INDUSTRYWIDE STUDIES REPORT:
A WALK-THROUGH SURVEY

OF

Professional Medical Products
P.O. Box 3288
Greenwood, SC 29648

SURVEY CONDUCTED BY:

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DATE OF SURVEY:
June 3-4, 1985

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PURPOSE:	To evaluate the industrial hygiene records, production processes, and personnel records to determine the suitability of including this facility in the NIOSH Industrywide Studies Branch mortality/industrial hygiene study of ethylene oxide (ETO).
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EMPLOYEE REPRESENTATIVE CONTACTED	None (no union)
STANDARD INDUSTRIAL CLASSIFICATION OF PLANT:	3841 - Surgical and Medical Instruments and Apparatus

Abstract

On June 3-4, 1985, a site visit to the Professional Medical Products plant in Greenwood, South Carolina, was conducted to gather data and to determine the feasibility of including this facility in the NIOSH mortality/industrial hygiene study of workers exposed to ethylene oxide (ETO).

This plant has used ethylene oxide from 1962-1985 to sterlize medical products such as dapers, vinyl examiniation gloves, sponges, and surgical drapes. ETO use was minimal from 1962-1966 until new sterilizers were purchased in 1966. The company now contracts out sterilization (off site).

During the visit, personnel records were evaluated and a walk-through survey of the facility was conducted. Industrial hygiene records were reviewed. The ETO exposure data submitted by the company, which is summarized in this report, indicate that the various control measures installed by the company did decrease the employees' exposure to ETO (documented via Qazi Ketcham tubes), however, general area sampling also conducted by the company (Qazi Ketcham tubes and a Miran^{R} (an infrared directed reading instrument) indicated that there were detectable levels of ETO throughout most of the plant.

Results of the epidemiologic evaluation of the records indicated that this facility meets all of the eligibility requirements as defined by the protocol for the mortality study. Therefore, this plant will be included in the mortality study of ETO. These requirements are: 1)the plant must contributed at least 400 person-years, 2) the plant must have adequate personnel records in order to identify who has been exposed, 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]

This walk-through survey was conducted to determine the suitability of including Professional Medical Products 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 FACILITY

This plant was owned by Parke-Davis Company from 1962 until 1970, and then by Warner-Lambert, until January 20, 1982 when it was bought by Professional Medical Products. For the purposes of this report, all plant descriptions will include the period from 1962 until 1985, regardless of ownership. There are two other plants in the area owned by Warner Lambert, Capsugel (next door) and Deseret Medical (in Honea Path, near Greenwood). These plants are not under consideration for the cohort mortality study.

This plant has manufactured diapers, vinyl examination gloves, sponges, surgical drapes, gauze in plastic packages, finger bandages, and other medical supplies. Since 1978 they have manufactured orthopedic products as well.

ETO has been used, from 1962-1985, as a 12/88 mixture of ETO and freon (FC12). Use of the gaseous mixture ranged from 153,000-317,000 pounds a year from 1978-1981, dropping to lower levels in more recent years. Data was not available for usage from earlier years.

DESCRIPTION OF THE WORKFORCE

There are approximately 750 people currently working at this plant, of whom approximately 515 are hourly, with the rest divided between exempt and nonexempt salaried employees. Employees are divided between two divisions, Patient Care and Orthopedic. There are approximately 100 Orthopedic hourly employees and 415 Patient Care hourly employees. Approximately 58% of the current workforce is male, and approximately 63% is white. In 1984 yearly turnover among hourly employees was approximately 7%, while it was 15% among salaried employees.

DESCRIPTION OF PROCESS

The description below reflects the process just before the discontinuation of on-site ETO product sterilization.

Professional Medical Products (PMP) produces soft medical products (gauze bandages, gauze rolls, and drapes). These products were sterilized with an ETO gas mixture (12% ETO, 88% Freon) in one of four (4) sterilizers (sterilizer 2 - 1280 ft^3, sterilizer 3 - 1280 ft^3, sterilizers 4 and 5 - 1208 ft^3 each). The first sterilizer used at this plant (sterilizer 1) was a 144 ft^3 unit installed in 1962 and removed in 1966. ETO has not been used at this facility to sterilize product since February, 1985. Steam is now used to sterilize some products, while the remainder is contracted out for gas sterilization.

