INDUSTRYWIDE STUDIES REPORT:
A WALK-THROUGH SURVEY

OF

CASTLE
Division of Sybron Corporation
P.O. Box 23077
Rochester, New York 14692

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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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STANDARD INDUSTRIAL CLASSIFICATION OF PLANT:	3842 - Orthopedic, Prosthetic, and Surgical Appliances and Supplies

ABSTRACT

On May 31-June 1, 1984, a walk-through survey was conducted at Castle, a division of Sybron Corporation in Rochester, New York, to evaluate industrial hygiene and personnel records, production processes, and document historic use of ethylene oxide (ETO). This survey was conducted as part of an industrywide study of mortality associated with an occupational exposure to ETO. Castle was founded in 1883, and introduced ETO into the plant for use in research and development in 1955. Production of ETO gas sterilizers began in 1958. ETO was used as a final check for leaks; gross leaks were found by compressed air or freon. The use of ETO in the factory to check for leaks was discontinued in 1979. Contract sterilization of bulk goods was conducted between 1963 and 1980. ETO is still used in research and development at this facility, in a very limited capacity.

There is very limited industrial hygiene data on ETO exposures in the facility. The validity of this data is in question, however, and therefore it was not included in this report. The lack of exposure data will make development of an exposure matrix at this facility very difficult. This plant meets the three eligibility requirements as defined in the protocol and therefore, should be included in the study. These requirements 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. ETO has not been used in the production of sterilizers at this plant since 1979, therefore there are no future industrial hygiene surveys planned at this time as part of this study.

Castle has several regional service offices, staffed by service representatives, located throughout the country. These persons will also be included in the 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. The biological warning properties are essentially useless since the (ether-like) odor threshold among individuals ranges from 300 to 1,500 parts per million (ppm) and adverse health effects may be elicited at levels much less than this.[1,2]

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.[3] 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.[4,5] 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.[4,5] Inorder 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 not part of the pilot study.

This walk-through survey was conducted to determine the suitability of including Castle, division of Sybron Corporation 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

Castle, a division of Sybron Corporation, was established in 1883. A gas mixtue of ETO and freon (12/88) was first used in 1955, in research and development. The first ETO gas sterilizers were manufactured in 1958. These sterilizers were designated as straight line (3.9 or 8.8 ft^3) or power claves (18, 24 or 30 ft^3). In the mid 1960s, floor loader (40 or 70 ft^3) and bulk (1000 ft^3) sterilizers were added to the product line. In 1972, Castle introduced two table top models (1 sterilizer, 1 aerator). These were discontinued in 1984. In 1978, post vaccum purge separators were introduced to the product line. These separators, which were added to in-use sterilizers, facilitated the capture of ETO gas into the sterilizer water drain following exhaust of the chamber. Prior to the addition of these kits, ETO was exhausted into the room where the sterilizer was being used. Castle has altered its current product line by making only one straight line (8.8 ft^3), all three power claves, and two floor loader models. The majority (99.9%) of these sterilizers are used in hospitals.

The production building, which was completed in 1955, had very few interior walls; this remains true at the time of this survey. The original building had large glass windows on all four sides which have been sealed or removed over the years. There is an on-site cafeteria where some of the employees eat. Others eat at the workstation or off-premises.

The use of ETO to test sterilizers was discontinued in 1979. Company personnel estimated 50,000-100,00 pounds of the 12/88 mixture were used per year. This is about 6000-12,000 pounds of ETO per year.

DESCRIPTION OF WORKFORCE

The current workforce numbers 870; 274 are hourly, 210 are salaried personnel who are in the field. There is little turnover in this plant. The average length of seniority is 14 years. Both females and minorities represent about 5-10% of total personnel currently. This plant has been unionized since 1966 by the International Association of Machinists (IAM). There is also a small union of polishers and buffers which includes only a few people.

