

**PART C - PUBLIC COMMENTS AND RESPONSES
TO THE DRAFT PART A AND PART B
ETHYLENE OXIDE REPORT**

**Prepared by the Staffs of the Air Resources Board
and the Department of Health Services**

April 1987

PART C - PUBLIC COMMENTS AND RESPONSES TO
THE DRAFT PART A AND PART B
ETHYLENE OXIDE REPORT

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I. Comments Received by
January 14, 1987

A. Sterile Design, Inc.



Sterile Design, Inc.

CORPORATE OFFICES
P.O. BOX 10077
15 S. LINCOLN
CLEARWATER, FL 33517-8077
(813) 442-3131

February 2, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

ATTN: Ethylene Oxide

Dear Mr. Loscutoff:

Subject: Ethylene Oxide Draft

Thank you for keeping us informed of the California emissions status of ethylene oxide. As Sterile Design no longer operates an EtO sterilizer in California, we will not be making any comments at this time. For your information, we discontinued all manufacturing operations at our Sacramento facility in December, 1985.

Sincerely,

John C. Hoffman
Director
Quality Assurance and
Regulatory Affairs

kh

B. Sterilization Services of California.



**Sterilization Services
of
California • Georgia • Tennessee**

January 9, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attention: Ethylene Oxide
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

We have reviewed the "Preliminary Draft Report on Ethylene Oxide" and we question the emission level reported for our company in Table III-1. We are permitted by the South Coast Air Quality Management District for a maximum daily emission of 40 lbs. of ethylene oxide. If we operated at the maximum emission level for 365 days per year, the emissions would total 7.3 tons as opposed to the 18 tons listed in the preliminary draft.

We do not have a copy of the reference study which listed our facility emissions at 18 tons per year so we are not able to evaluate the factors that may have been considered in developing the emission data. We will obtain copies of this study and analyze the data, but we add that Sterilization Services of California presently monitors chamber emissions and is in compliance with the permit restrictions.

We hope that this information is useful in completing an accurate assessment of EtO emissions and we are eager to work with you and the various state agencies to develop a safe and effective policy.

Respectfully,

Patterson Adams
General Manager

PA/jg

cc: Russell Skocypec

CALIFORNIA
1611 South Sunkist
Anaheim, CA 92806
(714) 937-5349

GEORGIA
6005 Boatrock Blvd.
Atlanta, GA 30336
(404) 344-8423

TENNESSEE
2396 Florida St.
Memphis, TN 38109
(901) 947-2217

C. Botanicals International



botanicals international

Division of Zuellig Botanicals, Inc.
2550 El Presidio/Long Beach, California 90810



January 9, 1987

Mr. William V. Loscutoff, Chief
TOXIC POLLUTANTS BRANCH
AIR RESOURCES BOARD
Attn: Ethylene Oxide
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Luscutoff,

Having recently received a copy of the "Preliminary Draft Report on Ethylene Oxide", I read through it completely and noticed one piece of data that is no longer accurate. On page III -6, table III -1, under "Fumigation (Food/Spice)" you list Botanicals International's EtO Emissions as 25 tons per year.

Beginning June 2, 1986, Botanicals International modified its EtO sterilization procedures to reduce the amount of Ethylene Oxide used per chamber load of product to be sterilized. We had three objectives when we initiated our change in procedures. Firstly, we wanted to reduce the potential for worker exposure to EtO during the product off-gassing period immediately after sterilization. Secondly, we wanted to reduce emissions to the atmosphere during the evacuation cycle of our chamber. Thirdly, we wanted to reduce the potential for EtO residuals in our finished products.

From June 2, 1986 through November 28, 1986, Botanicals International used exactly 10,000 pounds of Ethylene Oxide (25 drums @ 400 lbs ea). This is a 26 week period and our sterilization requirements are constant throughout the year, therefore, by doubling the quantity of EtO used during this time period you would have a very accurate estimate of our annual EtO usage (20,000 lbs. or 10 tons).

This represents a 60% reduction over the 1983 SCAQMD report and will have a significant impact on the Ethylene Oxide concentrations in the Exposure Area from all sources in the Inventory Area (Figure C-2).

In the interest of further reducing the potential for employee exposure and atmospheric emission of Ethylene Oxide, Botanicals International is negotiating the purchase of an Ethylene Oxide Emission Control System which has a Best Available Control Technology (BACT) Certification. This system will practically eliminate emissions to the atmosphere (99.9%).

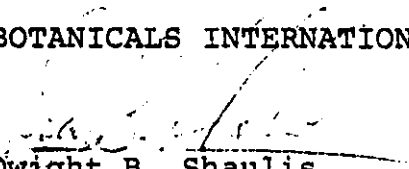
b

Air Resources Board (2)

I hope this information has been helpful and will be incorporated into the "revised" preliminary draft report. Should you have any questions or comments, please contact me. Thank you.

Sincerely,

BOTANICALS INTERNATIONAL


Dwight B. Shaulis
Production Manager

DBS:jh

D. Griffith Micro-Science, Inc.

GRIFFITH MICRO SCIENCE, INC.

7775 QUINCY STREET, WILLOWBROOK, IL 60521 • 312/325-6999

JOHN A. KJELLSTRAND

Vice President — Technical

January 13, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
1102 Q Street
P. O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

In response to your invitation to comment on the preliminary draft report on Ethylene Oxide, prepared by Mr. Ralph Propper, Principle Investigator, and published by the California Air Resources Board, on December 4, 1986, I have been authorized by Griffith Micro Science, Inc., formerly known as Micro-Biotrol, Inc., a subsidiary of Griffith Laboratories, Inc., to offer the following comments for your consideration.

Our company, and others we are aware of that are engaged in the sterilization of medical devices, both contract sterilizers and manufacturers of medical devices using Ethylene Oxide, have, or are in the process of installing emission control systems for Ethylene Oxide.

While we are aware that, currently, there are no specific regulations governing Ethylene Oxide emissions, Griffith Micro Science, Inc. has purchased an emission control system, and just recently received a verbal, temporary permit to construct and operate this unit, after a concerted effort on our part, working with the South Coast Air Quality Management District.

On several occasions, I had discussed our company's intent to install this system with Mr. Propper's staff, during conversations when they called regarding our company's activities in the State of California. We have cooperated with the Air Resources Board and the South Coast Air Quality Management District to the fullest extent in these efforts and appreciate the opportunity to comment on your preliminary draft.

