical conditions which require further

explanation or treatment. This written opinion must not reveal specific findings or diagnoses unrelated to occupational exposure to EtO, and a copy of the opinion must be provided to the affected employee.

The purpose in requiring the examining physician to supply the employer with a written opinion is to provide the employer with a medical basis to aid in the determination of initial placement of employees and to assess the employee's ability to use protective clothing and equipment.

Appendix D—Sampling and Analytical Methods for Ethylene Oxide

A number of methods are available for monitoring employee exposures to EtO. Most of these involve the use of charcoal tubes and sampling pumps, followed by analysis of the samples by gas chromatograph. The essential differences between the charcoal tube methods include, among others, the use of different desorbing solvents, the use of different lots of charcoal, and the use of different equipment for analysis of the samples.

Besides charcoal, methods using passive dosimeters, gas sampling bags, impingers, and detector tubes have been utilized for determination of EtO exposure. In addition, there are several commercially available portable gas analyzers and monitoring units.

This appendix contains details for the method which has been tested at the OSHA Analytical Laboratory in Salt Lake City. Inclusion of this method in the appendix does not mean that this method is the only one which will be satisfactory. Copies of descriptions of other methods available are available in the rulemaking record, and may be obtained from the OSHA Docket Office. These include the Union Carbide, Dow Chemical, 3M, and DuPont methods, as well as NIOSH Method S–286. These methods are briefly described at the end of this appendix.

Employers who note problems with sample breakthrough using the OSHA or other charcoal methods should try larger charcoal tubes. Tubes of larger capacity are available. In addition, lower flow rates and shorter sampling times should be beneficial in minimizing breakthrough problems. Whatever method the employer chooses, he must assure himself of the method's accuracy and precision under the unique conditions present in his workplace.

Ethylene Oxide

Method No.: 30.

Matrix: Air.

Target Concentration: 1.0 ppm (1.8 mg/m^3).

Procedure: Samples are collected on two charcoal tubes in series and desorbed with 1% CS_2 in benzene. The samples are derivatized with HBr and treated with sodium carbonate. Analysis is done by gas chromatography with an electron capture detector.

Recommended Air Volume and Sampling Rate: 1 liter and 0.05 Lpm.

Detection Limit of the Overall Procedure: 13.3 ppb (0.024 mg/m^3) (Based on 1.0 liter air sample).

Reliable Quantitation Limit: 52.2 ppb (0.094 mg/m^3) (Based on 1.0 liter air sample).

Standard Error of Estimate: 6.59% (See Backup Section 4.6).

Special Requirements: Samples must be analyzed within 15 days of sampling date.

Status of Method: The sampling and analytical method has been subjected to the established evaluation procedures of the Organic Method Evaluations Branch.

Date: August 1981.

Chemist: Wayne D. Potter.

Organic Solvents Branch, OSHA Analytical Laboratory, Salt Lake City, Utah

1. General Discussion.

1.1 Background.

1.1.1 History of Procedure.

Ethylene oxide samples analyzed at the OSHA Laboratory have normally been collected on activated charcoal and desorbed with carbon disulfide. The analysis is performed with a gas chromatograph equipped with a FID (Flame ionization detector) as described in NIOSH Method S286 (Ref. 5.1). This method is based on a PEL of 50 ppm and has a detection limit of about 1 ppm.

Recent studies have prompted the need for a method to analyze and detect ethylene oxide at very low concentrations.

Several attempts were made to form an ultraviolet (UV) sensitive derivative with ethylene oxide for analysis with HPLC. Among those tested that gave no detectable product were: p-anisidine, methylimidazole, aniline, and 2,3,6-trichlorobenzoic acid. Each was tested with catalysts such as triethylamine, aluminum chloride, methylene chloride and sulfuric acid but no detectable derivative was produced.

