INDUSTRYWIDE STUDIES REPORT OF WALK THROUGH SURVEY

OF

DAVIS AND GECK
(American Cyanamid)
Danbury, Connecticut

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 13-14, 1983

REPORT WRITTEN BY:
Virginia Ringenburg
Kyle Steenland
Alice Greife

DATE OF REPORT:
July 31, 1985

REPORT NUMBER: 67.21

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

Disclaimer

Mention of company names or products does not constitute endorsement by National Institute for Occupational Safety and Health (NIOSH).

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 by researchers from NIOSH to determine the suitability of including this facility in the mortality/industrial hygiene study of EtO.
EMPLOYER REPRESENTATIVE CONTACTED:	Mr. John Riley, Plant Manager, Davis and Geck (203) 743-4451 Mr. Sumner Kaufman, Manager of Safety Environment and Loss Prevention Davis and Geck (203) 743-4451
EMPLOYEE REPRESENTATIVES CONTACTED:	Ms. Linda Kunzer, President, Local 560, International Chemical Workers Union (ICWU) (914) 279-5985 Mr. Mike Dubos, Health and Safety Committee, ICWU, Local 560 (203) 792-9323
STANDARD INDUSTRIAL CLASSIFICATION OF PLANT:	3842 - Orthopedic, Prosthetic, and Surgical Appliances and Supplies

Table of Contents

Tables

Abstract

On December 13 and 14, 1983, a site visit to Davis and Geck, a division of the American Cyanamid Company, Danbury, Connecticut was conducted to gather data and determine the feasibility of including this facility in the NIOSH 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 Davis and Geck since 1977. 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, 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

Ethylene oxide (EtO) is one of the 25 chemicals of highest production volume in the United States.[1] The major portion of EtO produced 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]

EtO, a colorless gas at standard temperature and pressure or a liquid at higher pressures, 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.[2] 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.[3]

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 in the health care and medical supply industry, specifically those workers exposed to EtO in industrial sterilization processes, was the most adequate group to support a cohort mortality study.[4] This decision was supported by the findings of a 1977 survey conducted by National Institute for Occupational Safety and Health (NIOSH) researchers which showed that it is in this industry most of the employee exposures occur.[5,6] This survey estimated that approximately 75,000 health care workers were employed in EtO sterilization operations, with an additional 25,000 employees which may have incidental exposure resulting from inadequate engineering controls.[5,6] In order to develop and refine methods to be used for data collection and exposure classification of this selected cohort, a pilot study of six industrial sterilization facilities was initiated. The information gathered during the pilot study was incorporated into the final study protocol. This facility is/is not part of the pilot study.

This walk-through survey was conducted to determine the suitability of including Davis and Geck in the industrywide mortality and industrial hygiene study of workers potentially exposed to EtO in industrial sterilization processes. The suitability of including this facility was based on data gathered in this walk-through and is discussed in the Conclusion and Recommendation section. In addition, the data gathered during the walk-through survey 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. These exposure estimates will then 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.

The authority and responsibility for conducting and reporting on field studies in industry was given to NIOSH under the Occupational Safety and Health Act of 1970 (set forth by the 91st Congress, S.9123, Public Law 91-596). 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.

Description of Plant

The original site of Davis and Geck was Brooklyn, New York. On August 26, 1953, the plant opened at its present location in Danbury, Connecticut. Davis and Geck, a subsidiary of the American Cyanamid Company, manufactures approximately 2000 types of surgical sutures, hand scrub sponges, skin staplers, serum sample tubes, and burn dressings. Some of the sutures (with or without needles attached) are currently sterilized by ethylene oxide (EtO). An outside contractor sterilizes the other sutures by cobalt 60 gamma radiation.

The production departments and/or areas located on the 1st floor include: the Print Shop, Envelope Making, Atraumatic[R] (needle attaching) Department, Winding, Fiber Process, Braid Wash Area, and Hospital Products Department where an EtO solution is used to sterilize surgical scrub sponges. The second floor contains the Sterilization-Finishing Department which includes: two Sterilizer Rooms, Solution Room, Aseptic Holding Room, Alpha 65 Process Area (filling and sealing suture envelopes with EtO and alcohol mixture), Alpha 65 Reclaim Area (rework sutures and take care of suture envelope problems), Quality Control Lab, and Physical (tensile) Testing Computer Room. All materials received are stored in a climate controlled storage area. The Warehouse and Shipping Departments, originally on the first floor, were moved to a separate building in 1968. In 1969, a large first floor addition was built to handle the Dexon[R] fiber process; however, this operation was moved to Puerto Rico in 1975.

Description of the Workforce

The Davis and Geck plant employs approximately 600 hourly employees who work 2 shifts, 7:30 a.m. to 3:30 p.m. and 3:30 p.m. to 12:00 a.m. There were 1,100 employees in the early 1970's.

The employee turnover rate of the plant is low, about 1% per month. In fact, over 1/6th of the present workforce has been employed by Davis and Geck for 25 years. However, the job turnover within the plant is high, about 3 changes per person per year. This in part accounts for the large number of employees (3,500 out of 5,000) estimated by the company to have been potentially exposed to EtO. See Description of Personnel Record Keeping System (p.13) for the NIOSH epidemiologist's estimates.