Sincerely,


John A. Kjellstrand

JAK/mp

cc: Donald E. Alguire, Griffith Micro Science, Inc.
James S. Legg, Griffith Micro Science, Inc.

E. Liquid Carbonic Corp.



AREA CODE 415 592-7303

LIQUID CARBONIC

SPECIALTY GAS CORPORATION

767 INDUSTRIAL ROAD • SAN CARLOS, CALIFORNIA 94070

January 13, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attention: Ethylene Oxide
P.O. Box 2815
Sacramento, California 95812

Subject: Ethylene Oxide - Preliminary Draft Report

Dear Mr. Loscutoff,

This letter is in response to your request for comments and responses on the subject report. As a participant included in the report, we believe this report to be in error as follows:

Page III-4 Distribution Facilities

"Fugitive losses of less than 1/2 to 2% of total production occur from storage, handling, drumming and blending of ethylene oxide....."

Response: Our experience with ethylene oxide is estimated at less than 0.1% fugitive losses. Our experience with this material is based on working with closed piping systems and all transfer of material is followed by an inert gas (Nitrogen, Dichlorodifluoromethane). All residual raw material ethylene oxide is returned to the manufacturer and is not disposed of.

"Based upon discussions with distributors, ARB staff estimates that approximately 18% of the sterilant gas mixture is exhausted from cylinders at repackaging plants.

Response: Our experience indicates 18% to be high. We believe the figure to be more in the area of 10% or less. This is based on fifteen (15) years experience of handling returned sterilant cylinders.

Page D-2 Non-Pesticidal Sources

"Based upon information provided by the companies (see Section on emission sources in the main report for discussion), the following data was used as input to the ISCST model:

- 1) Liquid Carbonic Corp. - 3.39 pounds per hour emitted between 6:30 A.M. and 3:00 P.M. daily, from a three foot elevation."

January 13, 1987

Response: We sent a letter dated June 18, 1986 to Carol McLaughlin, clearly stating that our Los Angeles scrubbing equipment was used a maximum of four (4) hours per day. (see attached)

Page F-3

"The two Liquid Carbonic plants bubble the residual ethylene oxide gas through water at neutral or near neutral pH."

Response: In the same letter dated June 18, 1986 we stated that our Los Angeles plant used a 5% Sulfuric Acid/Water (wt/wt) solution as the scrubbing media. This solution would be clearly acidic and not "near neutral pH". This would result in a 90% or better conversion of the ethylene oxide to ethylene glycol. We would also like to point out that we currently have in place a 400 gallon commercial acid scrubber in Los Angeles with the same in process of being installed at our San Carlos plant within the next thirty (30) days. Both of these scrubbers will be capable of handling a 99% or better conversion. They are countercurrent packed tower scrubbers. The stack height is 30 feet.

Based on the foregoing comments, the results tabulated in your report will change as it relates to our Los Angeles facility.

Should you require additional clarification on this information please feel free to contact me at (415) 595-0334.

Sincerely,



J. A. Paine
Regional Manager
LIQUID CARBONIC
SPECIALTY GAS CORPORATION

JAP/dp



AREA CODE 415 662-7303

LIQUID CARBONIC

SPECIALTY GAS CORPORATION

787 INDUSTRIAL ROAD • SAN CARLOS, CALIFORNIA 94070

June 18, 1986

Carol McLaughlin
Stationary Source Division
Air Resources Board
P.O. Box 2815
Sacramento, Calif 95812

Re: Survey of Ethylene Oxide Use

In response to your request, the following information is submitted as requested:

1. Quantity of ETO sterilant gas mixture produced for sale during 1985.

San Carlos.....207,850 lbs.

Los Angeles.....619,040 lbs.

2. Quantity of pure ETO packaged for sale during 1985.

San Carlos.....1,600 lbs.

Los Angeles.....13,640 lbs.

Majority of this material is resold as purchased and therefore not repackaged.

3. Quantity of ETO purchased for processing.

San Carlos.....26,400 lbs.

Los Angeles.....86,400 lbs.

4. Detailed description of specific emissions control equipment in operation at our facilities.

San Carlos

Emissions control equipment is a 40-Gallon Water Type Scrubber (Custom Made).

a) Rate of Input.....10 CFM

b) Hours of Operation.....1½ per day

c) 100% Efficiency

Los Angeles

Emissions control equipment is a 55-Gallon Custom Made Scrubber filled with a 5% Sulfuric Acid/Water (wt/wt) solution.

- a) Rate of Input.....1 CFM
- b) Hours of Operation.....4 per day *max.*
- c) 100% Efficiency

We trust the foregoing information completes your request. Should you require further assistance please submit correspondence to the undersigned.

Sincerely,



J. A. Paine
Western Zone Manager

JAP:dp

F. Union Carbide Corp.
(Linde Division)



Union Carbide Corporation
Linde Division
19200 Hawthorne Boulevard
Torrance, California 90503

January 13, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff,

In response to your request for comments regarding the "Draft Report to the Air Resources Board on Ethylene Oxide", I wish to submit the following clarifications.

I am referenced on page F-3 of the "Emissions of Ethylene Oxide from Distribution Facilities" section, as saying that "18% of Ethylene Oxide(ETO) sold, was returned in used cylinders." While this number is accurate for ETO sold in cylinders as Oxyfume 12 (12% ETO, 88% Halocarbon-12) it is not true of all ETO sold.

Our facility sells ETO in several different mixtures which were not considered in the recovered product calculations. In addition, we sell Oxyfume 12 in bulk trailer quantities. These trailers are not processed through our recovery unit since they are either unloaded completely at the customer site or topped off when they return to our facility. We also sell pure ETO, of which, only a small amount (less than 2%) is returned. Further, the 18% return number was inflated by the fact that often times full, unused cylinders are returned for credit when they pass their expiration date.

Generally, product returned from hospital users tend to have a higher residual content than industrial users. Product returned from industrial users tends to be less than 5 or 6% of the product sold.

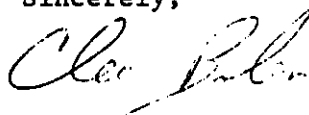
Combining all forms of product sold, recovered product represents a very small fraction of the total ETO sold. I estimate that this percentage would be less than 2%.

On page F-3 of this same section a reference is made to our scrubber unit with an efficiency rate of 90%. The new scrubber unit was completed in the summer of 1986 and has a design efficiency of 99.999%+. The old scrubber is therefore no longer in use. There was no mention, however, of the recovery/recycling system (the same as the South San Francisco system) used at our facility.