DESCRIPTION OF PROCESS

Castle currently produces three different sizes of sterilizers. The majority (99.9%) of the sterilizers are used by hospitals. The smallest is a straight line sterilizer which is about 8.8 ft^3. Power claves are the next size produced (18, 24 or 30 ft^3). The largest sterilizers produced are floor loader models (40 or 70 ft^3). Approximately 75% of the sterilizer parts are purchased, with the remainder of the parts fabricated

on-site. At the time of this survey, Castle was in the process of installing an automatic painting system.

Once the various metal components of a sterilizer have been received from various suppliers or fabricated in-house, they are sent to an assembly area which is located directly east of the test area or block. In the assembly area, the metal parts are assembled and the electronic components are added. The assembled sterilizer is then transported to the test area, where it will be checked by the tester, with freon or compressed air for leaks and proper gauge and electronic component function. Freon or compressed air has always been used for this check. Occasionally, an assembler will aid the tester. The assembled, tested sterilizer is run through a final check cycle using freon or compressed air. Prior to 1980, ETO (12/88) was used for this final check. The fully assembled and tested sterilizer is sent to packaging and shipping.

Contract sterilization, of various materials such as pacemakers, was also conducted at this plant between 1963 to 1979. This operation which used a 25 ft^3 unit was conducted 24 hour/day, 7 day/week in the research and development building. The product was room aerated. Very few individuals, all salaried, were exposed in this operation.

ETO is still used today at this facility, however, its use is limited to some research and development work, and a quality control check on biological test strips. These biological indicators are used as an indicator of ETO permeation through a sterilized load of material.

DESCRIPTION OF PAST EXPOSURES

There have been few modifications in the plant over the last several years that would have affected employee exposure to ETO, because the use of ETO in the production area has always been limited. The company estimates that about 6000-12,000 pounds of ETO were used per year. The only use of ETO in the production of the sterilizers was in the final check cycle, which consisted of one set-up and charging cycle. At the end of the cycle, one vacuum was drawn on the chamber, and the gas was dissolved in water circulating through the exhaust site. This water was sent directly into the drain in the test block which was not equipped with any ventilation. The company did not install any dedicated exhaust ventilation in the test block area to control ETO, however, there was good general ventilation in the facility. The use of ETO to test sterilizers was discontinued in 1979.

The company does have some extremely limited industrial hygiene data that was collected by the insurance carrier in late 1980, just prior to discontinuation of the use of ETO in the plant. The data is not included in this report, however, because there were several important test parameters which were not reported such as pump calibration (e.g. flow rate) and starting time and ending time of sample collection. In addition, depending upon humidity, a total sample of 6 to 8 liters of air should be collected with each tube. The total liters of air collected for each of the 3 samples were 0.3, 11.3, and 29.9 liters respectively. It is for these reasons that the validity of the data is suspect, therefore it is not reported.

DESCRIPTION OF MEDICAL, INDUSTRIAL HYGIENE AND SAFETY PROGRAMS

Medical

Castle has a medical department which is composed of a full-time nurse on first shift and part of the second shift. A physician is available as needed. The medical department is equipped to handle minor emergencies. All employees are given pre-employment physicals. The workers exposed to ETO were not given any routine follow-up examinations.

Industrial Hygiene and Safety

The company has had a general industrial hygiene program since 1969, which has been conducted since its inception by the insurance carrier. Extremely limited personal sampling for ETO was conducted by the insurance carrier in 1980. The validity of the data however is in question, and therefore, is not reported (see Past Exposure section). The company requires safety glasses and shoes. In specific areas, such as welding, respirators are required. Respirators have never been used in any areas where workers may have been exposed to ETO.

