INDUSTRYWIDE STUDIES REPORT OF WALK THROUGH SURVEY

OF

LEDERLE LABORATORIES DIVISION
American Cyanamid Company
Pearl River, New York

PROJECT NUMBER: P:84:12

SURVEY CONDUCTED BY:
Leslie Stayner, Epi II
Kyle Steenland, Epi I
Larry Elliott, IHS
Virginia Ringenburg, IHS

DATE OF SURVEY:
December 12-13, 1983

REPORT WRITTEN BY:
Virginia L. Ringenburg
Leslie Stayner
Alice Greife

DATE OF REPORT:
October 30, 1984

REPORT #:
67.20

Industrial Hygiene Section
Industrywide Studies Branch
Division of Surveillance, Hazard Evaluations and Field Studies
National Institute for Occupational Safety and Health
Centers for Disease Control
Cincinnati, Ohio

PURPOSE:	The purpose of this survey was to evaluate the industrial hygiene records, production processes, and personnel records as part of a pilot study for the ethylene oxide (EtO) mortality study. These areas were evaluated to determine the suitability of including this facility in the mortality/industrial hygiene study of EtO being conducted by researchers from NIOSH.
EMPLOYER REPRESENTATIVES CONTACTED:	Mr. Robert Parlante, Director of Safety and Environmental Services, Lederle (914) 735-5000 Mr. Douglas S. Bondor, Industrial Hygienist, Lederle (914) 735-5000
EMPLOYEE REPRESENTATIVE CONTACTED	Mr. William P. Siemers, Jr., President, Local 143, International Chemical Workers Union (ICWU) (914) 735-4874
STANDARD INDUSTRIAL CLASSIFICATION OF PLANT:	2834 - Pharmaceutical Preparations

Table of Contents

Tables

Abstract

On December 12 and 13, 1983, a site visit to Lederle Laboratories Division of the American Cyanamid Company, Pearl River, New York, was conducted to gather data and determine the feasibility of including this facility in the mortality/industrial hygiene study of EtO being conducted by researchers from NIOSH.

During the site visit, industrial hygiene records and personnel records were evaluated and a walk-through survey of the plant was conducted in order to observe all production processes related to EtO sterilization.

Personal and area sampling for EtO has been conducted by Lederle since 1978. An industrial hygiene evaluation of the monitoring data indicated that it would be possible to construct an exposure classification scheme for this facility.

In addition, this facility meets all the eligibility requirements as defined by the protocol and, therefore, should be included in the study. These requirements are: 1) the plant must contribute at least 400 person years (although the personnel records were not sampled, a crude estimate indicated there were about 7,000 person years at this plant), 2) the plant must have adequate personnel records or other records that can be used for identifying past and present workers exposed to EtO, and 3) the plant must not have any serious confounding exposure to a known leukemogen.

Introduction

Under the Occupational Safety and Health Act of 1970 (set forth by the 91st Congress, S.9123, Public Law 91-596), the National Institute for Occupational Safety and Health (NIOSH) was given the authority and responsibility for conducting and reporting on field research studies in industry. Section 20(a)7 states that NIOSH shall conduct and publish industrywide studies of the effects of chronic low level exposure to industrial materials, processes, and stresses on the potential for illness, disease, or loss of functional capacity in the aging adult.

Ethylene oxide (EtO) is a major industrial chemical and is one of the 25 chemicals of highest production volume in the United States.[1] The major portion of EtO is used in the production of ethylene glycol (antifreeze) and as a chemical intermediate for polyester films, fibers, and bottles. A small fraction of EtO, less than 0.24%, has been used by the health care and medical supply industries over the past 35-40 years to sterilize heat-sensitive medical supplies.[1] However, it is in this industry that most of the employee exposures occur. This was shown in a 1977 survey conducted by researchers from NIOSH in which it was estimated that 75,000 health care workers were employed in EtO sterilization operations.[2] In addition, another 25,000 employees might be incidentally exposed due to inadequate engineering controls.[3]

EtO is a colorless gas at standard temperature and pressure or a liquid at higher pressures. EtO is miscible with water, ethanol, ether, and most common organic solvents. In addition, it is highly explosive when in concentrations of 3 to 100% (EtO) in air. The biological warning properties are essentially useless since the (ether-like) odor threshold among individuals ranges from 300 to 1,500 parts per million (ppm) and adverse health effects may be elicited at levels much less than this.[1,4]

Due to the toxicity and possible carcinogenicity of EtO (see section on Toxicity), NIOSH researchers initiated an investigation in 1982 to assess the feasibility of conducting a cohort mortality study and industrial hygiene evaluation of workers exposed to EtO. Based on the data gathered during the feasibility study, it was concluded that the cohort of workers exposed to EtO in industrial sterilization processes was the most adequate group to support a cohort mortality study.[5] In order to develop a final protocol for this study, a pilot study of six facilities was initiated to further develop the methods used for data collection and exposure classification.

The purpose of this walk-through survey was to determine the suitability of including Lederle in an industrywide mortality and industrial hygiene study of workers potentially exposed to EtO in industrial sterilization processes. Specifically this walk-through evaluated the following:

1. The documentation of production processes which have a potential for worker exposure to EtO.

2. The documentation of changes in these processes, e.g., engineering controls, which may have altered potential worker exposure to EtO.

3. The determination of historic and current jobs and/or departments within these processes in which workers have a potential exposure to EtO.

4. The existence of historic as well as current production data which includes total amount of EtO used per given time, type of product sterilized, and form of EtO used.

5. The availability, quality, and completeness of any existing industrial hygiene records and/or programs documenting historic as well as current potential worker exposure to EtO.

6. The ability of these records to identify workers with peak exposures to EtO; and, the number and concentration levels of these peaks.

7. The identification of any additional exposures in the work environment which would confound the interpretation of the mortality or industrial hygiene results.

The data gathered in this walk-through will be used to develop, to the extent possible, estimates of exposure to EtO by department and/or job category, level and duration of continuous and peak exposures, and calendar year within this plant. If possible (during the future mortality/industrial hygiene study) these exposure estimates will be compiled into an exposure matrix which will be used to determine the existence of a dose response relationship with any positive association observed in the mortality study.

Description of Plant

Lederle Laboratories present site in Pearl River, New York, was founded in 1907 by Dr. Ernst J. Lederle. In 1930, Lederle became a subsidiary of the American Cyanamid Company of which it is now an operating division. The present day plant covers 700 acres and is divided into two separate facilities, one for research and the other for production. The production facility manufactures 300 products most of which are prescription drugs. These include: antibiotics, steroids, biologicals, pharmaceuticals, vitamins, hematinics, and vaccines. The products that are sterilized with EtO are: TB tine test, Thiotepa (anti-cancer drug), ascorbic acid (used in an injectable product), triamcinolone diacetate (steroid), and packaging supplies for the Sabin oral polio vaccine (Orimune). These parenteral and medical products are sterilized in Department 421 called the "sterile kitchen area" which is located on the fourth floor of Building 112.

Description of the Workforce

The Lederle plant employs 4000 workers; one-half in research and one-half in production. Of the 2000 workers in production, only 30 work in the EtO sterilizing department. Seven to eight of these employees work in the sterilizer area on a full-time basis, the other 22-23 work in this area approximately one day a week. Another six employees work in the EtO quarantine area and storage area.

Employees work one shift, five days a week, except the employee who operates the EtO sterilizer; this employee works overtime and weekends. There is a high turnover rate within the EtO sterilizing department because these jobs are considered entry level jobs. In fact, approximately 400 to 500 people have passed through these jobs in the past 28 years. The annual employee turnover rate of the plant is about 20%.

In the past, the plant workforce was 90-100% Caucasian and 80% female. At the present time, the workforce is 60% Caucasian and 65% female. Age has remained fairly constant over time with most employees falling in the mid-twenties to the late forties range. The union representing the Lederle employees is the International Chemical Workers Union, Local 143.