The raw materials were brought into the plant and processed as necessary. The completed goods were placed into ETO permeable packages, and overwrapped, and then placed into the shipping cases. Biological Indicator strips (BIs) were placed in and among the cases by the production personnel. The cases were then transferred to the sterilization area.

In the sterilizer area, the cases were placed onto aluminum pallets and loaded into the sterilizer. The total cycle time was about 24 hours. The exposure

time to ETO for the various products ranged from 6 - 19 hours. At the end of the exposure cycle, the chamber was exhausted directly to the outside of the building. The exhaust system consisted of an air intake and a automatic exhaust. The chamber door was equipped with a fail-safe lock which prevented the door from being opened until the exhaust cycle was completed. The exhaust water from the vacuum pump was sent to an aerator tank. In this tank, the ETO was separated from the water and sent directly to an exhaust vent on the roof. At the end of the exhaust cycle, the unload door (the vessel had a load and unload door) was partially opened. The exhaust system would then run for an additional 30 minutes before the product was unloaded.

The pallets were pulled from the chamber by the operator and the product cases were transferred to wooden pallets. During product loading and unloading, the operator wore a MSA^{R}-type air-purifying cartridge respirator. The wooden pallets were taken via fork-lift directly to "degassing racks" which were located in the quarantine area. These racks were placed directly in front of exhaust vents which aided in the aeration of the product. After the 24 hour aeration period, the product was returned to the pack-off area (directly behind the sterilizers). The BIs were then removed and sent to the Microbiology laboratory. The cases were manually sealed and transferred to the quarantine area, where they were held for 12 - 14 days. After that time, the cases were placed into the general warehouse or shipped.

DESCRIPTION OF PAST EXPOSURES

There have been many changes in this facility over the last several years which would have affected employee exposure to ETO. These changes can be divided into several areas: process changes, sterilizers, ventilation, and isolation.

Process Changes

The most important process change which reduced employee exposure to ETO was the discontinuation of ETO sterilization in February, 1985. Another important change in the production process involved the removal of the BIs from the sterilized product. Prior to 1979, the BIs were removed by hand from freshly sterilized product while the product was in the sterilizer area (for as long as one shift). The cases were then manually sealed and the product was sent directly into the quarantine area. After 1979, until the use of ETO was discontinued, the BIs were not removed from the product until it had aerated for 24 hours on the "degassing" racks in the quarantine area (see process description above).

Sterilizers

The first sterilizer acquired at this facility was a 144 ft^3 combination gas/steam unit in 1962. This unit was located in what is now the nonwoven department. This unit used the 12/88 ETO gas mixture, however the quantity of gas used is unknown. This unit was moved to the present sterilization area in 1966 and was not used as a gas unit after that time. In 1966, a second unit (sterilizer 2- 1280 ft^3) was purchased and also installed in the present sterilizer area. In 1969, a third unit (sterilizer 3 - 1280 ft^3) was

purchased and installed beside unit 2. The fourth and fifth units were purchased in 1970 and 1972 respectively. These units both had a volume of 1208 ft^3. All units were served by bottled ETO tanks which were located near the vessels. These bottles were not equipped with any local exhaust or quick release valves. In 1973, these bottles were replaced with a bulk tank which was located in the rear yard.

Ventilation

The major ventilation change which occurred was the installation of the direct exhaust system and fail safe door lock in late 1979 or early 1980. This system consisted of a automatic exhaust which flushed the units with air. The door lock prevented the units from being opened until the flush was complete. The general ventilation system (heating and air conditioning) for the sterilizer area was shared with the Sponge department from 1966 until 1981. At that time, the portion of the ventilation system serving the sterilizer area was separated from the rest of the system. The new sterilizer system had roof exhaust vents which were approximately 20 feet above the roof line. In addition, 100% make-up air was provided to this area.

Isolation

Isolation of the sterilization area occurred in 1980. Isolation was accomplished by the addition of a floor to ceiling cinder block wall. This physical separation of the sterilizers and devotion of a ventilation system to the sterilizer area in 1981 should have reduced ETO exposure in other areas of the plant.