The next derivatization attempt was to react ethylene oxide with HBr to form 2-bromoethanol. This reaction was successful. An ECD (electron capture detector) gave a very good response for 2-bromoethanol due to the presence of bromine. The use of carbon disulfide as the desorbing solvent gave too large a response and masked the 2-bromoethanol. Several other solvents were tested for both their response on the ECD and their ability to desorb ethylene oxide from the charcoal. Among those tested were toluene, xylene, ethyl benzene, hexane, cyclohexane and benzene. Benzene was the only solvent tested that gave a suitable response on the ECD and a high desorption. It was found that the desorption efficiency was improved by using 1% CS_2 with the benzene. The carbon disulfide did not significantly improve the recovery with the other solvents. SKC Lot 120 was used in all tests done with activated charcoal.

1.1.2 Physical Properties (Ref. 5.2–5.4).

Synonyms: Oxirane; dimethylene oxide, 1,2-epoxy-ethane; oxane; C_2H_4O; ETO;

Molecular Weight: 44.06

Boiling Point: 10.7 °C (51.3°)

Melting Point: −111 °C

Description: Colorless, flammable gas

Vapor Pressure: 1095 mm. at 20 °C

Odor: Ether-like odor

Lower Explosive Limits: 3.0% (by volume)

Flash Point (TOC): Below 0 °F

Molecular Structure: CH_2—CH_2

1.2 Limit Defining Parameters.

1.2.1 Detection Limit of the Analytical Procedure.

The detection limit of the analytical procedure is 12.0 picograms of ethylene oxide per injection. This is the amount of analyte which will give a peak whose height is five times the height of the baseline noise. (See Backup Data Section 4.1).

1.2.2 Detection Limit of the Overall Procedure.

The detection limit of the overall procedure is 24.0 ng of ethylene oxide per sample.

This is the amount of analyte spiked on the sampling device which allows recovery of an amount of analyte equivalent to the detection limit of the analytical procedure. (See Backup Data Section 4.2).

1.2.3 Reliable Quantitation Limit.

The reliable quantitation limit is 94.0 nanograms of ethylene oxide per sample. This is the smallest amount of analyte which can be quantitated within the requirements of 75% recovery and 95% confidence limits. (See Backup Data Section 4.2).

It must be recognized that the reliable quantitation limit and detection limits reported in the method are based upon optimization of the instrument for the smallest possible amount of analyte. When the target concentration of an

analyte is exceptionally higher than these limits, they may not be attainable at the routine operating parameters. In this case, the limits reported on analysis reports will be based on the operating parameters used during the analysis of the samples.

1.2.4 Sensitivity.

The sensitivity of the analytical procedure over a concentration range representing 0.5 to 2 times the target concentration based on the recommended air volume is 34105 area units per μg/mL. The sensitivity is determined by the slope of the calibration curve (See Backup Data Section 4.3).

The sensitivity will vary somewhat with the particular instrument used in the analysis.

1.2.5 Recovery.

The recovery of analyte from the collection medium must be 75% or greater. The average recovery from spiked samples over the range of 0.5 to 2 times the target concentration is 88.0% (See Backup Section 4.4). At lower concentrations the recovery appears to be non-linear.

1.2.6 Precision (Analytical Method Only).

The pooled coefficient of variation obtained from replicate determination of analytical standards at 0.5X, 1X and 2X the target concentration is 0.036 (See Backup Data Section 4.5).

1.2.7 Precision (Overall Procedure).

The overall procedure must provide results at the target concentration that are 25% of better at the 95% confidence level. The precision at the 95% confidence level for the 15 day storage test is plus or minus 12.9% (See Backup Data Section 4.6).

This includes an additional plus or minus 5% for sampling error.

1.3 Advantages.

1.3.1 The sampling procedure is convenient.

1.3.2 The analytical procedure is very sensitive and reproducible.

1.3.3 Reanalysis of samples is possible.

1.3.4 Samples are stable for at least 15 days at room temperature.

1.3.5 Interferences are reduced by the longer GC retention time of the new derivative.

1.4 Disadvantages.

1.4.1 Two tubes in series must be used because of possible breakthrough and migration.

1.4.2 The precision of the sampling rate may be limited by the reproducibility of the pressure drop across the tubes. The pumps are usually calibrated for one tube only.