With both the recovery unit and scrubber in operation our emissions are limited to fugitive emissions. For normal operation, I estimate that emissions from our facility are less than 100#/yr. This is supported by the use of a "Baseline" monitoring system which continuously samples 16 points in our facility for ETO concentration. With this system we are able to identify and correct problems before significant ETO exposure or releases can occur.

I hope these clarifications have cleared up any misunderstandings which may have occurred concerning ETO at the Torrance facility. If you have any further questions please feel free to contact me.

Sincerely,

A handwritten signature in cursive script, appearing to read "Cleo Bolen".

Cleo Bolen

CB/ph

G. Health Industry Manufacturers Association

January 13, 1987

Mr. William V. Loscutoff
Chief, Toxics Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
P.O. Box 2815
Sacramento, California 95812

Re: "Draft Report to the Air Resources Board on Ethylene Oxide,"
November 1986.

Dear Mr. Loscutoff:

The Health Industry Manufacturers Association is a trade group representing approximately 300 medical device and diagnostic product manufacturers. A number of HIMA member companies use Ethylene Oxide (EtO) to perform industrial sterilization of medical products. Our membership includes several manufacturers cited in the "Draft Report to the California Air Resources Board on Ethylene Oxide" (referred to herein as the "CARB Report"). We, therefore, are pleased to submit our Association's comments on the CARB Report.

1. EPA Activities

The CARB Report refers extensively to the Environmental Protection Agency's notice of intent to list EtO under Section 112 of the Clean Air Act, "Assessment of Ethylene Oxide as a Potentially Toxic Air Pollutant," (50 Federal Register 40286, October 2, 1985). HIMA submitted comprehensive comments (dated December 3, 1985) to EPA on the proposal. These comments are attached.

We urge CARB to review HIMA's 1985 position paper since it corrects several assumptions made by EPA in its proposal. Specifically, our comments emphasize that:

- Sources of EtO emissions have decreased in number as some manufacturers have ceased to use EtO, consolidated operations, increased the use of EtO contract sterilizers, used alternative methods of sterilization, and installed EtO emission devices.
- EtO emission control devices currently in use in the medical product manufacturing industry include chemical conversion units, scrubbers, incinerators, and reclamation units.
- A manufacturer of a highly effective chemical conversion control device had estimated (in late 1985) that by the end of 1986, 35-40% of sterilization facilities will have installed or committed to install a system for emissions control.

We have met several times with EPA representatives to provide additional information. In February 1986, HIMA submitted to EPA the results of a comprehensive survey of member companies regarding EtO use. EPA subsequently sent Section 114 information requests to medical product manufacturers not included in the HIMA survey. As a result, EPA now has an extensive database on EtO emissions sources and control practices, including California facilities cited in the CARB report. Since the CARB report acknowledges that data for some facilities date back to 1982, we recommend CARB review EPA's database, since it reflects 1985-1986 EtO use and control.

In summary, we believe CARB will benefit from a thorough review of the most recent data available from EPA on EtO use and emissions control, specifically at the California facilities. Additionally, since EPA is continuing to analyze our industry's information to determine risk from airborne EtO emissions, the Agency may significantly revise estimates/conclusions drawn in its October 1985 notice.

Revisions to the CARB Report should reflect EPA's database and EPA's most current conclusions on EtO use and emissions control. This would enhance the accuracy of the CARB report consistent with the goals of public health and safety. Mr. David Markwordt, an Environmental Engineer in EPA's Office of Air Quality Planning and Standards, has been coordinating EPA's analysis of our industry's data. He can be contacted at (919) 541-5671.

2. California Activities

The South Coast Air Quality Management District, and, most recently, the Bay Area Air Quality Management District, have a permit process for facilities using EtO. We have been informed by our members that the SCAQMD has, in the permit process, requested extensive data on EtO emissions. As a result of the permit process, these members have installed or are in the process of installing emissions control equipment.

The fact that this activity has occurred over the past two to three years, again shows the importance of a review by CARB of the most current data on emission sources.

3. Conclusion

A reduction of emissions sources and the increased installation of emission control devices has occurred since 1984. We recommend that CARB coordinate with EPA in the analysis of data for California facilities to ensure that the report reflects current company practice.

We appreciate the opportunity to comment on the draft CARB report. If you have any questions about these comments, please contact me.

Sincerely,



James F. Jorkasky
Director, Environmental, Occupational
and Small Business Programs

Attachment: EtO-87-1.1 HIMA 1985 Comments to EPA

health industry
manufacturers
association

hima

EtO-87-1.1

December 3, 1985

Central Docket Section [A-130]
Environmental Protection Agency
Docket No. A-85-10
401 M Street, S.W.
Washington, D.C. 20460

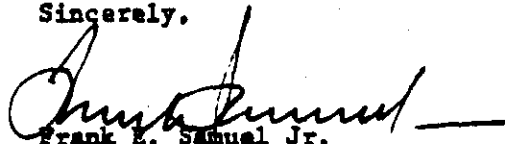
Re: Docket No. A-85-10, *Assessment of*
Ethylene Oxide As a Potentially Toxic
Air Pollutant (50 Fed. Reg. 40286,
October 2, 1985)

Dear Sir/Madam:

The Health Industry Manufacturers Association (HIMA), a trade Association representing 300 medical device and diagnostic product manufacturers, is pleased to submit the attached preliminary comments to EPA in connection with the Notice of Intent to List Ethylene Oxide (EtO). As discussed in the submission, HIMA is currently conducting a major survey of our industry to determine the extent of EtO emissions as well as the degree to which airborne EtO is already controlled.

HIMA anticipates providing more extensive comments to EPA in late January, 1986.

Sincerely,


Frank E. Samuel Jr.
President

FES:ldr

cc: Ms. Nancy Pate, EPA
Mr. Robert Schell, EPA
Mr. David Markwordt, EPA

JFJ/ldr

BEFORE THE
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Assessment of Ethylene Oxide)
as a Potentially Toxic Air)
Pollutant: 50 Fed. Reg. 40286)
(Oct. 2, 1985))

Docket No.
A-85-10

PRELIMINARY COMMENTS OF THE
HEALTH INDUSTRY MANUFACTURERS ASSOCIATION
ON THE NOTICE OF INTENT TO LIST
ETHYLENE OXIDE UNDER SECTION 112
OF THE CLEAN AIR ACT

Health Industry Manufacturers Association
1030 15th Street, N.W., Suite 1100
Washington, D.C. 20005
Frank E. Samuel Jr., President

December 3, 1985

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I. Executive Summary

HIMA submits these preliminary comments to the Environmental Protection Agency (EPA) in response to the Agency's Notice of Intent To List Ethylene Oxide (EtO) Under Section 112 of the Clean Air Act and Solicitation of Information published October 2, 1985 (50 FR 40286).