DESCRIPTION OF PERSONNEL RECORDS AND DEFINITION OF EXPOSED GROUP

(a) Personnel record system

Personnel records are divided between terminated hourly employees, terminated nonexempt employees, terminated exempt employees, active hourly employees, active nonexempt employees, and active exempt employees. Exempt and nonexempt will be discussed together as salaried employees. Active hourly employees are further divided between the Patient Care and Orthopedic Divisions. Records are arranged alphabetically. Records of employees terminated prior in 1967 or earlier have been microfiched, while all other records are maintained either on hard copy, or since 1977 are on computer (with hard copy back-ups in personnel file).

There are also approximately 50 retirees and 20 deceased individuals, who have retired and/or died since 1982, who are filed separately, but are kept in the same location as the files described above.

In addition, there are approximately 80 retirees and 40 former employees on long-term disability whose records were sent to Warner Lambert in Utah in 1982 when Professional Medical Products bought the plant. Names of all of these individuals are available, and their records can be sought from Warner Lambert.

In addition, records of appoximately 80 people who transferred to the nearby

Capsugel plant from 1980-1982 are currently kept at Capsugel. Subsequent to 1982 such transfers were not allowed, due to change in company ownership.

The approximate number of individuals in each of the filing systems described above is as follows:

1) Terminated hourly, 1968 to current, n=1050
2) Terminated hourly and salaried on fiche, terminated in prior to 1968, n=450
3) Terminated salaried, 1968 to current, n=450 (excluding about 180 exempt field personnel)
4) Active hourly, n=515
5) Active salaried, n=235

Personnel records include a work history which lists department and job over time, with the appropriate dates for any changes. Social Security numbers and date of birth are also available. Race data is available. Although departments have always had numerical codes, most of the early work history for any long term employee lists only the name of the department, without the numerical code. The company has provided a list of department names and their corresponding codes. Some departments have changed names often over time; job titles have changed less often. There are two sources which do list numerical department codes. These are the "change of employee status" sheets and the daily attendance records, which exist for the entire history of the plant. Thus it will be possible to develop detailed work histories with numerical department codes. Job titles themselves are not as important as department in determining exposure, and would not need to be coded at this plant.

Computerization began January 1977, and any employees who have worked at the plant since that date have that part of their work history on computer sheets. These computer sheets are entered into the personnel folder for terminated employees. For active employees hard copy computer sheets are also available in personnel folders for all jobs through the current one. Three different computer systems have been used. The first was used from January 1977 till January 1982. The second was used from January 1982 until March 1984. The third has been used since March 1984 until the present. Ordinarily work history can be obtained by using computer sheets from the first system and the current one. The second system is hard to read; much information has been coded and is hard to interpret. The work history from the second system is also available on the third.

Payroll records are available as an alternative list of employees who have worked at the plant. Payroll records back to 1971 are available at the Greenwood plant. Payroll records from 1970 back to 1963 are at Warner Lambert in Utah. These payroll records include not only employees from the plant in Greenwood, but also employees at the Capsugel plant in Greenwood, and the Deseret Medical plant in Honea Path, during the period when all three plants were owned and operated by Warner Lambert. However, it is possible from payroll records to distinguish at which plant employees were working.

(b) Definition of exposed group

Industrial hygiene data indicates that ETO moves from the sterilization area east throughout the rest of the plant. Although the highest exposure would have occurred in the sterilization area, and throughout that building (where gloves, sponges, and orthopedic products have been or are manufactured), exposure would have also occurred to the east in the building housing cotton production, and to the north in the warehouse where product offgassed. The only areas considered to be not exposed would have been the paper products area to the west of the sterilization area, and office areas to the south of the sterilization area. For the purposes of the mortality study, therefore, salaried employees will be considered nonexposed.

Furthermore, given that the amount of gas used prior to 1966 was small, exposure will be considered to have occurred only from January 1, 1966 onwards.

The exposed departments and their numbers are listed below. More recently three digit department numbers begin with the number "3." In the past, however, all Patient Care division departments began with the number "1". We will use the "100" series in referring to the Patient Care division.