1.4.3 The use of benzene as the desorption solvent increases the hazards of analysis because of the potential carcinogenic effects of benzene.

1.4.4 After repeated injections there can be a buildup of residue formed on the electron capture detector which decreases sensitivity.

1.4.5 Recovery from the charcoal tubes appears to be nonlinear at low concentrations.

2. Sampling Procedure.

2.1 Apparatus.

2.1.1 A calibrated personal sampling pump whose flow can be determined within plus or minus 5% of the recommended flow.

2.1.2 SKC Lot 120 Charcoal tubes: glass tube with both ends flame sealed, 7 cm long with a 6 mm O.D. and a 4-mm I.D., containing 2 sections of coconut shell charcoal separated by a 2-mm portion of urethane foam. The adsorbing section contains 100 mg of charcoal, the backup section 50 mg. A 3-mm portion of urethane foam is placed between the outlet end of the tube and the backup section. A plug of silylated glass wool is placed in front of the adsorbing section.

2.2 Reagents.

2.2.1 None required.

2.3 Sampling Technique.

2.3.1 Immediately before sampling, break the ends of the charcoal tubes. All tubes must be from the same lot.

2.3.2 Connect two tubes in series to the sampling pump with a short section of flexible tubing. A minimum amount of tubing is used to connect the two sampling tubes together. The tube closer to the pump is used as a backup. This tube should be identified as the backup tube.

2.3.3 The tubes should be placed in a vertical position during sampling to minimize channeling.

2.3.4 Air being sampled should not pass through any hose or tubing before entering the charcoal tubes.

2.3.5 Seal the charcoal tubes with plastic caps immediately after sampling. Also, seal each sample with OSHA seals lengthwise.

2.3.6 With each batch of samples, submit at least one blank tube from the same lot used for samples. This tube should be subjected to exactly the same handling as the samples (break, seal, transport) except that no air is drawn through it.

2.3.7 Transport the samples (and corresponding paperwork) to the lab for analysis.

2.3.8 If bulk samples are submitted for analysis, they shoud be transported in glass containers with Teflon-lined caps. These samples must be mailed separately from the container used for the charcoal tubes.

2.4 Breakthrough.

2.4.1 The breakthrough (5% breakthrough) volume for a 3.0 mg/m ethylene oxide sample stream at approximately 85% relative humidity, 22°C and 633 mm is 2.6 liters sampled at 0.05 liters per minute. This is equivalent to 7.8 μg of ethylene oxide. Upon saturation of the tube it appeared that the water may be displacing ethylene oxide during sampling.

2.5 Desorption Efficiency.

2.5.1 The desorption efficiency, from liquid injection onto charcoal tubes, averaged 88.0% from 0.5 to 2.0 x the target concentration for a 1.0 liter air sample. At lower ranges it appears that the desorption efficiency is non-linear (See Backup Data Section 4.2).

2.5.2 The desorption efficiency may vary from one laboratory to another and also from one lot of charcoal to another. Thus, it is necessary to determine the desorption efficiency for a particular lot of charcoal.

2.6 Recommended Air Volume and Sampling Rate.

2.6.1 The recommended air volume is 1.0 liter.

2.6.2 The recommended maximum sampling rate is 0.05 Lpm.

2.7 Interferences.

2.7.1 Ethylene glycol and Freon 12 at target concentration levels did not interfere with the collection of ethylene oxide.

2.7.2 Suspected interferences should be listed on the sample data sheets.

2.7.3 The relative humidity may affect the sampling procedure.

2.8 Safety Precautions.

2.8.1 Attach the sampling equipment to the employee so that it does not interfere with work performance.

2.8.2 Wear safety glasses when breaking the ends of the sampling tubes.

2.8.3 If possible, place the sampling tubes in a holder so the sharp end is not exposed while sampling.

3. Analytical Method.

3.1 Apparatus.

3.1.1 Gas chromatograph equipped with a linearized electron capture detector.

3.1.2 GC column capable of separating the derivative of ethylene oxide (2-bromoethanol) from any interferences and the 1% CS_2 in benzene solvent. The column used for validation studies was: 10 ft x ⅛ inch stainless steel 20% SP–2100, .1% Carbowax 1500 on 100/120 Supelcoport.