[R] T.M. American Cyanamid Company, Davis and Geck Division.

The percentage of females to males is 65% to 35%. Some of these employees were hired from a furrier/hat company where there was possible employee exposure to mercury. The union representing employees of Davis and Geck is the International Chemical Workers Union, Local 560.

Description of Process

There are essentially two EtO processes at Davis and Geck, surgical scrub sponge production and medical supply sterilization. In the scrub sponge process, the sponges are fed along a conveyor line which includes several tubs, application of heat and a vacuum, and a mixture containing EtO. This process was started in 1968. The finished sponges are transported from the plant to the warehouse for storage and shipping.

The suture sterilization process involves packaging sutures in partially sealed aluminum foil envelopes and sterilizing them with EtO in a chamber (open EtO sterilization process). The sterilized packages are then sealed and over-packaged in a Tyvek envelope (which is porous to EtO gas but not to bacteria) and sterilized again (closed EtO sterilization process) in order to sterilize the inner space between the two envelopes.

The chamber sterilization process is conducted under positive pressure in any one of several sterilizers (one is used for research and development purposes only). The product is loaded onto a pallet and pushed into the sterilizer where the humidity and temperature are increased and a mixture of 88 parts freon to 12 parts EtO is added to the sterilizer. After sterilization, the product remains in the sterilizers for a short time to reduce the EtO level and is then transferred to an aeration room. Transfer of the sterilized load is done on an off-shift between 5:00 a.m. and 7:00 a.m. before most employees arrive for work. After the aeration cycle is completed, the product is overwrapped and moved to the warehouse for quarantine, storage, and shipping.

Description of Past Exposures and Controls Used

In 1953, Davis and Geck sterilized sutures by first placing them in glass tubes, which were hermetically sealed and heat sterilized. The tubes were then placed into glass jars or tin cans with a solution of isopropanol and formaldehyde. Exhaust hoods were used to control exposure to isopropyl alcohol. In 1956, foil and mylar envelopes replaced the glass tubes and the product was contracted out for EtO sterilization. In 1957 and 1958, EtO sterilizers were purchased and used to sterilize open loads with a mixture of 80 parts carbon dioxide to 20 parts EtO. The gas mixture was stored in a class D explosion room. Leaks were detected by observing pressure changes on the chamber pressure recording chart and by monitoring chamber gas concentrations with an infrared analyzer.

In 1959, partitions and walls were removed on the main production floor, and Finishing, Atraumatic Attaching, and Winding Processes were conducted in the same room. The Aseptic Inner Sealing and Alpha Processes were enclosed segregated operations with separate air handling systems.

From 1959 to 1974, a mixture of liquid EtO was placed into envelopes holding the ligatures. Scotch Pak envelopes were then sealed around the envelopes containing the ligatures and sterilizing solution. The packs were placed under elevated temperature for several days which changed the liquid EtO to a gas. The EtO gas diffused into the interim space of the envelopes, sterilizing it. After sterilization, these loads were put into an aseptic transfer area; next, they went through an airlock and into an Aseptic Suite. Sealing of dry product (by machine) was done through a cutout in a glove box with a down-flow of filtered air. The box was under positive pressure with no exhaust.

In 1966, the surgical scrub sponge line was started. The sponges were initially sterilized by radiation from an electron beam accelerator. Starting in 1968, the sponges were sterilized by injection of a solution containing liquid EtO. Also, in 1968, the shipping and warehouse departments were relocated in another building and the suture assembly operation was moved from the 2nd to the 1st floor. In 1969, a large addition to the building was constructed for production of Dexon^{R} (polyglycolic acid suture), a synthetic absorbable braid. The vacuum sealing (used to pull out moisture) was conducted in a glove box, under positive pressure, with no exhaust. However, there was a separate ventilation system for the sterile suite.

In 1971, the Warehouse was moved from the first floor to a separate building, and in 1972, Winding, Atraumetic Attaching, Specialties, Maintenance, Engineering, Treated Stores, End Dip, and Control Lab were moved to the first floor.

Also, in 1971 and 1972, additional sterilizers were added.

In 1973, true glove boxes were added in which other products were sealed under aseptic conditions. The glove boxes were under positive pressure with no exhaust; air was supplied to the glove box through High Efficiency Particulate Air (HEPA) filters.

In 1975, the EtO gas mixture used for sterilization was changed to oxyfume (88 parts freon to 12 parts EtO). This was done to decrease the explosion hazard. Also, in 1975, Dexon^{R} (suture) production was moved to Puerto Rico, and some personnel were moved to another plant built for needle production.

In 1977, an 8-point Anarad infrared system was installed to monitor levels of EtO. This system could detect levels as low as 10 ppm. In addition, gaskets on sterilizer doors were changed from rubber to neoprene. Prior to this, gaskets were replaced approximately every two years, or when a leak was noted on the sterilizer chart. In 1977, slotted exhaust hoods were placed in the surgical scrub sponge area, vinyl drapes were hung for isolation, and positive pressure was obtained in the area. Walls were also constructed in 1977 to separate the finishing department from the sterilizing operation, and an exhaust hood was placed on the reclaim bench. Perimeter exhaust hoods were installed at the doors of chambers #3 and #4 to remove the initial EtO gas plume when the doors were cracked open.