HIMA's preliminary comments focus on the "Medical Supplies Manufacture" category described in EPA's notice. HIMA's comments are preliminary in that the Association is currently conducting a comprehensive survey of industry to determine EtO emissions and the extent of emissions control equipment already in place. HIMA anticipates providing further comments to EPA in late January, 1986.

HIMA makes the following points in these preliminary comments:

1. EtO is an essential sterilant for the medical device industry. It is used to sterilize 60-70% of industrially sterilized medical devices and is the only method for sterilizing certain materials that are sensitive to heat, moisture, or radiation. Less than 0.5% of EtO produced is used in all sterilization operations, including device manufacture, hospitals, clinics, and contract sterilization, as well as food processing and fumigation.
2. Sources of EtO emissions have decreased in number as some manufacturers have ceased to use EtO, consolidated operations, increased the use of EtO contract sterilizers, used alternative methods of sterilization, and installed EtO emission control devices.
3. EtO emission control devices are currently in use in the "Medical Supplies Manufacture" category. These devices include chemical conversion units, scrubbers, incinerators, and reclamation units.
4. Considerations to be made in the cost analyses of EtO emissions control devices include the size of sterilizer(s) to be controlled, the frequency of use of the sterilizer, the gas used (100% EtO or a mixture with FREONTM or Carbon Dioxide), the rated capacity of the control unit, and the engineering, installation, and annual operating costs.

II. Introduction

The Health Industry Manufacturers Association is pleased to submit the following preliminary comments to the Environmental Protection Agency (EPA) in response to the Agency's Notice of Intent To List Ethylene Oxide Under Section 112 of the Clean Air Act and Solicitation of Information, published October 2, 1985 (50 FR 40286).

HIMA is a trade association representing almost 300 domestic manufacturers of medical devices and diagnostic products. Approximately 100 HIMA members use or depend upon EtO for the sterilization of medical products. As documented herein, EtO is an essential sterilant for our industry and its continued use is crucial to the health care system.

HIMA's preliminary comments focus on the "Medical Supplies Manufacture" category described in EPA's notice of intent to list EtO.

The comments are preliminary in that HIMA is currently conducting a survey of the industry to determine the extent of EtO emissions and the number of EtO emissions control devices currently in place in member facilities. A copy of HIMA's survey form is attached as Appendix A. This survey is being conducted in cooperation with EPA, specifically the Emissions Standards and Engineering Division of the Office of Air Quality Planning and Standards.

In this present preliminary submission, HIMA provides information on our industry's use of EtO, current trends in sterilization, and emission control devices currently in use. Additionally, comments on major issues raised by the notice of intent to list are provided, as well as responses to the questions posed by EPA in the information solicitation.

HIMA anticipates providing more extensive comments on EPA's intent to list ethylene oxide at the completion of our survey, tentatively scheduled for late January, 1986.

III. Background Information on Ethylene Oxide

HIMA has previously presented a significant amount of information on the medical product industry's use of EtO in regulatory submissions to EPA [1] and OSHA [2-5]. The following is a brief summary of the areas of EtO use and alternatives to EtO sterilization.

A. Use of EtO - General

There are three basic groups of EtO users throughout industry in general. The first group, the converters, consumes over 99% of the EtO produced. This group consists of companies that produce or purchase the chemical as an intermediate or raw material for the manufacture of other products. Almost 90 percent of the EtO

produced is converted into other products by the firms that produce it. The second group is health product manufacturers and health care providers that use EtO to sterilize medical devices and supplies. The third group consists of companies that use EtO to fumigate miscellaneous items, including spices, black walnut meats, bird seed, books, furniture, textiles, empty bee equipment, empty cargo holds, cosmetic packaging, and dairy packaging. EtO is also used as a ripening agent. The second and third groups combined account for less than 0.5% of total EtO consumption.

B. Health Care Uses of EtO

Currently, EtO sterilization is the only available method for effectively sterilizing certain materials that are sensitive to heat, moisture, or radiation. Approximately 60-70 percent of industrially sterilized medical devices use EtO as a sterilant [6]. HIMA estimates that its members sterilize 10-12 billion items per year with EtO.

Conservatively, hospitals, clinics, and doctors sterilize an additional 200 million items per year with EtO [7]. Many common surgical procedures could not be safely undertaken without EtO-sterilized equipment [8].

For many medical devices, no suitable substitute for EtO has been identified. A 1977 NIOSH report [9] on EtO noted that "alternate methods [for sterilization of medical supplies] often are impractical, hazardous, undependable, or uneconomical" and concluded that "the continued use of EtO as a gaseous sterilant is highly desirable in many situations." The Food and Drug Administration (FDA), in publishing a proposed rule on EtO residues [10], also stated its belief that "the current use of EtO as a sterilant for certain drug products and medical devices is necessary for the delivery of required health care..." In 1977, Sherwin Gardner, then Acting Commissioner of the FDA, stated in a memorandum:

I wish to stress that precipitous action which would, in effect, severely limit the use of ethylene oxide for sterilizing devices or drugs could have a serious impact on the public's health. Many life-saving devices are sterilized by EtO both by industry, as well as individual hospitals or other similar facilities. The continuing availability of such devices is vital.

C. Alternatives to EtO

Alternatives to EtO sterilization include radiation (both gamma and electron beam), dry heat, steam, filtration, and use of other chemicals, such as formaldehyde and glutaraldehyde.

Although gamma radiation, using a radiation source such as cobalt-60, is a substitute for EtO, it is not acceptable for a large number of products because it affects the molecular structure of some materials and thus damages products composed of such substances. Additionally, the supply of Cobalt-60 is limited since there is only one major supplier in North America (Atomic Energy of Canada, Ltd), there currently are only 30-40 cobalt-60 radiation sterilization facilities in the country, and the construction of such facilities is a lengthy and costly process subject to regulation by the Nuclear Regulatory Commission. Several gamma radiation contract sterilizers are currently investigating the use of cesium for sterilization, but a sterilization methodology for this radiation source must still be validated.

Wet/dry heat is often unacceptable due to the heat-labile properties of many plastic formulations. Other chemical sterilants, such as formaldehyde, which is frequently used in high level disinfection, are also subject to regulatory concern with respect to workplace and environmental health and safety. Additionally, there has been little exploration of using these other chemicals for large scale industrial sterilization.