Description of Process

Initially, a batch of product is loaded onto a pallet which is pushed into a preconditioning chamber. This chamber load is conditioned overnight by increasing the temperature and humidity which in effect reduces the time required to sterilize each load. Next, the pallets are placed onto a screen topped cart on wheels and pushed by a large hook into the sterilizer (EtO #2). After the sterilizer is loaded the humidity is increased, the temperature is slightly elevated, and the EtO/carbon dioxide (CO_2) mixture (90 parts CO_2 to 10 parts EtO) is added to the sterilizer. The product is then sterilized for 11.5 to 21.5 hours; sterilizing time is dependent upon the absorption rate and capacity of the product. After the sterilization cycle, a vacuum is applied to remove the gas mixture from the sterilizer. The packaged products are then removed from the sterilizer and returned to the preconditioning chamber for aeration and off-gassing of EtO from the product. Aeration is conducted for a minimum of 10 hours under negative pressure at ambient temperature. After the aeration cycle is completed, the packaged products (in boxes) are moved via elevator to the quarantine area on the first floor. Sterilized bulk drug ingredients are taken to the parenteral manufacturing areas for vacuum scavenging and further processing. In the quarantine area the cardboard boxes containing the product are opened for an additional 72 hours of aeration. After this additional aeration the boxes are closed, stacked, and stored until a quality control (Q.C.) check is conducted. All products are then moved to other areas of the plant for further processing, packaging, and shipment.

Description of Past Exposures and Controls Used

Lederle's use of EtO as a sterilant began between the mid-forties and 1950. Since that time approximately the same amount, 1,300 pounds, of EtO has been used each year; however, the rate of use has changed. In the past, more cycles were run and less gas was used per load; today, the reverse is true. The first sterilizer used was a 55 gallon stainless steel drum to which powdered product and 2 pounds of EtO gas were added. The gas mixture used was 88 parts of Freon to 12 parts of EtO. The drum was rolled overnight and EtO removed from the powder by vacuum scavenging and vented outside the building. The batches were small and only one person handled the entire operation in an isolated area on the third floor. Keeping the number of people to a minimum was done in order to decrease the possibility of contamination of the sterile product.

In 1955, sterilizer EtO #1 was purchased. EtO #1's overall size was approximately 140 cubic feet (ft^3); it could be used for steam or EtO sterilization. The sterilizer was run under positive pressure; its exhaust was vented 15 feet (ft) above the roof. The gas mixture of 90 parts CO_2 to 10 parts of EtO was used.

Since 1962, boxes of sterilized product were opened after sterilization for aeration purposes. Currently, four employees carry out this task and probably receive an intermittent exposure to EtO of one hour or less per day. Prior to 1980, however, exposure of these employees was on a more consistent basis, since aeration of the product was carried out in the sterilizer room.

From 1964 to 1974, formaldehyde was present in trace amounts in certain products handled in the sterile kitchen area. Handling was conducted under conditions using closed systems and sealed containers. Formaldehyde fumigation was not conducted in the kitchen area, although other sterile processing areas were fumigated.

In 1970, sterilizer EtO #2 was purchased and is still in use today. Sterilizer EtO #2's capacity is approximately 126 ft^3 and it is used for EtO sterilization only. Sterilizer EtO #2 is run under positive pressure and its exhaust is vented 15 ft above the roof.

For a time prior to 1975, a reaction changing chloroform to 1,1-trichloroethane was conducted in an exhaust hood in the kitchen area. The practice was terminated in 1975.

In 1975, a low volume non-recirculating area exhaust was added to the general kitchen area. During the mid to late seventies, the door gasket material was changed in order to reduce the number of EtO leaks. Industrial hygiene sampling was first conducted in 1978 (see Table I for EtO sampling methods and data). In 1979, a multi-point Wilks Miran^R infrared monitor was installed in the kitchen area. An alarm system, set to signal immediate employee evacuation of the kitchen area at 30 ppm of EtO, was attached to this monitor. In addition, employees began wearing organic vapor cartridge (OVA) half-face respirators while unloading sterilizers. A respirator program including maintenance, cleaning and replacement, and fit testing was started. However, the OVA cartridge respirators were not approved by NIOSH for protection against exposure to EtO. Lederle also revised the standard practice instructions regarding safety work permits to introduce appropriate procedures for each class of work. (The Standard Practice Instruction form may be found in Appendix 1.)

During 1980, an outside consultant/contractor was retained and equipment and controls were upgraded. During this time two incidents of EtO exposure occurred. On June 5, 1980, a contractor inserted an incorrect size orifice in the sterilizer causing a blow-out of a threaded plug, resulting in an EtO leak. The released EtO set off alarms and employees were removed from the area. About 75 ppm of EtO was measured (grab samples) about five minutes after the accident. On July 1, 1980, the contractor committed a piping error and vented EtO outside the kitchen window. The EtO was picked up by the building's ventilation intake and recirculated. Again, the alarms were

set off, employees were evacuated, Scott Air Pacs were put on, and EtO samples were taken. Levels ranged from 25 to greater than 100 ppm in the sterilizer area.

Additional controls installed in 1980 included: check valves on tank lines, a validated electrochemical total hydrocarbon detector (Enmet) on the sterilizer, a pre-conditioning/off-gassing chamber, a local exhaust on the chamber drain, a wheeled pallet and hook arrangement for remote sterilizer loading, and a ventilation purge to the post-sterilization cycle. In addition, the company voluntarily lowered its Permissible Exposure Limit (PEL) for EtO to 10 ppm as an 8-hour Time-Weighted Average (TWAg). Also, Safety Program and Safety Training/Industrial Hygiene booklets were developed and instituted.

In February, 1981, EtO#1 was completely shut down and many products were transferred to Puerto Rico. Lederle also replaced the OVA respirators with Scott full-face pressure demand repsirators which were worn at the end of the sterilization cycle through degassing of the chamber. (NIOSH has issued approval for use of air supplied respirators for protection against exposure to EtO.) Lederle also tried to remove as many items as possible from EtO sterilization. These products are now sent outside of the company for sterilization by Cobalt 60 (gamma) radiation. Also in 1981, the company voluntarily lowered its PEL for EtO to 1 ppm.

In 1982, a specific Job Hazard Analysis-Safe Job Procedures form was put into use for employees operating EtO sterilizer #2. (This form may be found in Appendix 2.) Also, the use of updated, bound industrial hygiene chemical exposure monitoring record forms was started.

In 1983, safety training documentation forms were developed and instituted.

Description of Industrial Hygiene, Safety, and Medical Programs

Industrial Hygiene

Lederle employs a staff of three industrial hygienists, two of whom are certified, and a certified industrial hygiene technician. The industrial hygiene (I.H.) program was formed around 1958 and is part of the Safety Department. Yearly audits of this department were conducted by the corporate I.H. Department through 1980. EtO monitoring began in 1978 and continues today. Personal TWA and/or area TWA and grab sampling has been conducted with charcoal tubes (standard size and Qazi-Ketchum), direct reading detector tubes, 3-M badges, and a direct reading instrument (Wilks Miran multi-point infrared detector). The charcoal tubes were analyzed by an American Industrial Hygiene Association (AIHA) certified laboratory. Also, ventilation measurements are routinely conducted and engineering controls have been added periodically since 1955.

Safety

Sterilizer operators also wear respirators, safety glasses and shoes, uniforms, and leather gloves. Lederle's safety program includes: new personnel orientation, safety training programs, safety meetings,

promotional and incentive programs, literature distribution, and off-the-job safety programs.

Medical Program

Lederle employs 3 physicians, 7 nurses, 1 X-ray technician, and 1 laboratory technician. An on-site 8-bed clinic is provided.

Pre-employment physical examinations are required for all employees. Periodic physical examinations are made available to all employees.

Description and Review of the Personnel Record Keeping System

A. Description:
Blank copies of the various types of personnel records were obtained from the company, and several r cord systems were identified that would be useful for the study.

1. Computerized Records
In 1980, the company intiated a computerized personnel system. All workers active at this time, and those who have since joined the company are included in this system. This file contains relevant data on social security numbers, date of birth, race, and sex. An abbreviated work history containing the last three jobs held and the dates of employment in these jobs is available from this file.

2. Personnel File Folders
All active and terminated employees have a personnel file folder, which is maintained forever, according to company policy. These folders contain an application form, and a sheet that is completed each time an individual makes a job change. These records contain information on date of birth, social security number, and sex. Information on race is not always available in these records. A complete job history can be constructed by reviewing the job change sheets.