Prior to 1977, there was no respiratory protection and the chambers were loaded and unloaded manually, which required approximately 1 1/2 hours per day. In 1977, a respirator program was instituted. From 1977 to August, 1981, half-face organic vapor cartridge respirators were worn by the sterilizer attendants. The cartridges were changed after each shift. In addition, boat hooks were incorporated to pull the loads out of the chambers.

Prior to 1980, closed-load sterilized product was removed from the chamber and allowed to aerate in the open; therefore, it was possible for EtO to diffuse throughout the second floor. No personnel were permitted entry to the aeration room during the 8-hour aeration period.

In late 1980, a sterilizer was relocated and an aeration room built. One sterilizer was removed from service, and another dual entry sterilizer was added, as well as a small 12 ft^3 sterilizer for research and development purposes. An aseptic holding room for the clean side of one sterilizer was provided, as well as a remote control inner door which was interlocked with the exhaust system. EtO monitoring increased and an Enmet alarm system (sound and flashing lights) was installed to detect EtO concentrations greater than 100 ppm. The Aseptic Suite was also rebuilt.

In January, 1981, an administrative change transferred unloading of sterilized (closed-load) product to off-shift hours. For a sterilizer a post-cycle vacuum pull-down was implemented and this sterilizer operated as a pass-through for open load sutures. In August, 1981, the half-face OVA cartridge respirators were replaced with half-face Robert Shaw supplied air respirators (SARS) which were worn by workers who unloaded chambers, replaced EtO cylinders, and prepared solutions containing EtO. SARS were also assigned to maintenance workers and validation technicians. The respirators have undergone annual preventive maintenance checks by the manufacturer.

EtO sterilization was decreased due to a production change to cobalt 60 sterilization. Slotted exhausts were put on glove box ports, shut-off valves were placed on EtO cylinders, and a log book for EtO use was instituted. Carts for transporting EtO products were pulled instead of being pushed; and a delay period of 3 hours was instituted before employees were allowed to enter the closed-load aeration room. Residence time for workers in the aeration room was limited to two hours.

In 1982, the surgical sponge area was enclosed with walls (replacing the vinyl drapes). A perimeter slot hood exhaust was added to a sterilizer door and a separator was put on the EtO chamber drain. All EtO cylinders, upon receipt, were checked for leaks with an infrared (IR) analyzer.

In 1983, the 8-point Anarad EtO monitoring system was replaced with an interim 15-point gas chromatograph (GC) with photoionization (PID) and flame ionization detector (FID) and recorder. This was replaced with a 30-point, continuous GC with PID. In 1984, chamber #2 was removed from service. Recorded accidental exposures include the following:

1981 - A chamber gasket rupture resulted in setting off of the alarm, immediate emptying of the chamber, and evacuation of employees.

June 28, 1982 - A loose level gauge caused approximately a 10 liter (L) leak. No employees were in the area, and self-contained breathing apparatus (SCBA) was used for clean-up.

February 25, 1983 - An EtO solution leak of about 3 L occurred during a break period in the surgical scrub sponge area. Three people cleaned the spill and no personal protective equipment was used.

April 29, 1983 - Approximately 1 L of EtO solution leaked in the surgical scrub sponge area, workers were evacuated, and SCBA was used when the area was cleaned.

July, 1983 - A beaker containing about 60 milliliters of EtO was broken in the laboratory. SCBA was used while the area was being cleaned.

In the past, complaints of smelling EtO, congestion, and rash have been reported by employees.

Industrial Hygiene, Safety, and Medical Programs

Industrial Hygiene

An industrial hygiene program was started around 1963. From 1963 through 1977, industrial hygiene (I.H.) work was conducted once a year by the company physician and corporate (American Cyanamid) industrial hygienist. From 1978 to April 1980, I.H. work was conducted by a Davis and Geck chemist (who received I.H. training at Lederle in Pearl River, N.Y.). From April 1980 to the present, the senior safety engineer has conducted the I.H. work. Personal and area sampling commenced in 1977, i.e., Time-Weighted Averages (TWAs) and area short-term sampling have been conducted with various types of charcoal tubes (standard, 1977; NIOSH, 1978; and Qazi-Ketchum, 1979) and 3M EtO badges. The charcoal tubes were analyzed at Cyanamid's Stanford Industrial Hygiene Laboratory, an accredited laboratory, using NIOSH Method S286.[20] Area sampling was also conducted with a direct-reading instrument, a Century/Foxboro Organic Vapor Analyzer (OVA) Model 128, and with direct reading Draeger tubes.

Monthly ventilation checks are conducted on all engineering controls such as slotted hoods and vents which have been added periodically since 1977. All make-up air for the sterilization area comes from the plant; and there is no recirculation of this air.

Safety

In addition to a Safety Department, there are 3 regular and 3 alternate union safety representatives for the plant. Personal protective clothing in use included: respirators, latex gloves, caps, lab coats, safety glasses, safety shoes, and hearing protection.