Patient Care Division:

General Products	153
Glove Products (Adhesive and General)(Paper and Glove)	154
Sterilization	155
Adhesive Plaster (Tape)	161
Elastic Bandage	162
Readi-Bandage	163
(Readi-Bandage Bench)	863
Gauze Bleaching	164
Gauze Slitting (Stretch Gauze)	165
(Stretch Gauze Bench)	865
Packaging (Cotton and Rayon, Cotton and Gauze, Woven and Nonwoven)	166
Cotton Bleaching and Picking	168
Carding (Card Room)	170
Nonwoven	171 (178)
Gauze Sponge (Sponge)	176,177,179
(Sponge Bench)	876
Plant Engineering and Maintenance	183
W-Pack and Readi-Pad	177 (174)
Receiving and Material Storage	196
Cotton Baling	964

Orthopedic Division:

Pope Manufacturing	341
Chick Production (Assembly, Mach Shop, Framing, GTD Man)	342-7(303,397)
Realastic Mfg.	349

The departments with the most direct exposure were in the building with the sterilizers. These include the sterilization department (155), the sponge

department (176,177,179), the glove department (154) and the Realastic department (149)(since 1978). "Bench" departments are essentially the same as their corresponding department.

(c) Sampling the personnel records and estimating person-years to be contributed by this plant

Random samples were drawn from the various files described above for hourly employees. The number of records sampled for each file is shown in Table 1. The column headings in Table 1 refer to the total number of individuals in each file, the number of individuals sampled, the number of exposed individuals in the sample, the average date of hire and date of birth of the exposed individuals in the sample, and the number of males among the exposed in the sample.

In the sampling, an employee was considered to be exposed if they worked in an exposed department at anytime between 1966 and 1977, for more than 3 months. The first phase of the mortality study will include only those who were exposed prior to 1978.

Table I shows the results of the sampling. In Table I, file 1 refers to hourly terminated employees, who terminated from 1968 onwards. File 2 refers to the hourly/salaried employees on microfiche,all of whom had terminated prior to 1968. File 3 refers to active hourly workers. File 4 refers to retirees and individuals who had died, which including both hourly and salaried individuals. (file 4).

Applying the percentages of exposed in the sample to the total number of individuals who have been employed at the plant, it is expected that 786 individuals have been exposed at this plant, with an average date of hire of 1969, and an average date of birth of 1941. About 22% of the exposed will be males. Here it is assumed that the average date of hire corresponds to the average year of first exposure, an assumption which will hold true for most of these individuals. Given the above, and assuming that each individual will contribute an average of 13 person-years to the study (1969-1982), then it is expected that approximately 10,000 person-years of experience to be contributed by this plant.

Approximately 120 individuals (retirees and long-term disabled whose records are at Warner Lambert) have not been included in these calculations. The records of these individuals can probably be obtained. About 80 individuals who transferred to Capsugel in 1980-82 have also not been included. It is probable that the records of these individuals can also be obtained. These missing individuals represent about 7% of the employees who have worked at this plant.

DESCRIPTION OF MEDICAL, INDUSTRIAL HYGIENE, AND SAFETY PROGRAMS

(a) Medical

This plant employs a full time occupational nurse. There is a physician available who has conducted physicals on the employees from 1962-1983. All employees undergo a pre-employment physical. Certain management exempt employees undergo a routine periodic physical. Starting in 1980, all sterilizer operators and packers received an annual physical exam. This exam consisted of a brief medical and family history and a physical examination. There has been no cytogenetic testing.

(b) Industrial Hygiene and Safety

This facility began a formal in-house sampling program for ETO in late 1979. This program, which was initially conducted by corporate personnel, became the responsibility of the plant personnel in 1981. The initial industrial hygiene sampling and analysis for ETO was conducted as described by Qazi and Ketcham in 1977[25]. Qazi Ketcham (QK) charcoal tubes were used to collect both personal (see Table II) and general area samples (see Table III). The personal sampling was conducted on the same job titles and in general, on the same individuals from 1979 to 1981. The ETO gas and steam operators had essentially the same exposures to ETO, because the steam and gas vessels were located side by side. These exposures do decrease with time as a result of the installation of various controls (about 30 ppm 8 hr TWA-1979, <1.0 ppm 8 hrTWA-1981). The general area samples were also, in general, taken in the same locations over time from 1979 to 1981. There is also a decrease in these levels to less than 1.0 ppm in the manufacturing areas (Sponge and Realastic) in 1981, due to the installation of various controls.