Personnel file folders for active workers and about one year of terminated workers are kept on file in the main personnel office. Approximately 3700 active files are housed in this area.

File folders for workers terminated more than one year ago are stored in a warehouse area. There are approximately 20 full file cabinet drawers containing personnel files in this area. For workers terminated prior to 1969, files are stored in numbered drawers. An alphabetic index of the individual names in each numbered drawer is maintained in the personnel office. These file drawers are roughly in chronologic order, since approximately once a year a new drawer is sent to the warehouse. File folders terminated prior to 1969 are maintained in a file system that is in alphabetical order by last name.

3. Cardex Records
An index card record system is available for all terminated employees. These records contain information on social security number, date of birth, and sex. Information on race is only available on the more recent terminations.

Cards for hourly workers terminated prior to 1969 are filed with cards for all terminated salaried workers. These cards are in alphabetical order. It was estimated that this file contain approximately 17,200 cards. The cards for hourly workers and salaried workers terminated prior to 1969 appeared to contain complete work histories which included department codes, job titles, and dates of employment. For salaried workers terminated after 1969, only the first and last job history cards are in the file; therefore, the job histories are not complete for these workers. The missing cards were sent to the personnel file folders.

Cards for hourly workers terminated after 1969 are in a separate file cabinet. These files have only the first and last job history cards, and are thus not complete. It was estimated that the total number of records in this file system is 4900.

Based on the number of cards in the cardex system, it has been estimated that the company has a total of 22,100 inactive personnel records on file.

4. Other Potentially Useful Record Systems
   a. Payroll Records are available for the last seven years. These records are organized by social security number and contain a department code.

   b. Every employee has a medical file which is maintained forever. At the very least, this record contains a preemployment physical form. These records contain job titles at the time of the physical, but are not complete enough to construct a detailed occupational history. The preemployment medical exam form contains information on date of birth and sex.

B. Identification of Exposed and Nonexposed Workers
Workers potentially exposed to ethylene oxide can be identified from the personnel records by the department number which corresponds to the "sterile kitchen area" where EtO was used. From 1950 to 1979 this number was 712, from 1980 to 1982 it was 721, and from 1983 to the present it has been 421. The quarantine area workers can also be identified from the personnel records. These workers were employed in department number 824.

The job titles are not always available from the personnel records, and thus it may not always be possible to determine which workers operated the sterilizer units. However, the supervisor of the "sterile kitchen area", who has been with the company for as long as the company has used EtO, may be able to identify which employees were sterilizer operators.

C. Sampling from the Personnel Records

In order to validate the completeness of the personnel files, a list was obtained of 10 individuals that the plant management knew were potentially exposed to ethylene oxide. The cardex and personnel file folder systems were checked to see if these individuals could be found, and if their job histories would accurately reflect their length of employment in potentially EtO exposed areas. All 10 individuals were located in both file systems. The personnel files correctly identified all 10 workers as having worked in the EtO exposed departments (712 or 721). Seven out of the 10 workers' cardex records indicated that they had worked in the EtO department. However, when compared to the information in the personnel file folder, only one of the individuals had a cardex record with a complete job history from the EtO exposed department. This is because all of these workers left employment after 1969; and, as mentioned earlier, the cardex system does not contain complete job histories for workers terminated after 1969.

It was not possible, due to time constraints, to randomly sample the personnel record systems to determine the percentage of exposed workers. Out of approximately 20,000 records on file at this location, only 500 workers (2.5%) are believed to have been potentially exposed to ethylene oxide.

Toxicity

Evidence from animal studies suggests that EtO may have carcinogenic properties.[6,7] A group of EtO manufacturers sponsored a study at the Bushy Run Research Center in which male and female Fischer 344 rats were exposed to EtO at airborne concentrations of 10, 33, or 100 parts per million (ppm) for 6 hours per day, 5 days per week for two years.[6] Two other groups of animals served as controls. Initially, there were 120 animals of each sex, in each exposure group. The researchers observed a statistically significant increase in the incidence of mononuclear cell leukemia among the female rats, and peritoneal mesothelioma among the male rats exposed to EtO. The increase in leukemia incidence was found to increase linearly as a function of EtO exposure. An elevation in mortality from brain cancers (glial type) was also observed in the rats exposed to EtO.

NIOSH researchers have recently reported on the results from an animal experiment which corroborated the findings of the Bushy Run Study.[7] Male Fischer 344 rats were exposed to EtO for 7 hours/day, 5 days/week for 2 years at airborne concentrations of 0, 50, or 100 ppm. There were 80 rats in each exposure group. Increases in the incidence of mononuclear leukemia, peritoneal mesothelioma, and cerebral gliomas were observed among the EtO exposed rats, relative to nonexposed controls.

Only a few epidemiologic studies have examined the potential human carcinogenicity of EtO.[8-10] Hogstedt, et al, conducted a retrospective cohort mortality study of a group of workers in a Swedish chemical factory that had previously been included in a hematologic investigation.[8] This facility produced EtO via the chlorohydrin process in which, in addition to EtO, there was potential exposure to ethylene, ethylene chlorohydrin, ethylene dichloride, and small amounts of bis(2-chloro-ethyl) ether. Among

89 "full-time" exposed workers, a statistically significant (p less than .01) excess of leukemia mortality was observed (2 observed versus 0.14 expected). In addition, a statistically significant (p less than .01) excess of stomach cancer was observed (3 observed versus 0.4 expected). Because of the mixed exposures, these findings could not be attributed to EtO; however, ethylene oxide and ethylene dichloride were the prime suspects.

[illegible] et al, conducted a retrospective cohort mortality study of workers involved in the production of EtO at a Texaco Facility.[9] A total of 850 workers were included in the study, of which 767 were potentially exposed to EtO. No EtO was detected in most samples taken in the production area, and all measurements in this area were below 10 ppm. No cases of leukemia were observed in this study; however, the authors estimated that the lowest relative risk that they had a high probability of detecting (80% power) was 10.5.

Hogstedt also reported on three cases of leukemia that occurred in a small group of workers at a Swedish company.[10] The company used a mixture of 50% EtO and 50% methyl formate to sterilize hospital equipment. The 8-hour TWA exposure for EtO at this facility was estimated at 20 ppm. According to national statistics, only 0.2 deaths due to leukemia were expected in this cohort. One of the cases was exposed to benzene, a known leukemogen, and it was speculated that the combined exposure of EtO and methyl formate might produce a special risk.

EtO is also a potent alkylating agent capable of causing irreversible changes or mutations in cellular proteins and DNA in animals.[11,12] EtO is also a positive mutagen in several in vitro systems such as Salmonella typhimurium, viruses, and Tradescantia poludosa.[3]

Chromosomal aberrations related to EtO exposure have been observed in a number of animal studies and epidemiologic investigations.[7,12-19] Yager and Benz observed a dose related increase in sister chromatid exchanges (SCEs) among New Zealand white rabbits that were exposed via inhalation to 50 to 250 ppm of EtO.[13] NIOSH (Lynch, et al) recently reported preliminary findings in which cynomolgus monkeys were exposed to 0, 50, or 100 ppm of EtO for 7 hours per day, 5 days per week.[7] After 24 months of exposure, statistically significant increases were observed in the frequency of chromosomal aberrations (including quadriradial chromosomes) and SCEs in the peripheral lymphocytes of the 50 and 100 ppm exposed groups versus the controls.

Garry, et al, examined the occurrence of SCE in the peripheral lymphocytes of 12 EtO exposed workers and 12 nonexposed controls in a hospital sterilization facility.[14] The exposed group showed statistically significant elevations in the number of SCEs compared to the controls. Particularly high SCE frequencies were observed among 4 workers that had reported either neurologic or respiratory symptoms. The maximum peak exposure level of EtO measured at this facility was 36 ppm.

Cytogenetic abnormalities have also been observed in several studies of workers exposed to EtO. Ehrenberg, in a study of workers at a factory manufacturing and using EtO, observed a high frequency of chromosomal

aberrations in 8 workers who were accidentally exposed to high concentrations of EtO. One case of leukemia was also observed among the 37 workers studied.[15]

American Hospital Supply initiated a cytogenetic survey of workers that were exposed to EtO in the sterilization of medical devices in 1972.[16,17] Seventy-five exposed workers at 9 facilities were studied, as well as 37 nonexposed workers who served as controls. Compared to controls, exposed workers were found to have statistically significant increased frequencies of SCEs and chromosomal aberrations.

