

INDUSTRYWIDE STUDIES REPORT:
A WALK-THROUGH SURVEY
OF
AMERICAN MCGAW (AMERICAN HOSPITAL SUPPLY CORPORATION)
P.O. Box K
Milledgeville, GA 31061

PROJECT NUMBER: P:85:15

SURVEY CONDUCTED BY:
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DATE OF SURVEY:
January 23-24, 1985

REPORT WRITTEN BY:
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Industrial Hygiene Section
Industrywide Studies Branch
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National Institute for Occupational Safety and Health
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Cincinnati, Ohio

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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).

EMPLOYER REPRESENTATIVES

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EMPLOYEE REPRESENTATIVES

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None

**STANDARD INDUSTRIAL
CLASSIFICATION OF PLANT**

2834 - Pharmaceutical Preparations

ABSTRACT

On January 23-24, 1985, a walk-through survey was conducted at the American McGaw, a division of American Hospital Supply, in Milledgeville, Georgia. The primary purpose of this survey was to determine the feasibility of including this facility in the NIOSH mortality and industrial hygiene study of workers exposed to ETO.

American McGaw used ETO between 1962 and 1975 to sterilize IV administration sets. This process was moved in 1975 to an American McGaw facility in Puerto Rico. Sterilization was performed with a 12/88 percent mixture of ETO and freon. There have not been any Industrial Hygiene evaluations for ETO at this facility.

The eligibility requirements, as defined by the study's protocol, for inclusion of a facility in the NIOSH ETO mortality study are 1) the plant must contribute at least 200 person-years to the high exposure group, or 400 person-years total, 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. This facility failed to meet criteria number 2, since in most cases it was not possible to reliably determine whether or not a worker was exposed to ETO based on the job descriptions in the personnel file, and therefore this facility will not be included in this study.

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 American McGaw's facility in Milledgeville, Georgia, 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 THE FACILITY

This facility was constructed in 1959 by the American Sterilizer Company (AMSCO). It was purchased by American McGaw (AM) in 1962. There was little change in the production process, or the personnel at the time of this purchase.

This plant currently produces intravenous(IV) saline, glucose and nutritional solutions. This plant also produced IV administration sets up until 1975 when this operation was moved to a facility in Puerto Rico.

The IV bottles are sterilized with steam. The IV sets were sterilized with a 12% ETO and 88% freon (12/88) mixture. ETO has been used by the company for this purpose, since it purchased the facility in 1962 up until 1975 when the production of IV sets was moved to Puerto Rico. ETO was probably also used during the time period (1959-1962) when AMSCO owned the facility.

A 2 pallet AMSCO sterilizing unit was purchased with the plant in 1962 and was used up until the early 1970's. A 5 pallet Vacudyne sterilizer was purchased and installed in 1970. Both sterilizers have been moved to other AM facilities.

Based on a review of its purchasing records, the company has estimated annual usage of 12/88 ETO gas mixture to have been 92,560 pounds in 1971, 103,520 pounds in 1972, 169,520 pounds in 1973, 146,640 pounds in 1974, and 76,000 pounds in 1975.

About 1974, a warehouse was built in Atlanta, which served as a distribution center. Following release of the product from quarantine, it was taken to this warehouse for further distribution. There is an on-site cafeteria where most of the employees eat.

DESCRIPTION OF THE WORKFORCE

According to the plants' management about 40% of the workers at this facility are male; although most of the sterilizer operators are men. The average age of workers at this plant has been about 36 for the last few years. Employee turnover at the plant has been approximately 9% per year. Most operations at this plant are run on 2 shifts.

DESCRIPTION OF THE PROCESS

The IV administration sets were sterilized with an ETO and freon gas mixture (12/88). The IV fluids were sterilized with steam. Once the various components of the IV administration sets had been received as raw materials and assembled, they were packed, wrapped, and palletized. Biological Indicators (BI) were placed in the pallets, and the pallets were loaded into the sterilizer. (From 1962 to 1972 a 2 pallet vessel was used. This unit was replaced in 1972 with a 5 pallet unit, which had separate loading and unloading ends.) At the end of the cycle time, ETO exposure time of 3.5 to 4.0 hours, the vessel was unloaded, and the BIs were removed. The IV sets were transferred to a designated area in quarantine, where room aeration of the product occurred. The product remained there for 7-12 days. At the end of the quarantine period, the product was transferred to shipping. The residency time in shipping was relatively short, before the product was released and loaded onto trucks. Receiving and shipping were in separate ends of the warehouse.