Medical

Davis and Geck has a medical department; all employees undergo a preemployment physical examination and periodic voluntary physical examinations.

Description of the Personnel Record Keeping System

A. Description of Record Systems

There are three main file systems. There are approximately 600 hourly workers who are current in the active file (a separate file exists for the 320 salaried workers; in previous years the percentage of salaried workers in the total workforce was lower). There are several hundred hourly and salaried workers in the inactive files who have terminated in the last five years. Finally, there are several thousand hourly and salaried workers who terminated more than five years ago. For the latter workers, full personnel folders no longer exist. Instead, a card system is retained; the card lists the work history of the individual as well as demographic information. All files are alphabetical.

Information in the files is usually adequate to determine who is exposed. Individuals are given a department number which indicates where they work. In addition, a job description is also assigned, which is usually written in the work history, and which in addition may be deduced from a two-digit number which accompanies the two-digit department code.

B. Tentative Definition of Exposed Workers

In this plant the majority of employees, over time, have probably been exposed. Exposed job categories, for the purposes of this study, will include almost any job on the second floor where the chambers are located, and jobs on the first floor near the sponge area where an EtO solution is used. Jobs in the sponge area are entry level jobs and many employees have worked there for a short period of time before moving to other jobs. Exposed job categories tentatively include anyone in sponges (department 72), and anyone in the finishing department (department 65), which includes sterilizer operators who are called solvent attendants, as well as operators involved in handling products in the area. In addition, the following jobs will be included: inspectors (department 53), building maintenance (department 38), production mechanics (department 48), porters (department 40), quality control technicians (department 49), end dipping and cutting (department 62) (prior to 1972), strip packers (department 73), sterility assurance (department 60), inspection control stock clerks (department 47), and shipping (department 59). Prior to 1972, most of the production processes, including winding, atraumatics and all suture assembly were on the second floor with the EtO operations and were potentially exposed. The only operations which were not on the second floor, and hence were not potentially exposed during this time period, were the silk plant (department 85), the machine shop (department 52), data processing (department 32), accounting (department 32), film processing

(department 54), personnel (department 54), medical (department 55), needle plant (department 74-81), and soft gut (department 86). Workers from Research and Development and Engineering (department 45) will also be excluded from the study, even though they have had some potential for EtO exposure. This is being done because exposures in these departments were extremely infrequent since their exposures were primarily related to short-term projects in the sterilization areas.

C. Sampling From the Personnel Records

Industrywide Studies Branch (IWSB) epidemiologists reviewed a random sample of 121 records, from the card system of individuals who had terminated more than 5 years ago. These records were reviewed in order to identify workers that would be included in the study. To be included as an exposed worker eligible for the study, an individual had to have been employed for at least 3 months, worked in a job with potential exposure to EtO, and must have worked at the company in 1958 or later. Other individuals had worked less than 3 months or had been employed in Brooklyn before 1953 and had never worked in Danbury (the plant moved in 1953).

In the file of individuals who had terminated in the last five years, 100 personnel files were randomly sampled and reviewed. Of these, 43 (43%) were exposed and eligible for inclusion in the study. Others had worked less than 3 months. In a few cases, personnel records were insufficient to determine whether an individual was exposed, although querying other personnel would probably clarify the situation.

In the active file, 50 records of hourly individuals were randomly sampled and reviewed.

Applying these proportions to the total number of files, it is anticipated that about 1800 workers may have been exposed and are eligible for inclusion in the study.

Since completing this review, the list of potentially exposed job categories has been expanded to include individuals who worked in Suture Assembly, Winding, and Atraumatics prior to 1972, when these operations were moved to the first floor. Thus, the following estimates of the number of workers eligible for inclusion in the study are probably underestimates.

The average date of first employment for the eligible workers in the sample was 1969 (n=104), the percentage of males was 26%, and the average year of birth was 1939. About 15% of the individuals sampled had been first employed as of 1978 or later and would not be eligible for the first phase of the mortality study.

Overall, it is estimated that there have been several thousand individuals who have worked at this plant, of whom approximately 1800 have been exposed to EtO for three months or more. Approximately 15% of these 1800 were first exposed subsequent to 1978, leaving 1530 for the first phase of the mortality study. Assuming follow-up from the average date of first employment (1969) to 1983, it is estimated that this group would minimally contribute 21,420 (14 x 1530) person-years to the mortality study.

Toxicity

Evidence from animal studies suggests that EtO may have carcinogenic properties.[7,8] 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.[7] 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.[8] 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.[9-11] 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.[9] 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.