In response to the findings from the American Hospital Supply study, Johnson and Johnson initiated a cytogenetic study of workers that were also exposed to EtO in the sterilization of medical products.[18,19] Approximately 50 workers not exposed to EtO were compared to 50 exposed workers at three facilities with 8-hour Time-Weighted Average (TWA) exposures to EtO of less than 1 ppm, 1-10 ppm, and 25-200 ppm, respectively. Statistically significant elevations in SCE frequency were observed in the latter two facilities, and these changes have persisted after one year. The frequency of SCEs appeared to increase in a dose response manner. Chromosomal aberrations were also elevated in the high exposure groups; however, these findings were not statistically significant.

Applicable Standards and Recommended Levels

Prior to June 22, 1984, the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for EtO was 50 ppm as a TWA concentration for an 8-hour workshift, and the Immediately Dangerous to Life and Health (IDLH) level was 800 ppm.[20] However, OSHA established a new PEL of 1 ppm as an 8-hour TWA; this final standard will become effective on August 21, 1984.[21] In addition, an "action level" of 0.5 ppm as an 8-hour TWA was established (by OSHA) as the level above which employers must initiate periodic employee exposure monitoring and medical surveillance. The Environmental Protection Agency (EPA) supported the OSHA PEL of 1 ppm in the Federal Register (June 22, 1984).[22]

In 1977, NIOSH recommended a ceiling level of 75 ppm for 15 minutes.[3] This level, however, was set prior to the recognition of the carcinogenic potential of EtO. Based on recent findings, NIOSH recommends that EtO exposures not exceed 5 ppm for a maximum of 10 minutes per day and that exposures be controlled to less than 0.1 ppm determined as an 8-hour TWA (NIOSH Policy Statement, July 20, 1983). The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a Threshold Limit Value (TLV) of 10 ppm for an 8-hour TWA based on data available prior to 1982.[23] However, in 1982, the ACGIH issued a notice of intended change in which it was proposed that the TWA concentration be lowered to 1 ppm. This recommendation will be reviewed in 1984.

Discussion of Company Monitoring Data

The results of the company EtO sample analyses, the specific sampling location, and process description are presented in Table 1. Table 2 contains the plant controls implemented to reduce EtO exposure levels.

The data presented in Table 1 indicate that EtO was present in the work environment at this facility. A variety of sampling media and pumps was used during the years that sampling was conducted at Lederle (1978-1983). In 1978, standard size (150 milligram) charcoal tubes were used as sampling media. This size charcoal tube has been found to be inadequate for EtO sampling because the migration ability of EtO may result in a percentage of sample breakthrough (movement of EtO into and out of the back-up section of the charcoal tube).

Therefore, the EtO level of 976 ppm found while charging the drum in 1978, may be low. The lowest documented level in 1978, less than 0.012, is questionable since this level was below the quantitation limit of the analytical method used (NIOSH S286).[24] The second type of sampling media used, Draeger detector tubes, are only adequate for a general quantitative determination of EtO levels. Draeger EtO 25/a detector tubes may have an error rate greater than plus or minus 20 to 30%; in addition, detector tubes are no longer certified by NIOSH (as of September 30, 1983).[25]

The later sampling media used, Qazi Ketchum charcoal tubes and 3M badges, were more reliable media for EtO monitoring. However, the accuracy of the extremely low values listed, i.e., less than 0.03 and 0.01 ppm may be questionable, due to limits of the available analytical methods.

Overall, there was a decrease in EtO exposure levels over time. This was specifically noted in 1981 since several engineering and administrative controls had been implemented in late 1980. However, the migration ability of EtO was still apparent. Personal TWA levels of EtO found behind a partition in the sterile kitchen area (1981) and 30 to 40 feet from the sterilizer (1983) were higher than the TWA levels found at the chamber during unloading of product. (See Table 1.)

The job operations that appear to have the highest exposure to EtO (prior to 1981) are charging of the 55 gallon drum sterilizer (less than 1 ppm to 976 ppm due to an accidental leak), opening the chamber door after sterilizing and unloading of the chamber [both EtO #1 (less than 1 ppm to 154 ppm) and EtO #2 (less than 1 ppm-1000 ppm)], and stacking the load of freshly sterilized product outside of the chamber (30 ppm-100 ppm). Prior to 1981, the chamber drain presented an additional source of EtO exposure. During venting of the chamber (after a test run), EtO levels found at the drain ranged from 60 to 200 ppm. Eighteen hours after the test run, the EtO concentration level at the drain was 20 ppm. (See Table 1.)

From 1981 to 1983, the job operations that appear to have the highest exposure to EtO are removal of biological indicators from sterilized product (1.8-3.1 ppm in 1981) and syringe machine operations (1.3-1.4 ppm in 1983). These operations are located around the periphery of the sterilizer area. Some of the EtO levels found in these operations were in the same ranges as those found during chamber unloading, however, those employees unlike the sterilizer operators were not wearing air supplied respirators.

Another difference in the data is length of sampling time of EtO. Earlier sampling periods were short term--usually 7-20 minutes during which peaks were usually measured. TWAs were not obtained until 1980. During 1980 and

1981 both short term and TWA sampling were conducted; therefore, difference in peak and TWA levels may be compared. Overall, the TWA results were much lower than the short term sample results (0.1-8.0 ppm vs. 1.9-1000 ppm, respectively). (See Table 1.)

In 1982 and 1983, all sampling represented TWA exposure to airborne EtO.

Conclusions

Lederle has industrial hygiene data dating back to 1978. Therefore, it would be possible to construct an exposure classification scheme for job categories. In addition, based on the findings of this report, this plant meets all of the eligibility requirements as defined by the protocol and should be included in the study. These requirements are: 1) the plant must contribute at least 400 person years, 2) the plant must have adequate personnel records or other records that can be used for identifying past and present workers exposed to EtO, and 3) the plant must not have any serious confounding exposure to a known leukemogen.

Recommendations

Isolate the syringe machine operations in order to reduce the syringe machine operators' exposure levels to EtO. Continue the industrial hygiene monitoring program for EtO.

Table 1

History of EtO Usage at Lederle Laboratories
Pearl River, New York

Date	Type Sterilizer and Gas Mixture Used	How Sterilized	Potential # of Workers Exposed	Type of Sample	PPM of EtO Monitored (& year)	Description of Process and Sampling Location
About 1950-1981	55 gal stainless steel drum 88:12 freon:EtO	2 lb. EtO gas added to powdered product --rolled drum overnight	Only 1 worker in isolated area on 3rd floor	Ceil[a,b]-BZ[c]	< 0.01 (1978)	Release of EtO from drum into room
				Ceil[b]-BZ	976 (1978)	Charging of drum
				Grab sample -BZ[d]	20 (1980)	Charging of drum
				TWA8-pe,f	1.1-3.1 (1981)	Charging of drum
1955-1981	EtO #1 (steam or EtO) 126 ft^3, positive pressure 90:10 CO_2:EtO	Gas mixture piped into sterilizer--operated under positive pressure	7-8 workers in local EtO sterilizer area	Grab sample -BZ[d]	< 20 (1980)	Outside chamber during door opening and unloading
		past: less gas used, but more cycles run	24-25 workers in general EtO sterilizer area	Grab sample -BZ[d]	50 (1980)	Above sterilizer door as door opened and chamber unloaded
		present: more gas used, but less cycles run		TWA8-Pg	0.2-8.0 (1980)	Unloading sterilizer
				Ceil-BZg	<1.9-65.0 (1980)	Outside chamber during door opening and unloading
				Ceil-BZg	154.4 (1980)	Outside chamber during door opening and inside chamber during unloading

Table 1 (continued)