In summary, EtO sterilization is the only available method for sterilizing a large number of medical devices composed of certain materials that are heat, moisture or radiation sensitive.

IV. Current Trends in EtO Sterilization

Regulatory initiatives at the Occupational Safety and Health Administration (OSHA) and industry trends in general have had a significant impact on the current level of use of EtO in industry.

A. Use of EtO/Use of Contractors

Even before OSHA issued its advance notice of proposed rulemaking concerning EtO, HIMA member companies were voluntarily maintaining internal exposure targets well below the then - current OSHA standard. OSHA's revision of the workplace Permissible Exposure Limit downward to a 1 ppm eight-hour time-weighted average has resulted in manufacturers modifying their use of EtO. Several manufacturers, realizing they could not meet the new exposure standard, ceased sterilization operations, consolidated sterilization operations, or sent their products to contract

sterilizers to be processed. FDA, in its 1982 Compliance Program Evaluation Report [11], acknowledged the overall decrease in the use of EtO and the increased use of contract firms:

The trends in sterilization and its attendant technology over the past four years indicate that fewer firms are using ethylene oxide as a sterilant for the devices and that more firms are now using contract sterilizers.

As a result, the number of EtO emissions sources has declined and will continue to decline as sterilization operations become more centralized or consolidated.

In HIMA's 1983 Submission to OSHA on the Agency's proposal to reduce the Permissible Exposure Limit for EtO [2], HIMA estimated there were 132 sterilization sites representing 351 sterilization units. These units vary in size from small (one cubic foot) research sterilization units to large (1000 cubic feet) industrial sterilization units. HIMA's current survey of EtO use will indicate to what extent this number has changed over the past two years.

B. Increased Use of Alternatives

FDA's Compliance Program Evaluation Report [11] also acknowledges the increased use of sterilization methodologies other than EtO, particularly radiation sterilization. Advances in the stabilization of plastics and changes in the dosage of radiation to which products are exposed have increased the use of cobalt-60 as an alternative to EtO. Although cobalt-60 irradiation is still limited somewhat by materials effects, availability of facilities and the supply of Cobalt-60, it has gained increased acceptance at the expense of EtO sterilization.

C. Installation of Emissions Control Devices

Many health care manufacturers, in response to state regulatory activities, have installed, ordered, or plan to order highly effective control devices that significantly reduce EtO emissions from sterilization units. As a result, a portion of the "Medical Supplies Manufacture" category already has EtO emissions under control (See Section V). HIMA's current survey will indicate to what extent emissions are already under control in this category.

In summary, a number of factors have acted to reduce the amount of EtO used and, therefore, decrease the EtO emissions sources in the health care manufacturing industry. These factors include:

- cessation of use of EtO;
- consolidation of sterilization operations;
- increased use of EtO contract sterilization facilities;
- increased use of alternative methods of sterilization; and
- installation of EtO emission control devices;

V. EtO Emission Control Devices in Place

Although HIMA will be providing further information on EtO emission control devices in its future submission to the Agency, this section will briefly discuss the devices currently in use.

Due to state regulatory initiatives, a number of HIMA members have installed, ordered, or plan to order highly effective control devices that will significantly reduce EtO emissions from sterilization units. Chemrox, Inc.* a manufacturer of a highly effective chemical conversion control device, has estimated that by the end of 1986, 35-40% of sterilization facilities will have installed or committed to install a DEOXXTM system for emissions control [12].

HIMA members have indicated that the EtO emissions control processes that currently exist in the "Medical Supplies Manufacture" category include:

- Chemical Conversion - In this process, a weak acid solution is used to convert EtO gas to ethylene glycol liquid, which is then sold off to reprocessors or disposed. The device is greater than 99% effective;
- Scrubbing - In this process, the EtO exhaust stream is passed through water, producing a limited conversion to ethylene glycol. The system is minimally effective, in the 10-20% efficiency range;
- Incineration - In this process, EtO is burned to complete combustion by using a common fuel such as propane. The process is greater than 99% effective; and
- Reclamation - In this process, refrigeration is used to liquify the EtO gas for reuse. The system is specially designed for use in sterilization by a gas mixture of 12% EtO - 88% FREONTM. The system is greater than 99% effective.

*Chemrox, Inc. is an example of one such company. The DEOXXTM system is Chemrox's brand of chemical conversion system.

The various EtO emission control devices differ in the degree of efficiency in which they remove EtO vented from the sterilizer. Additionally, the type of control devices used and the attendant engineering depends on the size of the sterilizer unit (cubic feet of sterilizer capacity), the type of gas mixture used (100% of EtO or an EtO mixture with FREONTM or Carbon Dioxide), frequency of use of the sterilizer, and how many sterilization units may be manifolded into the control device.

VI. Comments on Major Issues Raised by the Notice of Intent To List

The Ethylene Oxide Industry Council (EOIC) has commented extensively to EPA [13] regarding the Hazard Assessment Document and the Exposure Assessment. The EOIC also presented these comments at the October 3-4, 1984 meeting of EPA's Science Advisory Board (SAB). We share EOIC's concerns about these documents and support its comments regarding the scientific validity of the assessments.

A. Hazard Assessment Document

With respect to the Hazard Assessment Document, we concur with the EOIC that EPA has not complied with the recommendations of the Science Advisory Board regarding the document. EPA has failed to:

- present maximum likelihood estimates of the extrapolated risk as part of a discussion of the range of plausible estimates;
- prepare a sensitivity analysis; and
- use the entire data base to quantify the potential carcinogenic risk (almost all of the risk associated with exposure to EtO consists of a mathematical extrapolation from rat inhalation studies).

EOIC has submitted to EPA and OSHA a scientific risk characterization for EtO, conducted by Dr. Leon Golberg. Dr. Golberg's assessment of the hazards posed by EtO relies primarily upon his scientific evaluation of the totality of the available data. Although numerical extrapolations from the Busby Run rat inhalation study results are presented, they are used by Dr. Golberg as only one component of the overall assessment.

The Hazard Assessment discusses extensively the uncertainties in the evaluation. Dr. Golberg considers the qualitative and quantitative aspects of the various phenomena reported to be associated with exposure to EtO and characterizes the hazard associated with EtO exposure, using three quantitative zones of eight-hour time-weighted exposure:

The Zone of Increased Probability for Potential Adverse Health Effects. In Dr. Golberg's judgment, it is highly probable that adverse health effects would occur only at levels above 10 ppm.