Morgan, et al, conducted a retrospective cohort mortality study of workers involved in the production of EtO at a Texaco Facility.[10] 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.[11] 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.[12,13] EtO is also a positive mutagen in several in vitro systems such as Salmonella typhimurium, viruses, and Tradescantia poludosa.[6]

Chromosomal aberrations related to EtO exposure have been observed in a number of animal studies and epidemiologic investigations.[8,13-20] 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.[14] 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.[8] 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.[15] 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.[16]

American Hospital Supply initiated a cytogenetic survey of workers that were exposed to EtO in the sterilization of medical devices in 1978.[17,18] 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.[19,20] 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.[21] OSHA established a new PEL of 1 ppm as an 8-hour TWA on August 21, 1984.[22] 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).[23]

In 1977, NIOSH recommended a ceiling level of 75 ppm as determined during a 15 minute sampling period.[6] 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.[24] 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 was reviewed and adopted in 1984. ACGIH has also designated ETO as an A2 carcinogen.[24] An A2 carcinogen is defined as an industrial substance suspected of having carcinogenic potential for man. This designation is based on either (1) limited epidemiologic evidence, exclusive of clinical reports of single cases, or (2) demonstration of carcinogenesis in one or more animal species by appropriate methods.

Discussion of Company Monitoring Data

The results of the company EtO sample analyses, the specific sampling location, and statistical analyses of the data (arithmetic and geometric means and geometric standard deviation) are presented in Table I. Table II contains the plant controls implemented to reduce EtO exposure levels.

The data presented in Table I indicate that EtO was present in the work environment at this facility. A variety of sampling media and pumps were used during the years that sampling was conducted at Davis and Geck (1977-1983). In 1977, standard size [150 milligram (mg)] 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 sample breakthrough (movement of EtO into and out of the back-up section of the charcoal tube). Therefore, the EtO levels documented in 1977-78 (10.4-271.0 ppm) may be low. The lowest documented level in 1977, 0.4 ppm, is questionable since this level was below the quantitation limit of the analytical method used (NIOSH S286).[25] Another type of sampling media used (1980 and 1981), detector tubes, are only adequate for a general quantitative determination of EtO levels. Detector tubes may have an error rate of greater than plus or minus 30-50%; in addition, it should be noted that detector tubes are no longer certified by NIOSH (as of September 30, 1983).[26]

Other sampling media used, Qazi-Ketchum charcoal tubes (1979-1982) and 3M badges (1981-1983), were more reliable media for EtO monitoring. However, the accuracy of the low values listed, i.e., < 0.05-0.1 ppm, may be questionable due to limits of the available analytical methods and/or the method used to calculate the 8-hour TWA.

A direct reading Century-Foxboro Organic Vapor Analyzer (OVA) was used in 1982-1983 to give instantaneous readings of EtO exposure levels. The OVA is fitted with a GC option which allows separation of organic vapors on the basis of column retention time. The sensitivity of the different OVA models to methane (the gas with which the OVA is factory calibrated) is listed from 0.2 to 1 ppm.[27] However, the OVA provides only a relative response to various organics; therefore, the 0-1 ppm levels documented at this facility may have been underestimated.

Prior to 1981, the Finishing Department, chamber area, and Sponge Department were the only locations sampled for EtO. The highest ranges of EtO levels monitored in the chamber area were non-detectable (ND) to 7.7 ppm personal TWAs in 1979, and 50 to 400 ppm area instantaneous measurements in 1980; the latter representing conditions inside a chamber prior to unloading. The highest ranges of EtO exposure levels documented in the Sponge Department were 1.2 to 14.1 ppm personal TWAs in 1979, and 26.8 to 71.5 ppm area short-term measurements in 1978.

After 1980, other plant areas were also monitored for EtO. The highest personal EtO exposure levels monitored after 1980 were 80.0 and 91.7 ppm as 1-hour TWAs in the Physical Testing Department in 1982; 8-hour TWAs were 10.5 and 8.3 ppm, respectively. The highest area EtO levels monitored (with detector tubes) ranged from 25 to 150 ppm as instantaneous measurements in the chamber area in 1981. However, use of air supplied respirators was instituted in 1981.

For the most part, the engineering and administrative controls instituted in 1982 effectively reduced EtO exposure levels for those areas monitored in 1983 (see Table II). The EtO exposure levels monitored in 1983 ranged from less than 0.1 to 1.3 ppm for personal TWAs and 1.0 ppm for an area instantaneous reading.

KEY TO TABLE I

1) A = area sample

2) STEL = Short-Term Exposure Level (usually 15 or 20 minutes)

3) D = Dupont air pumps; D4 = Dupont P4000 (500 cc/min flow rate); D2 = Dupont P200 (50 cc/min flow rate)

4) CT = Charcoal tube (1977-78: standard size; 1979: Qazi-Ketchum)

5) P = Personal sample

6) TWA_8 = 8-hour Time-Weighted Average

7) S = Sipin pump

8) N.D. = Non-detectable

9) ASR = air supplied respirator

10) ASR Partial = sterilizer operator wore the ASR part of the day (e.g, while unloading an EtO sterilizer).

11) IN = Instantaneous sample

One-half of the LOD was used as the N.D. value when calculating arithmetic means.