History of EtO Usage at Lederle Laboratories
Pearl River, New York

Date	Type Sterilizer and Gas Mixture Used	How Sterilized	Potential # of Workers Exposed	Type of Sample	PPM of EtO Monitored (& year)	Description of Process and Sampling Location
1970-Present	EtO #2 (EtO only) 126 ft^3, positive pressure 90:10 CO_2:EtO	Gas mixture piped into sterilizer--operated under positive pressure	7-8 workers in local sterilizer area	Ceil-BZ[g]	4.7 (1978)	Outside chamber during door opening
			24-25 workers in general EtO sterilizer area	Ceil-BZ[g]	6.7 (1978)	5 ft from chamber 30 min after unloading
		past: less gas used, but more cycles run				
		present: more gas used, but fewer cycles run		Grab sample -BZ[d]	100-1000 (1980)	Outside chamber door during door opening
				Grab sample -BZ[d]	100 (1980)	Stacking load--outside chamber
				Grab sample -BZ[d]	40 (1980)	Stacking load outside chamber 20 min after door opening
				Grab sample -BZ[d]	30 (1980)	Stacking load outside chamber 25 min after door opening
				Grab sample -BZ[d]	90-1000 (1980)	Inside chamber

Table 1 (continued)

History of EtO Usage at Lederle Laboratories
Pearl River, New York

Date	Type Sterilizer and Gas Mixture Used	How Sterilized	Potential # of Workers Exposed	Type of Sample	PPM of EtO Monitored (& year)	Description of Process and Sampling Location
1970-Present (continued)	EtO #2 (EtO only) 126 ft^3, positive pressure	Gas mixture piped into sterilizer--operated under positive pressure	7-8 workers in local EtO sterilizer area	Grab sample[d] -area	100 (1980)	One inch above pallet, 10 min after unloading
	90:10 CO_2:EtO	past: less gas used, but more cycles run	24-25 workers in general EtO sterilizer area	Grab sample[d] -area	20 (1980)	One inch above pallet, one hour after unloading
		present: more gas used, but fewer cycles run		Grab sample[h] -BZ	40 (1980)	In front of chamber 10 min after venting (empty chamber test run)
				Grab sample[h] -area	200 (1980)	Chamber drain (empty chamber test run)
				Grab sample[d] -area	60-150 (1980)	Chamber drain (empty chamber test run)
				Grab sample[d] -area	20 (1980)	Chamber drain, 18 hrs after test run
				Ceil-area[g]	56 (1980)	6 in above product-immediately after unloadin

Table 1 (continued)

History of EtO Usage at Lederle Laboratories
Pearl River, New York

Date	Type Sterilizer and Gas Mixture Used	How Sterilized	Potential # of Workers Exposed	Type of Sample	PPM of EtO Monitored (& year)	Description of Process and Sampling Location
1970-Present (continued)	EtO #2 (EtO only) 126 ft^3, positive pressure	Gas mixture piped into sterilizer--operated under positive pressure	7-8 workers in local sterilizer area	Ceil-area[g]	18 (1980)	6 in above product one hour after unloading
	90:10 Co_2:EtO	past: less gas used, but more cycles run	24-25 workers in general EtO sterilizer area	TWA[g]-P[g]	0.1-0.4 (1980)	Unloading chamber
		present: more gas used, but fewer cycles run		TWA[g]-P[g]	4.1 (1980)	Validation run--cylinder leak
				TWA[g]-P[g]	0.1-0.6 (1981)	Unloading droppers or pipettes 25 ft from EtO #1
				TWA[g]-P[g,i,j]	0.2-3.2 (1981)	Removing TB tines from inside sterilizer
				TWA[g]-P[g,j]	1.0-1.1 (1981)	Working inside partition, sterile kitchen area
				TWA[g]-P[g]	1.2-2.6 (1981)	Working behind partition, sterile kitchen area

Table 1 (continued)

History of EtO Usage at Lederle Laboratories
Pearl River, New York

Date	Type Sterilizer and Gas Mixture Used	How Sterilized	Potential # of Workers Exposed	Type of Sample	PPM of EtO Monitored (& year)	Description of Process and Sampling Location
1970-Present (continued)	EtO #2 (EtO only) 126 ft^3, positive pressure	Gas mixture piped into sterilizer--operated under positive pressure	7-8 workers in local sterilizer area	TWA8-Pg,k	0.7 (1981)	Removing droppers from EtO #2 and degassing chamber
	90:10 CO_2:EtO	past: less gas used, but more cycles run	24-25 workers in general EtO sterilizer area	TWA8-Pg	0.1 (1981)	25 ft from sterilizer
		present: more gas used, but fewer cycles run		TWA8-Pf,i	0.3-2.7 (1981)	Loading or unloading product from chamber
				TWA8-Pf,i	1.8-3.1 (1981)	Testing sterilized product behind partition
				TWA8-areag	6.3 (1982)	Inside box of product
				TWA8-Pg	0.03-0.9 (1982)	Removing product from sterilizer
				TWA8-Pf	1.7 (1982)	Removing product from sterilizer
				TWA8-Pg	0.1 (1982)	Working 20 & 25 ft from chamber

Table 1 (continued)

History of EtO Usage at Lederle Laboratories
Pearl River, New York

Date	Type Sterilizer and Gas Mixture Used	How Sterilized	Potential # of Workers Exposed	Type of Sample	PPM of EtO Monitored (& year)	Description of Process and Sampling Location
1970-Present (continued)	EtO #2 (EtO only) 126 ft3, positve pressure 90:12 CO2:EtO	Gas mixture piped into sterilizer--operated under positive pressure	7-8 workers in local sterilizer area	TWAg-Pg	< 0.03 (1982)	Quality control quarantine area
				TWAg-Pf	0.5-0.9 (1983)	Removing product from chamber and loading degassing chamber
		past: less gas used, but more cycles run	24-25 workers in general EtO sterilizer area			
		present: more gas used, but fewer cycles run		TWAg-Pf	1.3-1.4 (1983)	Syringe machine 30-40 ft from chamber unloading
				TWAg-Pf	< 0.1 (1983)	Opening boxes of EtO sterilized product in quality control quarantine area
				Area[f] (2.6 days)	< 0.01 (1983)	Above quarantine door and 5 ft from 45 open boxes of sterilized product

Table 1 - Footnotes

a) Ceil = ceiling or short term samples, usually for 15-20 minutes.

b) Standard size charcoal tubes used as sampling media.

c) BZ = breathing zone

d) EtO 25/a detector tubes used as sampling media.

e) TWA_8-P = Personal 8-hour time-weighted average

f) 3M Badge

g) Two Gazi-Ketchum charcoal tubes in series used as sampling media.

h) DT = Draeger tube

i) Workers wore air supplied respirators.

j) TWA calculated from 2 hours of sampling.

k) Operator does not enter sterilizer--uses wheeled pallet.

Table 2

Controls Implemented to Reduce EtO
Exposure Levels at Lederle Laboratories
Pearl River, New York

Date	Engineering Controls	Administrative Controls	Range of EtO Exposure Levels Measured (ppm)
1955-Present	Sterilizer exhaust vented 15 ft above roof		
1975	Low volume area exhaust added to sterilizer area		
1978		Industrial hygiene sampling first conducted	< 1-976
1979	EtO monitor/alarm (30 ppm) system installed in sterilizer area	Safety instruction for safety work permits revised	
		Wearing of organic vapor cartridge respirators initiated during sterilizer unloading	
1980	Check valves added to EtO tank lines	Consultant called in; process controls updated	< 1-1000
	Local exhaust added to to chamber drain	Wheeled pallet & hook arrangement implemented for remote sterilizer loading	
	Pre-conditioning/off-gassing chamber added		
	EtO detector (Enmet) installed on sterilizer #2	Company voluntarily lowered exposure limit to 10 ppm TWA8	
	Ventilation purge added to post-sterilization cycle	Safety Program and Safety Training/Industrial Hygiene booklets in use	

Table 2 (continued)

Controls Implemented to Reduce EtO
Exposure Levels at Lederle Laboratories
Pearl River, New York

Date	Engineering Controls	Administrative Controls	Range of EtO Exposure Levels Measured (ppm)
1981	No engineering control measures added	EtO sterilizer #1 shut down, tagged and locked out Transfer of products to Puerto Rico Use of air-line respirators instituted Many products sent outside plant for radiation sterilization Company voluntarily lowered EtO exposure limit to 1 ppm TWA[8]	< 1-3.2
1982	No engineering control measures added	Job Hazard Analysis-Safe Job Procedures form developed and instituted (for EtO #2 sterilizer operators)	< 1-1.7
1983	No engineering control measures added	Safety Training Documentation forms developed and instituted	< 1-1.4

REFERENCES

1. NIOSH. Current Intelligence Bulletin 35 - Ethylene Oxide (EtO). DHHS (NIOSH) Publication No. 81-130, May 22, 1981.

2. National Occupational Hazard Survey, National Institute for Occupational Safety and Health, 1977.

3. Glazer, Z.R., Special occupational hazard review with control recommendations for the use of ethylene oxide as a sterilant in medical facilities. National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 77-200, 1977.