3.1.3 An electronic integrator or some other suitable method of measuring peak areas.

3.1.4 Two milliliter vials with Teflon-lined caps.

3.1.5 Gas tight syringe—500 μL or other convenient sizes for preparing standards.

3.1.6 Microliter syringes—10 μL or other convenient sizes for diluting standards and 1 μL for sample injections.

3.1.7 Pipets for dispensing the 1% CS_2 in benzene solvent. The Glenco 1 mL dispenser is adequate and convenient.

3.1.8 Volumetric flasks—5 mL and other convenient sizes for preparing standards.

3.1.9 Disposable Pasteur pipets.

3.2 Reagents.

3.2.1 Benzene, reagent grade.

3.2.2 Carbon Disulfide, reagent grade.

3.2.3 Ethylene oxide, 99.7% pure.

3.2.4 Hydrobromic Acid, 48% reagent grade.

3.2.5 Sodium Carbonate, anhydrous, reagent grade.

3.2.6 Desorbing reagent, 99% Benzene/1% CS_2.

3.3 Sample Preparation.

3.3.1 The front and back sections of each sample are transferred to separate 2-mL vials.

3.3.2 Each sample is desorbed with 1.0 mL of desorbing reagent.

3.3.3 The vials are sealed immediately and allowed to desorb for one hour with occasional shaking.

3.3.4 Desorbing reagent is drawn off the charcoal with a disposable pipet and put into clean 2-mL vials.

3.3.5 One drop of HBr is added to each vial. Vials are resealed and HBr is mixed well with the desorbing reagent.

3.3.6 About 0.15 gram of sodium carbonate is carefully added to each vial. Vials are again resealed and mixed well.

3.4 Standard Preparation.

3.4.1 Standards are prepared by injecting the pure ethylene oxide gas into the desorbing reagent.

3.4.2 A range of standards are prepared to make a calibration curve. A concentration of 1.0 μL of ethylene oxide gas per 1 mL desorbing reagent is equivalent to 1.0 ppm air concentration (all gas volumes at 25°C and 760 mm) for the recommended 1 liter air sample. This amount is uncorrected for desorption efficiency (See Backup Data Section 4.2. for desorption efficiency corrections).

3.4.3 One drop of HBr per mL of standard is added and mixed well.

3.4.4 About 0.15 grams of sodium carbonate is carefully added for each drop of HBr (A small reaction will occur).

3.5 Analysis.

3.5.1 GC Conditions.

Nitrogen flow rate—10mL/min.
Injector Temperature—250°C
Detector Temperature—300°C
Column Temperature—100°C
Injection size—0.8 μL
Elution time—3.9 minutes

3.5.2 Peak areas are measured by an integrator or other suitable means.

3.5.3 The integrator results are in area units and a calibration curve is set up with concentration vs. area units.

3.6 Interferences.

3.6.1 Any compound having the same retention time of 2-bromoethanol is a potential interference. Possible interferences should be listed on the sample data sheets.

3.6.2 GC parameters may be changed to circumvent interferences.

3.6.3 There are usually trace contaminants in benzene. These contaminants, however, posed no problem of interference.

3.6.4 Retention time data on a single column is not considered proof of chemical identity. Samples over the 1.0 ppm target level should be confirmed by GC/Mass Spec or other suitable means.

3.7 Calculations

3.7.1 The concentration in μg/mL for a sample is determined by comparing the area of a particular sample to the calibration curve, which has been prepared from analytical standards.

3.7.2 The amount of analyte in each sample is corrected for desorption efficiency by use of a desorption curve.

3.7.3 Analytical results (A) from the two tubes that compose a particular air sample are added together.

3.7.4 The concentration for a sample is calculated by the following equation:

$$\text{ETO, mg/m}^3 = \frac{AXB}{C}$$

where:
A = μg/mL
B = desorption volume in milliliters
C = air volume in liters.