DESCRIPTION OF PAST EXPOSURES

This facility used ETO (12/88) from 1962 to 1975 to sterilize IV administration sets. In 1975, this product line, including the ETO sterilization process, was transferred to Puerto Rico. There have been some changes in this facility which would have affected potential employee exposure to ETO.

Sterilizer Vessels

The company began operations in 1962 with an AMSCO 2 pallet vessel (81 ft³). The vessel, which set in a pit, was loaded and unloaded from the same end with a forklift. A steam injector was used to introduce the ETO into the vessel. The ETO tanks, which stood next to the vessel, were changed by the operator. The cycle time for this vessel was about eight (8) hours, therefore three (3) loads could be run every 24 hours. The exhaust from this vessel went directly to the roof. After the product had been removed from the vessel, the BIs, which had been previously inserted into the pallets by the microbiology QC group, were removed. The product would sit outside the vessel, which was near the IV set assembly area, for about 24 hours, before it was transferred to quarantine. The vessel maintenance was done by AMSCO, the vessel manufacturer. Some point in time before 1970, this vessel was moved to an area called "The Shed". This area, which contained the steam sterilizer vessels, was located outside the building, but shared a common wall. In 1970, the two pallet vessel was replaced with a five pallet Vacudyne vessel. Maintenance on this vessel was done by plant maintenance personnel.

The 5 pallet vessel had separate loading and unloading doors. The operator did not have to enter the vessel to load or unload, as the vessel had rollers on which the pallets would slide. In 1972, the vessel was moved from "The Shed" to an enclosed room adjacent to the IV set assembly and packaging department. The room, which contained the vessel, did not have any dedicated ventilation system, however the vessel exhaust went directly to the roof. The ETO tanks were also located in this room, and it was the responsibility of the sterilizer operator to change the tanks. Product was sterilized on all three shifts, therefore, the cycle time was about eight (8) hours. The company estimates an average annual use (1971 to 1975) of ETO to be 120,000 pounds. Following removal of the product from the vessel, the operators would remove the BIs from the pallets. The microbiology QC group would retrieve the BIs. The product would sit outside the vessel only a short time before it was transferred to quarantine, which was located in the warehouse.

Quarantine

The quarantine area has always been located in the warehouse, however, the location of the actual quarantine area has changed as the warehouse area expanded. The quarantine area was always contiguous with the rest of the warehouse, as it was only separated by a chain link fence. Product would stay in this area for 7-12 days before it was sent to shipping. Shipping was located in the same end of the building complex as the quarantine area. Product could stay in shipping for a day or two before it was sent out. About 1974, the shipping function was transferred to a warehouse in Atlanta.

Product Aeration

This facility did not have a designated aeration area, therefore the product would aerate the entire time it was in the facility. The amount of ETO aerated from the product at any given time, however, is unknown.

Major Leaks or Accidents

The company does not report any major leaks or accidents involving ETO. There was only one individual who reported smelling ETO when the 5 pallet vessel was opened, following a sterilization cycle. This would indicate that the airborne ETO concentration at this particular time may have ranged from 300 to 1500 PPM. ³ The mean odor threshold, however, is 700 PPM.

DESCRIPTION OF THE MEDICAL, INDUSTRIAL HYGIENE, AND SAFETY PROGRAMS

Medical

The company established a medical program in 1962, when they began operations. On the first and second shifts a first-aid technician administered minor first aid, and kept a record of all in-plant accidents. In 1971, a full-time registered nurse (RN) was employed on the first shift. The RN was responsible for administering minor first-aid, and maintaining all health records required by the newly implemented OSHA Act. In the mid 1970s, physical exams were offered to all employees. About this time, a Licensed Practical Nurse (LPN) was employed on second shift. At the time of this walk-through survey, a physician assistant was employed on the first shift, and a LPN serves on the second shift.