4. Chemical Economics Handbook, SRI International, Ethylene Oxide, January, 1980.

5. NIOSH. Draft Feasibility Study for a Cohort Mortality Study of Workers Exposed to Ethylene Oxide. Internal report from the Industrywide Studies Branch, June, 1983.

6. Snelling, W.M.; Weill, C.S.; and Maronport, R.R., Final report on ethylene oxide two-year inhalation study on rats. Project Report 44-20, Bushy Run Research Center, January 28, 1981. Submitted by Union Carbide Corporation to the U.S. Environmental Protection Agency under section 8(e) of the Toxic Substances Control Act, on behalf of co-sponsors of the study (February, 1981).

7. Lynch, D.W.; Lewis, T.R.; Moorman, W.J.; Sabharwal, P.S.; and Burg, J.R., Chronic inhalation toxicity of ethylene oxide and propylene oxide in rats and monkeys -- a preliminary report. Presented at the 21st Annual Society of Toxicology Meeting, Boston, Massachusetts, February 22-26, 1982.

8. Hogstedt, C.; Rohlen, O.; Berndtsson, B.S.; Axelson, O.; and Ehrenberg, L., A cohort study of mortality and cancer incidence in ethylene oxide production workers. Br. J. Ind. Med., 39:276-280, 1979.

9. Morgan, R.W.; Claxton, K.W.; Divine, B.J.; Kaplan, S.D.; and Harris, V.B, Mortality Among Ethylene Oxide Exposed Workers. J. Occ. Med., 23:767-770, 1981.

10. Hogstedt, C.; Malmqvist, N.; and Wadman, B., Leukemia in workers exposed to ethylene oxide. JAMA, 241:1132-1133, 1979.

11. Calleman, C.J.; Ehrenberg, L.; Jansson, B.; Osterman-Golkar, S.; Segerback, K.; and Wachtmeister, C.A., Monitoring and risk assessment by means of alkyl groups in hemoglobin in persons occupationally exposed to ethylene oxide. J. Environ. Pathol. Toxicol., 2:427-442, 1978.

12. Ehrenberg, L.; Heische, K.D.; Osterman-Golkar, S; and Wennberg, I., Evaluation of genetic risks of alkylating agents: Tissue doses in the mouse from air contaminants with Ethylene Oxide. Mutat. Res., 24:83-103, 1974.

13. Yager, J.W., and Benz, R.D., Sister chromatid exchanges induced in rabbit lymphocytes by ethylene oxide after inhalation exposure. Environ. Mutagen., 4:121-134, 1982.

14. Garry, V.E.; Hozier, J.; Jacobs, D.; Wade, R.; and Gray, D., Ethylene Oxide: evidence of human chromosomal effects. Env. Mutag., 1:375-382, 1979.

15. Ehrenberg, L., and Hallstrom, T., Haematologic studies on persons occupationally exposed to ethylene oxide. In: International Atomic Energy Agency Report, SM 92/26, pp. 327-334, 1967.

16. Abrahams, R.H., Recent studies with workers exposed to ethylene oxide, in The Safe Use of Ethylene Oxide. J.F. Jorkasky, ed. Health Industry Manufacturers Association, Washington, D.C., HIMA Report No. 80-4: 211-220, 1980.

17. Abrahams, R.H., Chromosomal changes in workers exposed to ethylene oxide -- an update. Ethylene Oxide Worker Safety Issues. J.F. Jorkasky, ed., Washington, D.C., HIMA Report No. 82-2:27-38, 1982.

18. Herman, A.A., (Johnson and Johnson Corporate Submittal to OSHA). Pilot research chromosome study of workers at sites where ethylene oxide gas is utilized as a sterilant. Submitted to OSHA, March 30, 1982.

19. Jones, J.P., Chromosomal changes in employees exposed to ethylene oxide. Ethylene Oxide Worker Safety Issues. J.F. Jorkasky, ed., Washington, D.C., HIMA Report No. 82-2, 5-25, 1982.

20. Occupational Safety and Health Administration (OSHA), Safety and Health Standards 29 CFR 1910, General Industry Standards, OSHA 2206, Revised, June, 1981.

21. Federal Register, Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910, Occupational Exposure to Ethylene Oxide. 49(122):25734-25809, June 22, 1984.

22. Federal Register, Ethylene Oxide; Certain Pesticide Products Registered for the Sterilization of Equipment and Supplies in Hospitals and Health Care Facilities. 49(122):25675-25676, June 14, 1984.

23. Threshold Limit Values for Chemical Substances and Physical Agents in the Work Environment with Intended Changes for 1983-84, American Conference of Governmental Industrial Hygienists, 1983.

24. NIOSH Manual of Analytical Methods, Second Edition, Vol. 3, DHEW (NIOSH) Pub. No. 77-157-C, 1977.

25. Federal Register, Notice of Termination of Voluntary Testing and Certification Programs for Gas Detector Tube Units and Industrial Sound Level Meters. 48(191):44931-44032, 1983.

APPENDIX 1

1. PURPOSE

To specify when a Safety Work Permit (LPR 102) shall be used, the responsibilities of personnel concerned, and the procedure to be followed. Compliance with this procedure is mandatory for all Lederle and Medical Research Division personnel at the Pearl River facility. Other Lederle locations are responsible for designing procedures to implement the provisions of this instruction as appropriate for local conditions.

2. DEFINITIONS

a. Class A Safety Work Permits

These Safety Work Permits require approval by primary and authorized secondary operating supervision and inspection of the job site by both secondary operating supervision and the work crew supervisor immediately prior to the start of the work.

Class A Safety Work Permits are required for work of a more hazardous nature such as:

1) Hot work - any open flame such as welding, oxy-acetylene burning, etc. and the use of portable spark or heat producing equipment, except when performed in properly equipped maintenance shops and designated adjacent outside area.

2) Entrance into confined spaces, i.e., operating vessels, holding tanks or pits (See SPI PR 2K3).

3) Breaking into lines used for toxic, flammable, high pressure, or corrosive materials as indicated in SPI PR 2K6, 4. a. 3) f) 1), page 6.

4) Fumigation work.

b. Class B Safety Work Permits. For all other hazardous work.

c. Primary operating supervisor. First line supervision in an operating department. This includes such managers as supervisors, group leaders, department heads, and superintendents.

d. Secondary Supervision. Department head, superintendent or staff engineer designated by their section managers to approve Class A Safety Work Permits.

e. Operating Department. Defined for the purposes of this procedure as an area utilized and/or charged to any departmental unit within Medical Research Division or the Lederle, Davis and Geck Departments.

4. SCOPE (All Safety Work Permits)

A Safety Work Permit must be issued to any person or persons on Lederle premises before he performs work of the types described below. It shall be initiated by the maintenance supervisor or coordinator and approved and signed by the operating supervisor or as designated below for the specific type of work to be done. This Safety Work Permit must be signed and thereby made valid before the following types of activities are started:

a. Hot Work - any open flame such as welding, oxy-acetylene burning, etc. and the use of portable spark or heat producing equipment, except when performed in properly equipped maintenance shops and designated adjacent outside area. APPROVAL BY AUTHORIZED PRIMARY AND SECONDARY OPERATING SUPERVISION IS REQUIRED.