DEFINITION OF EXPOSED GROUP AND DESCRIPTION OF RECORDS

There are few walls in the production area, and gas is likely to have moved freely throughout the plant. However, given that the volume of gas used was relatively low (for example, compared to medical supply companies) it is believed that the exposed group should include primarily those who worked in the same direct area where the gas was used. Therefore the exposed will be defined as those who worked as assemblers and testers in departments 75 (bulk assembly) and 82 (testing). Individuals who worked in department 80, which no longer exists but which included quality assurance technicians who tested sterilizers with ETO, should also be included in the exposed group. Prior to January 1, 1964, all testers, hourly and salaried, were in department 80. After 1964, hourly testers were grouped in department 82, but salaried personnel (quality assurance) continued in department 80 for a number of years, until that department was abolished. Lamp and table top assemblers (department 50) will be excluded.

Model makers in department 006 (also 706) will also be included, because they tested new prototypes of sterilizers. There are very few individuals in this job category (perhaps 5). The repair department between 1974-1980 repaired table top sterilizers and individuals who worked in this department (department 17) should be included in the exposed group. There are only about 5 such people. Contract sterilization has involved only a handful of people over the years, and these have been salaried personnel who are not easily identified via records. Based on an interview with a field representative who explained that these men may have been exposed to high peaks, field representatives should also be included in the exposed group. These individuals are salaried, but are easily identified via records.

There are 8 types of files in personnel records. These file systems are described below, along with the number of records sampled from each, the

percentage of the total records in that file system, the number exposed in the sample, and the percentage of individuals in the sample who were exposed.

Type of File System		# Sampled (%)	# Exposed (%)
1)	Active hourly (salaried separate) (n=270)	35 (13%)	3 (9%)
2)	Terminated before 1975-76, with work history card only in files (n=1700)	107 (6%)	12 (11%)
3)	Retired (n=150)	27 (18%)	4 (15%)
4)	Vested but not yet retired (n=80)	20 (25%)	7 (35%)
5)	Terminated 1975-79 on microfiche (n=420)	40 (10%)	11 (28%)
6)	Terminated after 1979 and not on fiche (n=200)	21 (10%)	2 (9%)
7)	Decreased on microfiche (n=70)	not sampled	
8)	Active salaried (n=519; 210 are field reps)	21 (4%)	7 (33%)
Total	n=3339 (excl. #7)	271 (8%)	46 (17%)

The number for the total records in each file system are estimates. File systems 2-7 include salaried individuals mixed with the hourly. File system 2 includes individuals who worked at the plant prior to 1958, but in our estimate of the total number of these records we attempted to exclude such individuals. The company made a separate listing of 177 assemblers and testers from file system 2, but some of the assemblers included in their list did not assemble sterilizers. In addition to these sources, payroll records by department exist back to 1964. These could be very useful in identifying the exposed. The company has also compiled a list of all field representatives who terminated prior to 1979, and these number 166. All together it is estimated that approximately 415 field service representatives, including terminated and active employees, have worked at Castle.

The company apparently has copies of all microfiche data on microfilm, which will help the later copying of records. The company is now putting more records (eg, retirees) on fiche, but will retain hard copy until after their records have been copied.

The results above indicate that overall approximately 17% of all employees who have ever worked at Castle have had potential exposure, or approximately 570 people.

The average year of birth and year of hire for the exposed was 1937 and 1968 respectively. Sixty-five of the exposed, about 11%, were first hired in 1978 or later. It is estimated that those first exposed prior to 1978 will contribute about 7200 person years to the study.

TOXICITY

Evidence from animal studies suggests that ETO may have carcinogenic properties.[6,7] A group of ETO manufacturers sponsored a study at the Bushy Run Research Center in which male and female Fischer 344 rats were exposed to ETO at airborne concentrations of 10, 33, or 100 parts per million (ppm) for 6 hours per day, 5 days per week for two years.[6] Two other groups of animals served as controls. Initially, there were 120 animals of each sex, in each exposure group. The researchers observed a

statistically significant increase in the incidence of mononuclear cell leukemia among the female rats, and peritoneal mesothelioma among the male rats exposed to ETO. The increase in leukemia incidence was found to increase linearly as a function of ETO exposure. An elevation in mortality from brain cancers (glial type) was also observed in the rats exposed to ETO.