TABLE I
HISTORY OF EtO SAMPLING METHODS AND DATA
AT DAVIS AND GECK
DANBURY, CONNECTICUT

DATE	SAMPLING LOCATION	TYPE OF SAMPLE AND EQUIPMENT	RANGE OF EtO CONCENTRATION (ppm)	NO. OF SAMPLES	ARITH. MEAN $\bar{X}$	GEOMETRIC MEAN	GEOMETRIC STANDARD DEVIATION	COMMENTS
1977	Finishing Dept., Chamber Area	A-STEL D/CT	0.8-15.2	4	5.5	3.1	3.5	
	Finishing Dept., Chamber Area	P-TWA_8	0.4	1	--	--	--	
	Sponge Dept.	A-STEL D/CT	2.1	1	--	--	--	
1978	Finishing Dept., Chamber Area	A-STEL D4/CT	2.1-271.0	16	71.0	34.7	4.0	
	Sponge Dept.	A-STEL D/CT	26.8-71.5	4	46.1	42.1	1.6	
1979	Sponge Dept.	A-TWA_8 D2/CT	7.7-17.7	3	14.0	13.1	1.6	Hoods not installed.
	Sponge Dept.	P-TWA_8 D2/CT	1.2-14.1	5	8.2	6.1	2.7	Hoods not installed. Hoods installed but not operational.
	Sponge Dept.	A-STEL D4/CT	1.9-8.6	4	4.8	4.2	1.9	1.9-3.3, hood on 5.6-8.6, hood off
1980	Finishing Dept., Chamber Area	P-TWA_8 S and/or D2/CT	N.D.*-7.7	9	4.0	1.8	7.2	7 of 9 workers sampled were wearing cartridge respirators.
	Finishing Dept., Chamber Area	P-STEL D4/CT	N.D.*	1	--	--	--	

*LOD for Q-K charcoal tubes = 0.06 ppm for an 8-hr TWA and 0.07 ppm for a 15 min STEL
LOD for 3M badges = 0.08 ppm

TABLE I (continued)
HISTORY OF EtO SAMPLING METHODS AND DATA
AT DAVIS AND GECK
DANBURY, CONNECTICUT

DATE	SAMPLING LOCATION	TYPE OF SAMPLE AND EQUIPMENT	RANGE OF EtO CONCENTRATION (ppm)	NO. OF SAMPLES	ARITH. MEAN $\bar{X}$	GEOMETRIC MEAN	GEOMETRIC STANDARD DEVIATION	COMMENTS
1980	Finishing Dept., Chamber Area	A-STEL D2/CT	1.5-215.0	22	28.4	12.3	3.6	
	Finishing Dept., Chamber Area	A-STEL D4/CT	0.4-29.4	32	5.8	2.9	3.4	
	Finishing Dept., Chamber Area	A-IN Draeger	50.0-400.0	16	140.0	109.5	2.0	
	Finishing Dept., Chamber Area	A-STEL D4/CT	0.9-31.3[a]	10	11.8	7.8	3.0	
	Sponge Dept.	A-STEL D4/CT	0.8-1.1	5	1.0	1.0	1.1	
	Sponge Dept.	P-TWA8 D4/CT	0.4-0.6	2	0.5	--	--	
	Sponge Dept.	P-TWA8 D2/CT	N.D.*	1	--	--	--	
1981	Finishing Dept., Outer Seal Area	P-TWA8 D4/CT	0.3-0.5	5	0.4	0.4	1.3	
	Finishing Dept., Outer Seal Area	P-TWA8 D2/CT	0.2-0.3	2	0.3	--	--	
	Finishing Dept., Outer Seal Area	P-TWA 3M Badge	N.D.*-13.0[a]	7	2.1	0.5	4.7	

*LOD for Q-K charcoal tubes = 0.06 ppm for an 8-hr TWA and 0.07 ppm for a 15 min STEL
LOD for 3M badges = 0.08 ppm
a) Company notation: questionable

TABLE I (continued)
HISTORY OF EtO SAMPLING METHODS AND DATA
AT DAVIS AND GECK
DANBURY, CONNECTICUT

DATE	SAMPLING LOCATION	TYPE OF SAMPLE AND EQUIPMENT	RANGE OF EtO CONCENTRATION (ppm)	NO. OF SAMPLES	ARITH. MEAN $\bar{X}$	GEOMETRIC MEAN	GEOMETRIC STANDARD DEVIATION	COMMENTS
1981	Finishing Dept., Overwrap Area	P-TWA$_8$ D2/CT	0.1	1	--	--	--	
	Finishing Dept., Overwrap Area	P-TWA$_8$ 3M Badge	N.D.*-0.3	3	0.2	0.2	1.8	
	Finishing Dept., Chamber Area	A-STEL D4/CT	<6.1-28.6	22	12.5	11.2	1.6	
	Finishing Dept., Chamber Area	P-TWA$_{(1-8)}$ D2/CT	<1.6-6.7	2	4.2	--	--	Cartridge respirators in use for 6.7 ppm exposure level
	Finishing Dept., Chamber Area	A-IN Draeger	25.0-150.0	15	95.0	84.6	1.8	Obtained during chamber unloading
	Finishing Dept., Aseptic Sealing Area	P-TWA$_8$ D4/CT	> 4.0-4.5	2	4.3	--	--	
	Finishing Dept., Aseptic Sealing Area	P-TWA$_8$ D2/CT	1.1-4.7	4	2.7	2.2	2.1	
	Finishing Dept., Aseptic Sealing Area	A-1hr. D2/CT	< 0.7- 0.8	2	0.7	--	--	