NOTE: Maintenance use of electric hand tools requires a Safety Work Permit only when they are to be used in an explosion proof or other hazardous area.

b. Electrical and piping lockouts as required in SPI PR 2K6.

c. Entrance into confined spaces, i.e., operating vessels, holding tanks or pits (See SPI PR 2K3). APPROVAL BY AUTHORIZED PRIMARY AND SECONDARY OPERATING SUPERVISION IS REQUIRED.

d. Breaking into lines used for toxic, flammable, high pressure, or corrosive materials. APPROVAL BY AUTHORIZED PRIMARY AND SECONDARY OPERATING SUPERVISION IS REQUIRED.

e. Underground utility service installations (See SPI PR 2K9).

f. Exposure to corrosive, toxic, or infectious materials or to high pressures or high/low temperatures (See SPI PR 2K6).

g. Fumigation work. APPROVAL BY AUTHORIZED PRIMARY AND SECONDARY OPERATING SUPERVISION IS REQUIRED.

h. Exposure to pesticides, insecticides and bactericides.

i. Any unusual movement of heavy equipment, over building floors and roofs, into and on elevators, or over Plant roads.

j. Blasting and the use of EXPLOSIVE actuated tools.

k. Construction work on idle or abandoned pipelines (See E&M Standards 3A3 and 3A4).

l. Excavations, breaking or drilling of concrete.

m. ANY OTHER WORK WHICH THE OPERATING SUPERVISOR, OR WORK CREW SUPERVISOR OR COORDINATOR FEELS MAY PROVE HAZARDOUS TO PERSONNEL, PROPERTY PRODUCT OR EQUIPMENT.

Any deviation from 21 percent Oxygen or 0 percent of LEL should be investigated to find the cause of the deviation so that it can be eliminated. No work will be attempted until this is done.

e) To revoke the permit at any time to prevent occurrence of an unsafe act or condition.

4) Work crew supervisor or coordinator (supervisor responsible for the job being performed that shift).

a) To initiate the Safety Work Permit before any work requiring a permit is performed on the job; to initiate a new permit if the job continues beyond one shift unless the work is being completed by the original crew listed on the permit.

b) To make a PERSONAL INSPECTION of area involved prior to signing the permit and to discuss any unusual safety features and special precautions of the job with the operating supervisor. For Type A Safety Work Permit this must be done just prior to start of work.

c) To ensure conformance to all safety precautions.

d) To notify Guard Headquarters before entrance into confined spaces.

5) Operating supervisor and work crew supervisor.

a) Equal responsibility is placed on the operating supervisor directly responsible for the area where the work will be done (not a general service manager unless directly responsible) and on the person in charge of the crew doing the work. The former is responsible for inspecting the work site to make certain that conditions are safe and for the approval of the permit. The latter is responsible for initiating the Safety Work Permit before starting hazardous work and for seeing that the work crew perform their work in a safe manner and that the work crew leaves the areas in a safe condition.

b) Both the operating supervisor and the work crew supervisor have equal responsibility to revoke the Safety Work Permit if unsafe conditions arise.

NOTE: Service personnel (Fire CHief, Utility Department, Engineering Department, Accident Prevention Department) are available as required for consultation. Whenever possible, requests for consultation should be given 24 hours before job is to start.

6. PROCEDURE FOR FILLING OUT SAFETY WORK PERMIT

See exhibits A and B.

HEADING ON LPR 102	INSTRUCTIONS
1. Date - GOOD FOR THIS DATE AND SHIFT ONLY	Each permit is dated and is valid for the date and shift the work described on the permit is to begin. The permit must be signed by the operating supervisor and the maintenance supervisor or coordinator for their responsibilities. The Permit must be issued in the same shift or just prior to the shift in which the work is to be done. If work on the job in question extends beyond the authorized shift, the area must be reinspected and a new permit issued before the work continues, unless the work is being completed by the original crew listed on the permit as a continuation of the shift.
2. Dept.	Department number of department calling for work to be done.
3. Location	Detailed job location such as Building 120, 2nd Floor, Col. #
4. M.S.R. No.	Order number identifying the job, e.g., M.S.R. No.
5. Check One	If the work to be done is Hot Work, Hazardous, Piping, Vessel Entry or Fumigation, check the appropriate box. For work of this type you are required to get a secondary operating signature (See SPI 2 K 2). Other types of work are Class B.
6. Describe Work to be Done	Clear, concise explanation of work, e.g., "Check bottom bearing in fermenter #23."
7. Craft – Name	Crafts and Name such as EL - Name, WD - Name, etc. As additional crafts are introduced to the job add them to the permit.
8. Your Special Instructions	Any peculiarities relating to the particular area in question.
9. If you are not sure, ASK.	Request assistance from appropriate sources, e.g., Central Engineering, Accident Prevention, Fire Dept., etc.
10. Safety Equipment Required – Check-Off	Check all of the items required, under "OTHERS", describe any special equipment needed.
11. Checklist	Operating Supervisor to check Yes, No, or Does not apply (DNA) for each of the items listed. NOTE 1: Hot Work - any torch work such as welding, oxy-acetylene burning, etc., and the use of portable spark or heat producing equipment, except when performed in properly equipped maintenance shops and designated adjacent outside area. See check list on back of S.W.P. NOTE 2: Operating supervisor, and work crew supervisor or coordinator must concur in these decisions or refer to Accident Prevent Department for final decision. NOTE 3: A secondary authorized operating supervisors signature is required for: - Hot work SPI 2 K 2, 3a. - Confined space entry (other than underground utilities) SPI 2 K 3 - Breaking into corrosive, toxic, high pressure or flammable lines per SPI 2K6, 4, a. 3) f) 1) page 6. - Fumigation work. Safety work permits for these projects require inspection of the job site by both the work crew supervisor and the secondary signer immediately prior to the start of work.
12. Gas and Oxygen Test	Operating Supervisor to ensure that combustible gas test is taken, if required, and reported as Lower Explosion Limit (LEL) %; and that the oxygen level is within the requirements and that the actual oxygen % is entered. Test results are to be written at the issuance of Permit; and signed, dated and time indicated. Any deviation from 21 percent oxygen or 0 percent of LEL should be investigated to find the cause of the deviation so that it can be eliminated. No work will be attempted until this is done. When all required information has been entered on the Safety Work Permit, the operating supervisor and the work crew supervisor will sign and enter date and time.
13. Approval Signatures	When contract maintenance and construction work requires a Safety Work Permit, the contractor's representative on the job site shall sign and transmit safety instructions in the same manner as a Lederle maintenance supervisor. The project engineer and the operating supervisor will sign the permit in the "operating supervisor" box.
14. Secondary Signature	Secondary operating signature required for Type A S.W.P.
15. Completion of Work	Upon the completion or stoppage (for any reason) of the job, excluding authorized breaks or lunches, work crew supervisor or coordinator must indicate the status of the jobs by dating and signing in appropriate area. A new permit will be issued after any stoppage, if necessary to complete job.

LPR 102 - REVERSE - REV. 10/79 (CANARY)

CHECK LIST FOR HOT WORK

	YES	NO	DNA
Has the area and the equipment been tested for a safe level of combustible gases or vapors with a Combustible Gas Indicator Meter?			
Has piping been disconnected or blanked off?			
Has vessel and/or attached piping been drained, cleaned, purged and ventilation supplied?			
Have tanks or equipment being welded or burned been cleaned to remove flammable or combustible material (solvents, vapors, dusts, wastes)?			
Can sparks ignite material in vicinity, lower floors or levels?			
Have sewers been properly isolated to prevent ignition?			
Is adjacent equipment safe?			
Has all combustible material been relocated at least 35 feet from the work site?			
Have combustibles that are impractical to relocate been protected by using flame proof covers?			
Has the floor been swept clear of all combustibles for a radius of 35 feet from the work site?			
Will combustible floors be kept wet or covered?			
Have all wall or floor openings within 35 feet of the work site been covered to prevent passage of sparks to adjacent areas?			
Have ducts and conveyor systems that might carry sparks to distant combustibles been covered?			
Has processing of flammable liquids in the area been stopped?			
Have all vessels which contain flammables been closed?			
Have you explained any special precautions to be observed because of hazardous materials?			
Has adjacent operating force been informed of this work?			
Has the Fire Department been notified?			
Has location of fire extinguishers, safety showers and siren switches been reviewed with work crew?			
Is the sprinkler system in service?			
NOTE: Consult with the Fire Chief if you have any doubts about burning, welding or using an open flame in a safe manner.			
NOTE: Maintain a fire watch for a minimum of one-half hour after completion of a burning or welding operation.			

LPR 1858 11/79

MASTER CHECK LIST FOR CONFINED SPACE ENTRY. FOR USE TO DEVELOP CHECK LISTS FOR EACH PIECE OF EQUIPMENT THAT MAY REQUIRE ENTRY TO A CONFINED SPACE.