3.7.5 To convert mg/m³ to parts per million (ppm) the following relationship is used:

$$\text{ETO, ppm} = \frac{\text{mg/m}^3 \times 24.45}{44.05}$$

where:
mg/m³ = results from 3.7.4
24.45 = molar volume at 25 °C and 760mm Hg
44.05 = molecular weight of ETO.

3.8 Safety Precautions

3.8.1 Ethylene oxide and benzene are potential carcinogens and care must be exercised when working with these compounds.

3.8.2 All work done with the solvents (preparation of standards, desorption of samples, etc.) should be done in a hood.

3.8.3 Avoid any skin contact with all of the solvents.

3.8.4 Wear safety glasses at all times.

3.8.5 Avoid skin contact with HBr because it is highly toxic and a strong irritant to eyes and skin.

4. Backup Data.

4.1 Detection Limit Data.

The detection limit was determined by injecting 0.8 μL of a 0.015 μg/mL standard of ethylene oxide into 1% CS_2 in benzene. The detection limit of the analytical procedure is taken to be 1.20×10^{-5} μg per injection. This is equivalent to 8.3 ppb (0.015 mg/m³) for the recommended air volume.

4.2 Desorption Efficiency.

Ethylene oxide was spiked onto charcoal tubes and the following recovery data was obtained.

Amount spiked (μg)	Amount recovered (μg)	Percent recovery
4.5	4.32	96.0
3.0	2.61	87.0
2.25	2.025	90.0
1.5	1.365	91.0
1.5	1.38	92.0
.75	.6525	87.0
.375	.315	84.0
.375	.312	83.2
.1875	.151	80.5
.094	.070	74.5

At lower amounts the recovery appears to be non-linear.

4.3 Sensitivity Data.

The following data was used to determine the calibration curve.

Injection	0.5×.75 μg/mL	1×1.5 μg/mL	2×3.0 μg/mL
1	30904	59567	111778
2	30987	62914	106016
3	32555	58578	106122
4	32242	57173	109716
X	31672	59558	108408

Slope = 34.105.

4.4 Recovery.

The recovery was determined by spiking ethylene oxide onto lot 120 charcoal tubes and desorbing with 1% CS_2 in Benzene. Recoveries were done at 0.5, 1.0, and 2.0 X the target concentration (1 ppm) for the recommended air volume.

PERCENT RECOVERY

Sample	0.5x	1.0x	2.0x
1	88.7	95.0	91.7
2	83.8	95.0	87.3
3	84.2	91.0	86.0
4	88.0	91.0	83.0
5	88.0	86.0	85.0
X	86.5	90.5	87.0

Weighted Average = 88.2.

4.5 Precision of the Analytical Procedure.

The following data was used to determine the precision of the analytical method:

Concentration	0.5x.75 µg/mL	1X1.5 µg/mL	2X3.0 µg/mL
Injection	.7421	1.4899	3.1184
	.7441	1.5826	3.0447
	.7831	1.4628	2.9149
	.7753	1.4244	2.9185
Average	.7612	1.4899	2.9991
Standard Deviation	.0211	.0674	.0998
CV	.0277	.0452	.0333

$$CV = \frac{3(.0277)^2 + 3(.0452)^2 + 3(.0333)^2}{3+3+3}$$

CV+0.036

4.6 Storage Data.

Samples were generated at 1.5 mg/m³ ethylene oxide at 85% relative humidity, 22°C and 633 mm. All samples were taken for 20 minutes at 0.05 Lpm. Six samples were analyzed as soon as possible and fifteen samples were stored at refrigerated temperature (5°C) and fifteen samples were stored at ambient temperature (23°C). These stored samples were analyzed over a period of nineteen days.