In 1980, general area samples were also taken with a Miran 101^{R}, a direct reading infrared instrument. These samples were taken about every six (6) months in the same locations by the same individual. The samples indicate that ETO could migrate throughout most, if not all, of the entire plant (see Table IV). The data indicates that, as expected, the areas nearest to the sterilizers have the highest exposures to ETO. The data also indicates that in 1985, after many controls had been installed, the sponge area, which is adjacent to the sterilizers, had about the same ETO levels as the sterilizer area (3-4 ppm). This was unexpected, as data collected with QK tubes in 1981 indicated that these areas were less than 1.0 ppm. The variation in the industrial hygiene data may be dependent on several factors such as the type of product being sterilizer and the number of sterilizers being unloaded at the time the samples were collected. In addition, the Miran data reflects a one time (grab) sample while the QK data would be more representative of a full shift exposure, therefore, it is some what difficult to make a direct comparison of the variation of ETO levels with time.

In July 1983 until the use of ETO was discontinued in February 1985, all sterilizer area employees were issued Scott^{R} full-face back-pack type air-purifying respirators. These respirators were equipped with organic vapor cartridges. The cartridges were changed at the beginning of each shift. QA and maintenance personnel were also issued this equipment.

TOXICITY

Evidence from animal studies suggests that ETO may have carcinogenic properties.[8,9] 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.[8] 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.[9] 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.[10-12] 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.[10] 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.[11] 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.[12] 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.[13,14] 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.[9,14-21] 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.[15] 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.[9] 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.[16] 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.[17]

American Hospital Supply initiated a cytogenetic survey of workers that were exposed to ETO in the sterilization of medical devices in 1978.[18,19] 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.[20,21] 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.[22] OSHA established a new PEL of 1 ppm as an 8-hour TWA on August 21, 1984.[23] 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).[24]

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.[25] 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.[25] 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.

CONCLUSIONS

Personnel records are adequate to determine who was exposed based on department. Exposure data exists to broadly characterize exposure by department over time. Based on the findings of this survey, this plant meets the eligibility criteria to be included in the cohort mortality study (adequate personnel records, more than 400 person years, no serious confounding exposures).

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. Qazi, A; Ketcham, N., A new method for monitoring personal exposure to ethylene oxide in the occupational environment. Am. Ind. Hyg. J., 38 (11): 635-647, 1977.

8. 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).

9. 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.

10. 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.

11. 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.

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

13. 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.

14. 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.

15. 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.

16. 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.

17. 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.

18. 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.

19. 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.

20. 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.

21. 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.

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

23. 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.

24. 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.

25. 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.

TABLE I. SAMPLING THE PERSONNEL RECORDS*

File	Total#	#Sampled	#Exposed in sample(%)	Estimated total # exposed	Date 1st-emp	Av.DOB of exposed	#Male exposed
1	1050	46	14 (30)	315	1971	1944	5
2	450	30	8 (27)	121	1966	1939	7
3	515	25	16 (64)	330	1967	1937	9
4	50	10	4 (40)	20	1962	1923	4
Total	2065	111	42 (38)	786			

*Files 1-4 are for hourly employees who terminated from 1968 onwards, hourly/salaried employees who terminated prior to 1968, active hourly workers, and hourly/salaried retirees/decedents, respectively.