	YES	NO	DNA
Has a combustible gas and oxygen check been made?			
Has adequate ventilation been provided?			
NOTE: Do not use plant air for air supplied respirators; nor for ventilating tanks.			
Has a Scott air pack been brought to the work site for use if needed?			
Have arrangements been made for repeat oxygen and combustible gas tests after lunch breaks or job delays?			
NOTE: Continuously monitoring devices used for determining the presence of combustible gas or oxygen content have not proven reliable. Their use does not negate the need for making standard tests for combustible gas, or for 21% oxygen.			
Have switches and valves been properly set, tagged and locked?			
(Safety locks on push-buttons are not sufficient. Test local starter station)			
Has piping been disconnected or blanked off?			
Has vessel and/or attached piping been drained, cleaned, purged, and free of product residue?			
Is adjacent equipment safe?			
Are overhead structures within the confined space secure?			
Has cover of confined space been removed or secured open?			
Have electrical tools and extension cords been ground fault tested?			
Are all electrical tools and portable electric lights plugged into a ground fault circuit interrupter?			
Are tools in good condition?			
Have acetylene and other pressure hoses to be used on this job been tested for leaks?			
Has insulation been provided? (Required for electrical work)			
Has the ladder been tied?			
On vessels with manhole on top is there an eye bolt with attached pulley mounted above the opening for each life line in use?			
Has safety watch been posted and instructed?			
Have rescue procedures been reviewed and understood?			
Have you explained any special precautions to be observed because of hazardous materials or conditions?			
Has Guard Headquarters been notified of a confined space entry?			
Is employee entering confined space –			
fully clothed			
wearing proper eye protection and hard hat			
wearing an approved harness with a life line attached			

APPENDIX 2

DO NOT USE UNLESS STAMPED IN RED

JOB HAZARD ANALYSIS – SAFE JOB PROCEDURES DO NOT COPY 153

DATE ISSUED | JOB OPERATION: Operation of ETO No. 2 Sterilizer (NEW)

DEPARTMENT: 721 | SUPERVISOR: Sisto Pileggi

JOB CLASSIFICATIONS THAT ARE REQUIRED TO KNOW AND FOLLOW THIS PROCEDURE

Sterilization Worker

OPERATIONS	PERSONAL PROTECTIVE EQUIPMENT	PROCEDURES – SAFETY CONTROLS	HAZARDS
Loading Precon-ditioning Chamber	1) Safety shoes 2) Safety glasses 3) Leather gloves	1) Load carts into chambers close and latch doors carefully. Set cycle parameters, activate power and start preconditioning cycle.	1) Pinching or crushing hands and/or fingers
Handling - ETO 90:10 Cylinders	As Above	1) Use carry all cart to transport cylinders. 2) Place all cylinders behind chains. 3) Have necessary tools/wrenches readily available. 4) Connect gas line to cylinders making sure cylinder valve is "off" Inspect check valve in line for proper operation.	1) Possible back strain. 2) Prevent cylinders from falling. 3) Improper tools impose unnecessary dangers in handling.
Loading ETO Sterilizer	As Above	1) Install RH sensor in proper connection inside sterilizer. 2) Carefully push racks into chamber without entering chamber. 3) Close and lock chamber door tightly.	1) Injury to hand and/or fingers 2) Residual gas in chamber.
Exposure Cycle	As Above	1) Check main, wall-mounted ETO monitor for indications of gas leaks and possible sources of leaks. If yellow warning light comes on operator will: Put on Scott Air-Supplied respirator, investigate and correct cause of ETO leaks. Check ETO monitor to determine which sensor is nearest the leak. If leaks cannot be located or stopped, the run should be aborted. This includes venting the chamber and shutting off source. Notify supervisor. 2) If "RED" light comes on and alarm sounds, area must be evacuated. 3) Supervisor or operator if off-hours, will call Fire Dept. (x2600) for assistance in area. 4) Operator will enter area wearing Scott Air-Pak, accompanied by Fire Dept. back-up person also wearing a Scott-Pak and shut off cylinders and abort the run.	1) Leaks from chamber may release ETO gas into environment. 2) Second person needed with Scott Air-Pak in the event a rescuer is needed. Scott "Air-Pak" is a pressure demand self-contained breathing apparatus.

DO NOT USE UNLESS STAMPED IN RED

JOB HAZARD ANALYSIS – SAFE JOB PROCEDURES DO NOT COPY 153 (2)

DATE ISSUED | JOB OPERATION: Operation of ETO No. 2 Sterilizer (NEW)

DEPARTMENT: 721 | SUPERVISOR: Sisto Pileggi

JOB CLASSIFICATIONS THAT ARE REQUIRED TO KNOW AND FOLLOW THIS PROCEDURE

OPERATIONS	PERSONAL PROTECTIVE EQUIPMENT	PROCEDURES – SAFETY CONTROLS	HAZARDS
		Second person from Fire Dept. will keep operator in sight at all times. Turn on exhaust vent switch, if it is not already on; and open windows to aerate area. No one will re-enter area until "GREEN" light comes on for all sampling points.	
End of Cycle	As Above, Scott Air-Supplied Respirator.	1) When En-met detector in chamber vacuum line indicates ETO concentration to be very low-needle completely to left and the chamber pressure is 14.7 - 15.0; the load can be removed from the sterilizer and placed into the degassing chamber. Do not enter chamber; use metal hooks provided and wear Scott Air-Supplied Respirator. 2) Donning Procedure: Connect all lines and the face mask by pushing the couplings into the sockets. These fittings snap in and lock in place. Check to see that cylinders contain certified breathing air. Open both breathing air cylinder valves counter-clockwise 2 complete revolutions. Check to see that tanks have at least 600 lbs. pressure registering on supply gauge. Bring the mask and hose assembly over the shoulder and snap the clip onto a belt loop on the right side. Hold the face mask against the face and slowly turn the regulator valve clockwise to 100# air pressure on the delivery gauge (100# for 1 person, 125# for 3 persons). Glasses cannot be worn with their facepiece. A constant flow of air will be present in the facepiece. Don the facepiece, chin first, then pull down and center the rubber harness on the back of the head.	1) Potential ETO in area from sterilizer and load.

DATE (Initiated) | JOB OPERATION: Operation of ETO No. 2 Sterilizer (NEW)

DEPARTMENT: 721 | SUPERVISOR: Stat[redacted]ggi

JOB CLASSIFICATIONS THAT ARE REQUIRED TO [redacted] THIS PROCEDURE

OPERATIONS	PERSONAL PROTECTIVE EQUIPMENT	PROCEDURE / SAFETY CONTROLS	HAZARDS
		Adjust the straps until comfortable. Adjust the lower straps first, then the middle second and the top last. As the facepiece is donned, airflow will subside. A slight positive pressure will prevent any external contaminated environment from entering system.	
Unloading Sterilizer and Loading Degassing Chamber	As Above. Scott Air-Supplied Respirator	1) Open sterilizer door, place and attach floor cart to sterilizer, and roll sterilization pallet onto cart. Remove spore strips and roll cart into Degassing Chamber. Repeat with second cart. Do not enter chamber, but use steel hook provided for pulling cart out. 2) Set Cycle switch to Degas Mode and Timer to 10 hours. Push Start switch and allow to run for pre-set time. 3) Remove Air-Supplied Respirator. Shut off tank valves, bleed regulator by turning clockwise; then unscrew three times to relieve diaphragm spring pressure. Detach facepiece and hose from air supply line. Dissolve 1 packet of MSA respirator cleaner/disinfectant in a gallon of warm water in a bucket. Turn respirator upside down and immerse facepiece and mask up to the regulator. Do not immerse regulator or get it wet. Scrub off mask and facepiece with a sponge using the solution. Thoroughly rinse off the mask and facepiece with fresh warm water for 1 minute. Do not get regulator wet. Dry off excess water using a clean paper towel. Allow mask to air dry and put back in plastic storage bag on respirator cart.	
End of Degassing Cycle	As Above	1) Check to see that En-Met detector is below half-way mark at end of run. 2) Remove carts; unload material and send to quarantine area as soon as possible.	1) Potential ETO slow release into working environment.

RA 1/15/82