Industrial Hygiene and Safety Programs

In 1975, an insurance carrier began an Industrial Hygiene program at this facility. The carrier sampled only for noise. The safety activities began in 1976. All current Industrial Hygiene activities are conducted by an insurance carrier. The carrier did not conduct any air monitoring for ETO, as the use of ETO was discontinued about the same time the insurance carrier was employed.

There is no plant-wide use of personal protective equipment. Hearing protection, safety glasses, and safety shoes are required in some areas however. There was reported use of "rubber masks", assumed to be full-face, canister type respirators, by the sterilizer operators on the first shift in the late 1960s, however, no details were available.

DESCRIPTION AND REVIEW OF THE PERSONNEL AND OTHER RECORD SYSTEMS

Personnel

Personnel records exist for all current and former AM employees at this facility. Personnel records are not available for workers who were employed by AMSCO and not hired by AM when the plant was purchased in 1962. There are 721 personnel files for active employees on file in the Personnel Department. Out of the 721 files, 75 are for exempt (exempted from overtime requirements) salaried employees, 68 are for nonexempt salaried employees, and the remaining 578 files are for hourly employees. Approximately 470 personnel records for workers who terminated employment after 1978 are also on file in the Personnel Department. About 30 of these records are for exempt salaried workers, and the remainder are for nonexempt salaried and hourly workers. Personnel records for workers who terminated employment prior to 1978 are on microfilm. There are approximately 3244 hourly and nonexempt salaried files, and 37 exempt salaried files on microfilm.

The personnel files contain personnel change notices (PCNs), and performance appraisals. Files for exempt salaried workers employed after 1977 include a computer generated 'Employee Profile'. Personnel data was computerized in 1977. Information for hourly and nonexempt employees has also been entered in the computer, and 'Employee Profiles' could be generated. The 'Employee Profiles' contain personal information including name, social security number, date of birth, sex and race. They also include a detailed employment history, which may include work history prior to 1977 when the computer system was developed. Files for hourly and nonexempt salaried workers may include what the company calls a 'VISA' card. The 'VISA' card contains the name, social security number, date of birth and a detailed employment history. Work histories may also be constructed from the PCNs, which are placed in the personnel file each time a worker changes jobs, departments, or pay status.

Payroll

Payroll registers are available from 1969 for exempt salaried workers, and from 1970 for hourly and nonexempt salaried workers. These registers are organized by department number, and contain names and social security numbers. Quarterly earnings tax reports, which are prepared for the Internal Revenue Service are available from 1963 on. These reports do not indicate what jobs or departments an individual worked in.

Record Review

The company has prepared a list of 240 names of people they believe have been potentially exposed to ETO. This list was primarily generated by interviewing people who have worked in areas of the plant that are potentially exposed to ETO. A copy of this list was provided to the NIOSH investigators. Two names were selected from each job category on the list,

and the personnel records for these individuals were reviewed. The purpose of this review was to determine whether these workers could have been identified as having been potentially exposed to ETO based upon the personnel records.

A total of 16 personnel files were included in this review. Only 7 of the 16 files reviewed could be identified as having been potentially exposed to ETO based on the information in the personnel file. Basically the problem was that the job and department titles used were not specific enough to separate exposed from nonexposed workers. Based on this review, personnel records at this plant were judged to be inadequate for the purposes of the ETO 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. ⁴

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. ^{18,20} 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.

CONCLUSIONS AND RECOMMENDATIONS

Eligibility requirements, as defined by the study's protocol, for inclusion of a facility in the NIOSH ETO mortality study are 1) the plant must contribute at least 200 person-years to the high exposure group, or 400 person-years total, 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. This facility failed to meet criteria number 2, since it was not possible in most cases to reliably determine whether or not a worker was exposed to ETO based on the job descriptions in the personnel file and therefore this facility will not be included in this study.

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