TABLE II
PROFESSIONAL MEDICAL PRODUCTS
PERSONAL BREATHING ZONE SAMPLES°
QAZI-KETCHAM TUBES

DATE	JOB	8 hr TWA PPM
5-79		
	ETO Vessel Operator	33.1
	Steam Operator	25.0
	Pack-off Operator	28.7
12-79		
	ETO Vessel	1.6
	ETO Vessel Operator	13.9*
	Steam Vessel Operator	2.2
	Pack-off Operator (Steam Product)	2.4
	ETO Vessel Operator	1.9
	Steam Vessel Operator	2.3
	Pack-off Operator (Steam Product)	2.6
	Pack-off Operator ETO	15.0
11-80		
	ETO Vessel Operator	0.8
	Pack-off Operator	2.2
4-81		
	ETO Vessel Operator	0.13
	ETO Vessel Operator	0.92
	ETO Vessel Operator	0.42
	Steam Operator	0.13
	Pack-off Operator	0.12

°Data submitted by company
* Leak during sampling.

TABLE III

PROFESSIONAL MEDICAL PRODUCTS
GREENWOOD, SOUTH CAROLINA
GENERAL AREA SAMPLES*
QAZI KETCHAM TUBES

DATE	LOCATION	8 hr TWA PPM
5-79		
	Sponge Packaging (South perimeter of Sterilizer area)	28.9
	Sponge (East perimeter of Sterilizer area)	22.5
	Sterilizer area	21.9
12-79		
	Quarantine	25.3
	Sponge Packaging (South perimeter of Sterilizer area)	1.7
	Pack-off Area	4.1
4-80		
	Sponge Packaging (South perimeter of Sterilizer area)	2.9
	Realastic	4.0[a]
	Quarantine	10.0[b]
	Warehouse	0.73[c]
	Cafeteria	N.D.[d]
4-81		
	Sponge Department	0.20
	Realastic	0.1
	Quarantine	3.3

*Data submitted by company
a-20 minute sample
b-22 minute sample
c-32 minute sample
d-N.D. non-detectable assumed to be 0.15 ppm[25]

TABLE IV
PROFESSIONAL MEDICAL PRODUCTS
GREENWOOD, SOUTH CAROLINA
GENERAL AREA SAMPLES#
MIRAN 101

Location	11-80	6-81	12-81	6-82	11-82	6-83	12-83	6-84	8-84	1-85	X + S.D.°
Boiler Room (BR)	NA*	NA	NA	NA	NA	2.0	0	3.5	1.0	0.0	1.6 ± 1.5
Hallway Between BR and Paint Shop	NA	NA	NA	NA	NA	2.0	0	3.0	2.0	2.0	1.8 ± 1.3
Mechanical Stores	NA	NA	NA	NA	NA	0.0	1.0	2.5	0.0	1.0	0.9 ± 1.2
Mezzanine Above Engineering	NA	NA	NA	NA	NA	0.5	1.0	2.0	1.0	1.5	1.1 ± 0.6
Between Engineering and Waste Disposal	NA	NA	NA	NA	NA	1.5	1.0	2.0	1.0	3.0	1.4 ± 0.5
Waste Disposal Area	NA	NA	NA	NA	NA	1.5	0.5	2.0	0.5	5.0	1.9 ± 1.8
Warehouse "F"	2.7	1.5	0.0	0.25	2.5	2.0	1.0	2.5	3.0	3.0	1.9 ± 1.0
Above Suspended Ceiling Over Sterilizers	NA	NA	NA	NA	NA	2.5	4.0	3.0	5.0	8.0	4.5 ± 2.2
In Sponge Near First Aid	3.5	3.0	1.5	0.1	3.5	2.0	4.0	0.5	1.0	5.0	2.4 ± 1.3
In Sponge Near Canteen Door	3.0	3.5	2.0	0.1	3.5	2.0	3.0	0.5	3.5	3.0	2.6 ± 1.1
Near Area Production Supervisor Office	5.7	3.0	3.0	0.1	5.0	2.0	3.5	0.5	1.0	6.0	3.0 ± 1.8
Realastic	5.5	3.0	3.0	0.0	4.5	2.0	4.5	1.5	1.0	4.0	3.1 ± 1.6
Sterilizer Staging	12.0	3.0	3.5	1.0	5.0	1.0	2.0	3.0	2.0	7.0	4.0 ± 3.5
Quarantine	NA	NA	NA	NA	NA	1.5	2.0	2.0	3.0	4.5	2.1 ± 0.6

#Data submitted by company
*Data in question due to possible Miran malfunction (company remark).
° Data does not reflect 11-80.
@ NA-not available