Zone of Uncertain Consequence. Dr. Golberg has judged that exposure between 1 and 10 ppm represent the zone in which the occurrence of adverse health effects is uncertain.

Zone of Insignificant Exposure. Exposures at or below 1 ppm are considered by Dr. Golberg to be insignificant and to present no apparent hazard.

Although Dr. Golberg's evaluation was made in the context of employee exposure to EtO, it is also applicable to the public.

B. Exposure Assessment

EPA indicated in the Notice of Intent to List that information on the amount of EtO used, the location of use, and procedures for use and disposal of EtO in the health/sterilizer industry were "not as well characterized" as in the producer industry.

In arriving at the exposure assessment, EPA has made assumptions as to aggregate EtO emissions and locations of facilities. EPA has taken the total amount of EtO emissions (estimated as 4.5 million pounds, with no account as to emission control devices already in place) for the "Medical Supplies Manufacture" Category and distributed it over the 30-40 major population centers. Although HIMA does not have specific data on all of the sterilizer locations, we are generally aware that most sterilization facilities are not located in major population centers. Therefore, the estimates for exposure would be significantly decreased. We can only reiterate that our current survey of EtO use will more accurately identify the number and location of EtO emissions sources.

VII. Responses to EPA's Questions

1. Are there any adverse health effects other than those presented in the Health Assessment Document (HAD) associated with exposure to ethylene oxide via the ambient air and if so, at what concentrations exposure times are these effects observed?

EPA's Hazard Assessment Document (HAD) and other publications, such as the Preamble to OSHA's Ethylene Oxide Standard (29 CFR 1910.1000), have reviewed a number of health effects studies and we are not aware of any other such

studies. HIMA, in past submissions to the EPA [1] and OSHA [2-5] has presented comments questioning the scientific validity of studies presented by the Agencies to support regulatory action. Likewise the EOIC has submitted extensive comments to EPA [13]. EPA has failed to not only respond to EOIC's concerns, but has also not responded in the HAD to the recommendations raised by the Science Advisory Board.

2. Are there any available ambient air monitoring techniques for ethylene oxide?

In 1983 comments to OSHA on the then - proposed EtO standard [2], HIMA presented comprehensive comments on ambient air monitoring techniques for EtO. Since that time, little has changed regarding methodology except that increased sensitivity in gas chromatographic methods has lowered the level of detection of EtO to under 0.5 ppm, and there is currently a standardized charcoal tube monitoring method.

Four types of methods for measuring EtO concentrations are currently being used for personal and area monitoring. These are: charcoal tubes, passive diffusion samplers, direct reading tubes, and direct reading instruments. Preferences for the various monitoring techniques vary from company to company, depending in part upon in-house monitoring and analytical capabilities. Currently, charcoal tubes are most frequently employed. TedlarTM plastic bags and acid impingers can be used to measure EtO, but are not in general use.

• Charcoal Tubes

Monitoring with charcoal tubes involves the use of a calibrated sampling pump attached to a charcoal tube by a piece of TygonTM tubing. A known volume of air is drawn through the charcoal tube, and EtO is adsorbed onto the charcoal. The sampling pump and charcoal tube are placed on the employee, as close as possible to the breathing zone.

Through the use of appropriate methods, charcoal tube samples can measure down to 1 ppm \pm 20% in the laboratory and, under optimal conditions, 0.5 ppm or below at \pm 50%. Gas chromatographic equipment with flame or photoionization detection is in general use at a number of larger companies. Field use of this method requires that skilled personnel be used to obtain, preserve and analyze the samples. Careful attention must be paid to the analysis methodology.

The charcoal tube method offers a number of

advantages: (1) the sample device is small and portable, (2) interferences are minimal; (3) sample collection does not involve liquids; and (4) two or more organic substances suspected to be present in the air can usually be analyzed from the same sample. The charcoal tube method is, however, subject to certain restrictions and limitations. High temperatures and humidities interfere with the collection and desorption of EtO. Breakthrough can occur due to limited adsorption sites, necessitating that tubes be changed frequently. The flow rate is critical to allow time for the EtO to adsorb onto the charcoal, therefore charcoal is not suitable for short (generally less than fifteen minutes) sampling periods. Care must be taken to prevent channeling, and migration can occur if only one tube is used. Tubes must be refrigerated while transported and stored.

The American Society for Testing and Materials (ASTM) has issued a standardized charcoal tube monitoring method (ASTM D4413-85), which has been field validated by Clayton Environmental Consultants, Inc., under contract to the EOIC [14-15].

● Passive Diffusion Monitors

A number of companies are currently marketing different types of passive diffusion monitors. The basic principle for these devices is diffusion, the gradual spread of substances from an area of higher concentration to areas of lower concentrations. The devices are designed to measure time-weighted averages over a measured time interval of eight hours or less.

Passive diffusion monitors offer many advantages. The initial cost is low and no hoses, tubes, or pumps are required. The devices are compact, lightweight, and convenient to wear, and the method is simple and easy to use.

However, an analytical technique similar to that used for charcoal tubes is required, that is, a desorption of the badge and analysis using gas chromatography or colorimetric methods. Presently most companies are not analyzing the badges but returning them to the manufacturer for analysis.

Passive diffusion monitors have sufficient sensitivity to perform eight-hour sampling, but

they are limited in short term sampling (less than 15 minutes).

• Direct Reading Equipment

Direct reading equipment comes in three basic types: (1) infrared analyzers; (2) organic vapor analyzers; and (3) gas chromatographic equipment with flame ionization or electron capture. The infrared analyzer measures down to 1-2 ppm, but some models are subject to interference from chlorofluorocarbons, hydrocarbons, and humidity. The more expensive models reportedly have overcome this problem. The portable organic vapor analyzer is accurate to about 1 ppm, provided that there are no organic interferences. This device, however, measures all organics and is not specific for EtO.

There are a variety of continuous air monitors that consist of a gas chromatographic unit with flame ionization or electron capture capabilities. The lower detection limit is around 0.3 ppm. These instruments are large, expensive, not easily transportable, and must be carefully calibrated and validated.

• Other Methods

The TedlarTM bag and acid impinger methods are not in general use. In the TedlarTM bag method, a constant flow of air is pumped into an empty plastic (polyvinyl fluoride) bag for a specific period. After the sampling period, the pump is turned off and the bag is sealed. Analysis is done by gas chromatography. The advantages of TedlarTM bags are that they are reusable and not subject to interference by temperature and humidity. Problems with this method are that the bags are bulky and can be penetrated by sharp objects.