PERCENT RECOVERY

Day analyzed	Refrigerated	Ambient
1	87.0	87.0
1	93.0	93.0
1	94.0	94.0
1	92.0	92.0
4	92.0	91.0
4	93.0	88.0
4	91.0	89.0
6	92.0	
6	92.0	
8		92.0
8		86.0
10	91.7	
10	95.5	
10	95.7	
11		90.0
11		82.0
13	78.0	
13	81.4	
13	82.4	
14		78.5
14		72.1
18	66.0	
18	68.0	
19		64.0
19		77.0

4.7 Breakthrough Data.

Breakthrough studies were done at 2 ppm (3.6 mg/m³) at approximately 85% relative humidity at 22°C (ambient temperature). Two charcoal tubes were used in series. The backup tube was changed every 10 minutes and analyzed for breakthrough. The flow rate was 0.050 Lpm.

Tube No.	Time (minutes)	Percent breakthrough
1	10	(1)
2	20	(1)
3	30	(1)
4	40	1.23
5	50	3.46
6	60	18.71
7	70	39.2
8	80	53.3
9	90	72.0
10	100	96.0
11	110	113.0
12	120	133.9

[1] None.

The 5% breakthrough volume was reached when 2.6 liters of test atmosphere were drawn through the charcoal tubes.

5. References.

5.1 "NIOSH Manual of Analytical Methods," 2nd ed. NIOSH: Cincinnati, 1977; Method S286.

5.2 "IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man," International Agency for Research on Cancer: Lyon, 1976; Vol. II, p. 157.

5.3 Sax., N.I. "Dangerous Properties of Industrial Materials," 4th ed.; Van Nostrand Reinhold Company. New York, 1975; p. 741.

5.4 "The Condensed Chemical Dictionary", 9th ed.; Hawley, G.G., ed.; Van Nostrand Reinhold Company, New York, 1977; p. 361.

Summary of Other Sampling Procedures

OSHA believes that served other types of monitoring equipment and techniques exist for monitoring time-weighted averages. Considerable research and method development is currently being performed, which will lead to improvements and a wider variety of monitoring techniques. A combination of monitoring procedures can be used. There probably is no one best method for monitoring personal exposure to ethylene oxide in all cases. There are advantages, disadvantages, and limitations to each method. The method of choice will depend on the need and requirements. Some commonly used methods include the use of charcoal tubes, passive dosimeters, Tedler gas sampling bags, detector tubes, photoionization detection units, infrared detection units and gas chromatographs. A number of these methods are described below.

A. Charcoal Tube Sampling Procedures

Qazi-Ketcham method (Ex. 11–133)—This method consists of collecting EtO on Columbia JXC activated carbon, desorbing the EtO with carbon disulfide and analyzing by gas chromatography with flame ionization detection. Union Carbide has recently updated and revalidated this monitoring procedures. This method is capable of determining both eight-hour time-weighted average exposures and short-term exposures. The method was validated to 0.5 ppm. Like other charcoal collecting procedures, the method requires considerable analytical expertise.

ASTM-proposed method—The Ethylene Oxide Industry Council (EOIC) has contracted with Clayton Environmental Consultants, Inc. to conduct a collaborative study for the proposed method. The ASTM-Proposed method is similar to the method published by Qazi and Ketcham is the November 1977 American Industrial Hygiene Association Journal, and to the method of Pilney and Coyne, presented at the 1979 American Industrial Hygiene Conference. After the air to be sampled is drawn through an activated charcoal tube, the ethylene oxide is desorbed from the tube using carbon disulfide and is quantitated by gas chromatography utilizing a flame ionization detector. The ASTM-proposed method specifies a large two-section charcoal tube, shipment in dry ice, storage at less than −5°C, and analysis within three weeks to prevent migration and sample loss. Two types of charcoal tubes are being tested—Pittsburgh Coconut-Based (PCB) and Columbia JXC charcoal. This collaborative study will give an indication of the inter- and intralaboratory precision and accuracy of the ASTM-proposed method. Several laboratories have considerable expertise using the Qazi-Ketcham and Dow methods.