*LOD for Q-K charcoal tubes = 0.06 ppm for an 8-hr TWA and 0.07 ppm for a 15 min STEL
LOD for 3M badges = 0.08 ppm
a) Company notation: questionable

TABLE I (continued)
HISTORY OF EtO SAMPLING METHODS AND DATA
AT DAVIS AND GECK
DANBURY, CONNECTICUT

DATE	SAMPLING LOCATION	TYPE OF SAMPLE AND EQUIPMENT	RANGE OF EtO CONCENTRATION (ppm)	NO. OF SAMPLES	ARITH. MEAN $\bar{X}$	GEOMETRIC MEAN	GEOMETRIC STANDARD DEVIATION	COMMENTS
1981	Finishing Dept., Aseptic Sealing Area	P-TWA$_8$ 3M Badge	3.4-6.6[a]	8	4.4	4.2	1.3	
	Finishing Dept., Alpha Process Area	P-TWA$_8$ D2/CT	0.2	1	--	--	--	
		3M Badge	N.D.*	2	0.08	--	--	
1982	Warehouse	A-instantaneous Century Foxboro OVA	N.D.-4.0	10	--	--	--	
	Sponge Dept.	P-TWA$_{(5-8)}$ 3M Badge	0.5-3.0	9	1.2	1.0	2.0	
	Sponge Dept.	A-instantaneous Century Foxboro OVA	0-70	12	12.2	2.5	2.2	
	Physical QC Testing Dept.	P-STEL 3M Badge	60.8-96.8	2	78.8	--	--	
	Physical QC Testing Dept.	P-TWA$_1$ 3M Badge	80.0-91.7	2	85.9	--	--	
	Physical QC Testing Dept.	P-TWA$_8$ 3M Badge	0.3	1	--	--	--	
	Finishing Dept., Chamber Area	P-TWA$_{(1-4)}$ 3M Badge	1.6-4.6	3	3.3	3.0	1.7	TWA$_4$ (3.6 & 4.6) included PPG/EtO solution preparation, those workers wore ASR-partial

*LOD for Q-K charcoal tubes = 0.06 ppm for an 8-hr TWA and 0.07 ppm for a 15 min STEL
LOD for 3M badges = 0.08 ppm
a) Company notation: questionable

TABLE I (continued)
HISTORY OF EtO SAMPLING METHODS AND DATA
AT DAVIS AND GECK
DANBURY, CONNECTICUT

DATE	SAMPLING LOCATION	TYPE OF SAMPLE AND EQUIPMENT	RANGE OF EtO CONCENTRATION (ppm)	NO. OF SAMPLES	ARITH. MEAN $\bar{X}$	GEOMETRIC MEAN	GEOMETRIC STANDARD DEVIATION	COMMENTS
1982	Finishing Dept., Chamber Area	A-STEL D4/CT	6.6-130.0	16	28.4	18.4	2.4	Samples in various locations in aeration room after transport of sterilized loads
	Finishing Dept., Chamber Area	P-STEL D2&4/CT	1.7-37.3	13	11.5	8.2	2.4	Some workers wore ASR
	Finishing Dept., Chamber Area	P-TWA$_8$ D2&4/CT	1.2- > 1.8	2	1.5	--	--	ASR Partial
	Finishing Dept., Chamber Area	A-instantaneous Century Foxboro OVA	0-350.0	13	34.1	2.5	2.2	350 ppm level-probe inside tote box (aeration room)
	Finishing Dept., Aseptic Area	P-TWA$_8$ D2/CT	0.4-0.7	3	0.5	0.5	1.3	
	Finishing Dept., Alpha Process	A-instantaneous Century Foxboro OVA	3.5- > 47.0	6	15	9.7	2.7	
1983	Warehouse	P-TWA$_8$-3M	1.0	1	--	--	--	
	Physical Testing Dept.	P-TWA$_8$ 3M Badge	< 0.1-1.0	10	0.4	0.3	2.7	No exhaust for 2 samples-(0.94-0.98 ppm)
	Physical QC Testing Dept.	P-TWA$_8$ 3M Badge	0.2	1	--	--	--	

TABLE I (continued)
HISTORY OF EtO SAMPLING METHODS AND DATA
AT DAVIS AND GECK
DANBURY, CONNECTICUT

DATE	SAMPLING LOCATION	TYPE OF SAMPLE AND EQUIPMENT	RANGE OF EtO CONCENTRATION (ppm)	NO. OF SAMPLES	ARITH. MEAN $\bar{X}$	GEOMETRIC MEAN	GEOMETRIC STANDARD DEVIATION	COMMENTS
1983	Sterility Lab	P-TWA_8 3M Badge	0.05-0.07	2	0.06	--	--	TWA_8 calculated from monitored TWA_4
	Finishing Dept., Outer Seal Area	P-TWA_8 3M badge	0.1	3	--	--	--	
	Finishing Dept., Overwrap Area	P-TWA_8 3M Badge	0.1	1	--	--	--	
	Finishing Dept., Chamber Area	P-TWA_8 3M Badge	0.5-1.3	2	0.9	--	--	0.5 ppm exposure level includes EtO solution preparation
	Finishing Dept., Aseptic Seal Sterile Suite	P-TWA_8 3M Badge	0.1-0.7	3	0.3	0.2	2.4	
	Finishing Dept., Alpha Process Area	P-TWA_8 3M Badge	0.1	1	--	--	--	