In the acid impinger method, a known volume of air is bubbled through a sulfuric acid solution in an impinger, where EtO is converted to ethylene glycol and analyzed by gas chromatography. The impinger is weighed both before and after sampling to correct for any evaporation loss. This method has a lower detection limit of about 1 ppm, is unaffected by temperature and humidity problems and can be used over a wide range of flow rates and sampling sizes. However, the impinger method involves a cumbersome apparatus, the risk of spills, the hazard to personnel, and requires a

difficult analytical method.

These methods and their applicability to EtO have been described in greater detail in HIMA publications [16-18].

3. Are there sources other than those listed to Table 1 that are likely to emit ethylene oxide into the air?

In Section III A, HIMA described a variety of industries that use EtO as a sterilant/fumigant. The MITRE Corporation, under contract to EPA, specifically the Office of Pesticide Programs, has prepared a number of reports describing the sterilant/fumigant sources of EtO emissions [19].

4. What are the locations, emission rates and current control equipment for ethylene oxide sources?

As previously discussed, HIMA plans to submit to EPA in early 1986 more specific information on EtO emissions in the "Medical Supplies Manufacture" category.

5. What is the quantity of ethylene oxide being emitted from each ethylene oxide source category, including automobile exhaust and Publicly-owned treatment works (POTWs).

HIMA is currently conducting a survey to respond to this question.

VIII. Costs of Control

HIMA does not currently have specific data on the capital and annual operating costs of EtO emissions control devices. We understand that EPA has preliminary data from several manufacturers of such equipment. It is important for EPA to note in cost analyses that factors associated with control devices include:

- the size of sterilizer(s) (cubic feet) the control device will service;
- the rated capacity of the control unit;
- frequency of use of the sterilizer;
- the engineering/installation costs;
- associated material costs (e.g. insulation); and
- annual operating costs (manpower and materials).

HIMA represents a membership that is primarily small companies. 50% of HIMA's membership have sales of less than \$5 million, 66% have sales less than \$10 million and 75% have sales less than \$30 million. The majority of the HIMA members potentially affected by a requirement for control equipment are small entities and much of the financial impact

would be on these companies. The economic burden on small companies may be especially severe as they are generally less able to shift or pass along significant cost increases.

IX. Conclusion

Although HIMA will be providing further information to EPA on the extent of EtO emissions and the control devices currently in place in the "Medical Supplies Manufacture" category, these preliminary comments have concluded that:

1. Ethylene Oxide is an essential sterilant for the medical device industry. It is used to sterilize 60-70% of industrially sterilized medical devices and is the only available method for sterilizing certain materials that are sensitive to heat, moisture, or radiation.
2. Sources of EtO emissions have decreased in number as some manufacturers have ceased the use of EtO, consolidated operations, increased the use of EtO contract sterilizers, used alternative methods of sterilization, and installed EtO emissions control devices.
3. EtO emission control devices are currently in use in the "Medical Supplies Manufacture" category. These devices include chemical conversion units, scrubbers, incinerators, and reclamation units.

X. References

1. Health Industry Manufacturers Association, 1978 Submission to the Environmental Protection Agency to Notice of Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing Ethylene Oxide (May 15, 1978).
2. Health Industry Manufacturers Association Comments on Notice of Proposed Rulemaking to Revise the Standard for Ethylene Oxide (June 17, 1983).
3. Health Industry Manufacturers Association Post-Hearing Comments on Notice of Proposed Rulemaking to Revise the Standard for Ethylene Oxide (August 29, 1983).
4. Health Industry Manufacturers Association Post-Hearing Brief on the Proposed Rulemaking to Revise the Standard for Ethylene Oxide (September 19, 1983).
5. Health Industry Manufacturers Association Comments on A Short Term Exposure Limit for Ethylene Oxide (November 5, 1984).
6. HIMA, Ethylene Oxide Technical Report No. 78-3, 1978 at 159.
7. Id. at 17.
8. Id. at 167-192, 198-200.
9. Glazer, Z.R.: Special Occupational Hazard Review with Control Recommendations for the Use of Ethylene Oxide as a Sterilant in Medical Facilities, NIOSH, 1977.
10. 43 Fed. Reg. 3800 (January 27, 1978).
11. Sterilization of Medical Devices, Compliance Program Evaluation Report, Compliance Program Circular 7378. 008A, National Center for Devices and Radiological Health, Fiscal Year 1982.
12. Letter from Chemrox, Inc. to EPA, dated October 31, 1985.
13. Ethylene Oxide Industry Council Comments to the Environmental Health Committee on the Draft Health Assessment Document for Ethylene Oxide, September 12, 1984.
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15. Ethylene Oxide Field Validation Study for the Ethylene Oxide Industry Council, Chemical Manufacturers Association, by Clayton Environmental Consultants, Inc., September 13, 1985.

16. Jorkasky J.F., editor. The Safe Use of Ethylene Oxide, Health Industry Manufacturers Association, Report No. 80-4, December, 1980.
17. Jorkasky, J.F., editor. Monitoring Airborne Ethylene Oxide, Health Industry Manufacturers Association, Report No. 81-1, May, 1981.
18. Jorkasky, J.F., editor, Ethylene Oxide Worker Safety Issues, Health Industry Manufacturers Association, Report No. 82-2, December, 1982.
19. MITRE Corporation Reports Include:
 - o Preliminary Benefits Analysis of Ethylene Oxide as a Medical Sterilant, October, 1978.
 - o Preliminary Benefits Analysis of Ethylene Oxide at Transportation Sites, March, 1980.
 - o Preliminary Benefits Analysis of Ethylene Oxide as a Fumigant in Libraries, March, 1980.
 - o Preliminary Impacts Analysis of Ethylene Oxide as a Fumigant in Museums, March 1980.
 - o Preliminary Benefits Analysis of Ethylene Oxide as a Sterilant in Research Laboratories, April, 1980.
 - o Mitigation of Worker Exposure to Ethylene Oxide, March, 1981.
 - o Costs of Measures Used to Mitigate Worker Exposure to Ethylene Oxide, August, 1981.