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

Only a few epidemiologic studies have examined the potential human carcinogenicity of ETO.[8-10] Hogstedt, et al, conducted a retrospective cohort mortality study of a group of workers in a Swedish chemical factory that had previously been included in a hematologic investigation.[8] This facility produced ETO via the chlorohydrin process in which, in addition to ETO, there was potential exposure to ethylene, ethylene chlorohydrin, ethylene dichloride, and small amounts of bis(2-chloro-ethyl) ether. Among 89 "full-time" exposed workers, a statistically significant (p less than .01) excess of leukemia mortality was observed (2 observed versus 0.14 expected). In addition, a statistically significant (p less than .01) excess of stomach cancer was observed (3 observed versus 0.4 expected). Because of the mixed exposures, these findings could not be attributed to ETO; however, ethylene oxide and ethylene dichloride were the prime suspects.

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

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

ETO is also a potent alkylating agent capable of causing irreversible changes or mutations in cellular proteins and DNA in animals.[11,12] ETO is also a positive mutagen in several *in vitro* systems such as *Salmonella typhimurium*, viruses, and *Tradescantia poludosa*.[5]

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

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

Cytogenetic abnormalities have also been observed in several studies of workers exposed to ETO. Ehrenberg, in a study of workers at a factory manufacturing and using ETO, observed a high frequency of chromosomal aberrations in 8 workers who were accidentally exposed to high concentrations of ETO. One case of leukemia was also observed among the 37 workers studied.[15]

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

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

APPLICABLE STANDARDS AND RECOMMENDED LEVELS

Prior to June 22, 1984, the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for ETO was 50 ppm as a TWA concentration for an 8-hour workshift.[20] OSHA established a new PEL of 1 ppm as an 8-hour TWA on August 21, 1984.[21] In addition, an "action level" of 0.5 ppm as an 8-hour TWA was established (by OSHA) as the level above which employers must initiate periodic employee exposure monitoring and

medical surveillance. The Environmental Protection Agency (EPA) supported the OSHA PEL of 1 ppm in the Federal Register (June 22, 1984).[22]

In 1977, NIOSH recommended a ceiling level of 75 ppm as determined during a 15 minute sampling period.[5] This level, however, was set prior to the recognition of the carcinogenic potential of ETO. Based on recent findings, NIOSH recommends that ETO exposures not exceed 5 ppm for a maximum of 10 minutes per day and that exposures be controlled to less than 0.1 ppm determined as an 8-hour TWA (NIOSH Policy Statement, July 20, 1983). The American Conference of Governmental Industrial Hygienists (ACGIH) recommends a Threshold Limit Value (TLV) of 10 ppm for an 8-hour TWA based on data available prior to 1982.[23] However, in 1982, the ACGIH issued a notice of intended change in which it was proposed that the TWA concentration be lowered to 1 ppm. This recommendation was reviewed and adopted in 1984. ACGIH has also designated ETO as an A2 carcinogen.[23] 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

Personnel records were adequate to determine who was exposed based on job categories. Very limited industrial hygiene data does exist, however, the validity of the data is in question. Therefore, while it may be possible to construct a simple exposure matrix (i.e. high exposure category-direct exposure, low exposure category-indirect exposure) for this facility, it will be difficult.

Based on the findings of this report, this plant meets the three eligibility requirements as defined in the protocol and therefore, should be included in the study. These requirements are 1) the plant must contribute at least 200 person-years to the higher exposure groups, 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. ETO has not been used in the production of sterilized at this plant since 1979, therefore there are no future industrial hygiene surveys planned at this time as part of this study. Castle has several regional service offices staffed by service representatives located throughout the count.

It has been determined that the extent of exposure of these service representatives to ETO warrants their inclusion in the study.

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