B. Passive Monitors—Ethylene oxide diffuses into the monitor and is collected in the sampling media. The DuPont Pro-Tek badge collects EtO in an absorbing solution, which is analyzed colorimetrically to determine the amount of EtO present. The 3M 350 badge collects the EtO on chemically treated charcoal. Other passive monitors are currently being developed and tested. Both 3M and DuPont have submitted data indicating their dosimeters meet the precision and accuracy requirements of the proposed ethylene oxide standard. Both presented laboratory validation data to 0.2 ppm (Exs. 11–65, 4–20, 108, 109, 130).

C. Tedlar Gas Sampling Bags-Samples are collected by drawing a known volume of air into a Tedlar gas sampling bag. The ethylene oxide concentration is often determined on-site using a portable gas chromatograph or portable infrared spectometer.

D. Detector tubes—A known volume of air is drawn through a detector tube using a small hand pump. The concentration of EtO is related to the length of stain developed in the tube. Detector tubes are economical, easy to use, and give an immediate readout. Unfortunately, partly because they are nonspecific, their accuracy is often questionable. Since the sample is taken over a short period of time, they may be useful for determining the source of leaks.

E. Direct Reading Instruments—There are numerous types of direct reading instruments, each having its own strengths and weaknesses (Exs. 135B, 135C, 107, 11–78, 11–153). Many are relatively new, offering greater sensitivity and specificity. Popular ethylene oxide direct reading instruments include infrared detection units, photoionization detection units, and gas chromatographs.

Portable infrared analyzers provide an immediate, continuous indication of a concentration value; making them particularly useful for locating high concentration pockets, in leak detection and in ambient air monitoring. In infrared detection units, the amount of infrared light absorbed by the gas being analyzed at selected infrared wavelengths is related to the concentration of a particular component. Various models have either fixed or variable infrared filters, differing cell pathlengths, and microcomputer controls for greater sensitivity, automation, and interference elimination.

A fairly recent detection system is photoionization detection. The molecules are ionized by high energy ultraviolet light. The resulting current is measured. Since different substances have different ionization potentials, other organic compounds may be ionized. The lower the lamp energy, the better the selectivity. As a continuous monitor, photoionization detection can be useful for locating high concentration pockets, in leak detection, and continuous ambient air monitoring. Both portable and stationary gas chromatographs are available with various types of detectors, including photoionization detectors. A gas chromatograph with a photoionization detector retains the photionization sensitivity, but minimizes or eliminates interferences. For several GC/PID units, the sensitivity is in the 0.1–0.2 ppm EtO range. The GC/PID with microprocessors can sample up to 20 sample points sequentially, calculate and record data, and activate alarms or ventilation systems. Many are quite flexible and can be configured to meet the specific analysis needs for the workplace.

DuPont presented their laboratory validation data of the accuracy of the Qazi-Ketcham charcoal tube, the PCB charcoal tube, Miran 103 IR analyzer, 3M #3550 monitor and the Du Pont C–70 badge. Quoting Elbert V. Kring:

> We also beleive that OSHA's proposed accuracy in this standard is appropriate. At plus or minus 25 percent at one part per million, and plus or minus 35 percent below that. And, our data indicates there's only one monitoring method, right now, that we've tested thoroughly, that meets that accuracy requirements. That is the Du Pont Pro-Tek badge* * *. We also believe that this kind of data should be confirmed by another independent laboratory, using the same type dynamic chamber testing (Tr. 1470)

Additional data by an independent laboratory following their exact protocol was not submitted. However, information was submitted on comparisons and precision and accuracy of those monitoring procedures which indicate far better precision and accuracy of those monitoring procedures than that obtained by Du Pont (Ex. 4–20, 130, 11–68, 11–133, 130, 135A).

The accuracy of any method depends to a large degree upon the skills and experience of those who not only collect the samples but also those who analyze the samples. Even for methods that are collaboratively tested, some laboratories are closer to the true values than others. Some laboratories may meet the precision and accuracy requirements of the method; others may consistently far exceed them for the same method.

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