TABLE II

CONTROLS IMPLEMENTED TO REDUCE EtO EXPOSURE LEVELS AT DAVIS AND GECK DANBURY, CONNECTICUT

DATE	ENGINEERING CONTROLS	ADMINISTRATIVE CONTROLS	RANGE OF EtO LEVELS MEASURED (ppm)
1953	Exhaust hoods	None added	
1968	None added	Shipping and warehouse depts. relocated in different building; suture assembly moved from 2nd to 1st floor	
1969	Vacuum sealing conducted in glove box--no exhaust	None added	
1975	None added	EtO gas mixture changed from 80:20-CO_2:EtO to 88:12-freon:EtO Dexon sutures moved to Puerto Rico	
1977	Rubber sterilizer gaskets changed to neoprene	OV respirator program developed and instituted for sterilizer operators	0.4-15.2 (Chamber area)
	8-point Anarad EtO monitoring system installed	Boat hooks incorporated for pulling sterilized loads from sterilizer	
	Vinyl strips hung to isolate the scrub sponge area	Industrial hygiene sampling program started	2.1 (Sponge Dept.)
	Exhaust hood put on reclaim bench		
	Walls constructed to separate sterilizing operations from Finishing Dept.		
1978	None added	None added	2.1-271.0 (Chamber area) 26.8-71.5 (Sponge Dept.)

TABLE II (continued)

CONTROLS IMPLEMENTED TO REDUCE EtO EXPOSURE LEVELS AT DAVIS AND GECK DANBURY, CONNECTICUT

DATE	ENGINEERING CONTROLS	ADMINISTRATIVE CONTROLS	RANGE OF EtO LEVELS MEASURED (ppm)
1979	Slotted exhaust hoods installed on EtO scrub sponge line	None added	Hood off: 5.6-8.6 (Sponge Dept.) Hood on: 1.9-3.3 (Sponge Dept.)
1980	Remote control interdoor was interlocked with sterilizer exhaust system	Sterilizer relocated Sterilizer shutdown EtO exposure monitoring increased	N.D.-400 (Chamber area) N.D.-1.1 (Sponge Dept.)
	Degassing room built for sterilizers		
	Additional exhaust ports added to top of sterilizers		
	Aeration room built for clean side of sterilizer		
	Enmet alarm system installed		
	Aseptic Suite rebuilt		
1981	Slotted exhaust added to glove box ports	Use of supplied air respirators instituted Amount of EtO sterilization decreased Carts for transporting EtO sterilized product were pulled not pushed 3 hour delay period instituted before entry allowed in degassing room; entry limited to 1 hour	N.D.-150 (Chamber area)

TABLE II (continued)

CONTROLS IMPLEMENTED TO REDUCE EtO EXPOSURE LEVELS AT DAVIS AND GECK DANBURY, CONNECTICUT

DATE	ENGINEERING CONTROLS	ADMINISTRATIVE CONTROLS	RANGE OF EtO LEVELS MEASURED (ppm)
1982	Additional slot exhaust added to sterilizer door	Liquid EtO mixture changed	0.5-3.0 (TWA) 0-70.0 (instant/area) (Sponge Dept.)
	Surgical sponge area enclosed with walls	All EtO cylinders checked for leaks, upon receipt	1.2-130.0 (chamber area)
1983	Multi-point GC/FID EtO monitor installed	None added	< 0.05-1.3 (all areas sampled)
1984	Multi-point GC/PID EtO monitor installed	None added	--

Conclusions

Davis and Geck has industrial hygiene data dating back to 1977. Therefore, it may 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

1. Continue the industrial hygiene monitoring program for EtO.

2. Conduct additional 8-hr TWA EtO monitoring of the warehouse where the (1983) instantaneous monitoring result was 0.95 ppm.

3. Increase dilution ventilation or add local exhaust ventilation to the Physical Testing Department and Finishing Department, Chamber Area where the 8-hr TWA results were at or slightly greater than 1 ppm.

4. Continue conducting ventilation investigations to insure proper operation of the ventilation systems.

References

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

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

3. Clayton, G.D.; Clayton, F.E.; eds, Patty's Industrial Hygiene and Toxicology, 3rd Revised ed., Vol. 2A, John Wiley and Sons, New York, 1978.

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

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

6. 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.

7. 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, B thy Run Research Center, January 28, 1981. Submitted by Union Carbide C. poration 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).

8. 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.

9. 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.

10. 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.

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

12. 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.

13. 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.

14. 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.

15. 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.

16. 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.

17. 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.

18. 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.

19. 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.

20. 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.

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

22. 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.

23. 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.

24. 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.

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

26. 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.

27. Centurion, Century Systems Corp. Vol. 1, No. 2. May, 1979.