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January 8, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

We would like to take this opportunity to respond to your Draft Report on Ethylene Oxide (November, 1986). While analyzing the data presented on emissions from the various types of facilities in California, some of our calculations differ with yours. Conversations with several California blenders of 100% ETO with an inert gas such as a fluorocarbon indicate that their basic plant design and operation are similar to our own. At our facility, all transfer of 100% ETO liquid or vapor, into or out of (DOT 5-P) drums, is done in a closed system. The only exception to this would be when a drum must be opened, in which case a suction device covers the opening, and the captured vapors are passed through an acid scrubber to convert the 100% ETO to ethylene glycol. All piping connections in our system are leak-tested by pressurization with inert gas at installation before being placed in operation. Whenever a connection must be opened after ETO has been in the line, the line is first purged with inert gas which blows the liquid out of the line, also picking up the ETO vapors in the line. This inert gas/ETO mixture is then passed through the scrubber. When returned drums must be emptied of returned material (perhaps 1-2% of the amount shipped) the liquid ETO is passed through a closed system to a receiving drum, and inert

gas passed through the return drum to purge ETO vapor as well. Again, the inert gas/ETO mixture is passed through the scrubber to control emissions. The receiving drum is shipped to our facility in South Carolina for conversion in a closed system to ethylene glycol. This conversion process is similarly designed to minimize emissions; the ETO is transferred through a closed system into a closed reactor for conversion. With such tight controls on the method of transferring the 100% ETO, we find it difficult to accept that we could be losing 2-8 pounds (1/2-2% of 400 pounds) of ETO to the atmosphere per drum filled. We, therefore, must question the fugitive emissions value of 1/2-2% as stated by Zwiacher (1983), and suggest that the value (for blenders, at least) must be somewhat lower. Correcting the emission data for such reduced values is in order.

Conversations with one California blending (repackaging) facility provided us with data which indicate that the emissions from their facility are approximately 20% of the value reported in the ARB Draft Report. Our calculations indicate that the report used the 18% return figure plus some fugitive loss, without accounting for the 90% efficiency of the acid-water scrubber used to recover the material recovered from the cylinders. Additionally, this same facility reported a 5% return rate, on average, which is considerably lower than the 18% figure used in the calculations in the report. Another blender (repackager) contacted estimated their returns at only 2-3%, vs. the 18% assumed in the ARB Draft Report. These differences should alter your calculation of emissions by a factor of 3-6 times.

Another assumption made by the ARB staff is that all 100% ETO purchased by a California sterilizer facility is eventually released to the atmosphere as sterilizer discharge or off-gassing after unloading. While we cannot comment on what may have been true in the past prior to the alleged health affects of ETO, scrubber units such as the one in the enclosed short article (Attachment 1) will contribute significantly to a reduction of ETO emission from the (industrial) sterilizer. Conversations with some additional California sterilizer facilities indicate they may change their production methods to cycle the atmosphere in the sterilizer several times rather than "vent-and-open." This would have the effect of more complete ETO removal prior to opening the sterilizer, more ETO going through the scrubber, and less ETO remaining for the off-gassing

step. This would reduce the amount of ETO released to the atmosphere. Again, these engineering improvements will alter your emissions calculations by several magnitudes.

We have been in contact with several of the facilities listed in table III-1 which have indicated that they will be responding to the Draft Report separately and individually. Several had indicated their intention to add emission-control devices to their systems in the near future; several have already added such devices or improved existing ones between your collection of data and today.

At this point, a discussion of several points of the health effects data cited in your draft is in order. In the Executive Summary, pg. 1., you state that at current ambient levels of ETO, "no acute or noncarcinogenic effects are expected." We would agree with that statement, a later statement on the same page, suggesting increased incidences of stomach cancer and leukemia from occupational exposure to ETO, requires comment. A preliminary report of a University of Pennsylvania Medical Center study of a cohort at the Buffalo, NY plant of Johnson & Johnson (Attachment 2), dated April, 1986, found that of 442 of 513 persons who were regular employees of the company between July, 1974 and September, 1980 (104 males, 338 females participated; 18 males 53 females did not participate - 86% participation) there were 8 breast cancers (vs. 3.14 expected), 6 all other cancers in females (vs. 6.74 expected) and 0 cancers in males (vs. 1.74 expected). The incidence of breast cancers prompted a further analysis of tissue samples, where 10 cases from the Buffalo study were interspersed with 10 cases from the Pennsylvania Hospital, all samples being identified with code numbers only. The investigator, Dr. V. A. LiVolsi, M.D., was unable to microscopically detect by "grade of the tumor, the type of the tumor, or the surrounding breast tissue" any changes in the tissue which would indicate which samples had come from which source. In other words, Dr. LiVolsi could not pinpoint a specific cause of the breast cancers in the exposed worker samples. Therefore, although it is possible that ETO was the cause of the breast cancers in this cohort, microscopic examination could not support that conclusion.

The Snellings, et.al., study on Fisher 344 rats in 1984 concluded that "one or more biologically significant effects were demonstrated...at all three dose levels of ethylene oxide..." The conclusion is based on the (pg. 25 of the Draft Report, Part B) "numerically increased incidence of MNCL (mononuclear cell leukemia) in females at 10 ppm" and the "statistically significant increase in the number of rats with primary neoplasms". However, on pg. 20 (Part B), the MNCL incidence was reported as statistically significant only in the 100 ppm female rat group. The difference between "numerical increase" and "statistically significant increase" is very important. The authors switch from "statistically significant" to "numerical increase" to be able to state more than one biological effect at all levels (10, 33, 100 ppm). In fact, only one statistically significant effect occurred, and only for females (primary neoplasms) at all 3 levels. MNCL only showed a significant difference in females at 100 ppm, and no dose-related significance was shown in males. Therefore, no particular effect was shown to equally affect all animals of the study.

The Lynch, et.al., study from 1984 has claimed similar effects, however, the Lynch, et. al., study confined itself to levels of 50 ppm and 100 ppm. Using only these two levels of exposure, the authors state that no "No Observed Effect Level (NOEL)" was found. The Snellings study found some effects at 33 ppm (already lower than the Lynch Study), but effects at 10 ppm were questionable, at least. Thus, a level between 0-10 ppm might be considered the NOEL Lynch could not observe, because the exposures in the Lynch Study were so high.

Another aspect of the Snellings and Lynch Studies which affects the ability to translate the rat data to human risk assessment is the difference in breathing rates between rats and man. At an equivalent dose per body weight, rats will inhale 4-7 times as much ETO as man. Therefore, at the 33 ppm level in the Snellings study, the translation to human exposure would be in the range of 130-250 ppm. The 10 ppm level, where statistically significant cancers occurred in the females only -- not in the males, would translate to a human exposure of 40-70 ppm. Therefore, a NOEL is definitely a possibility where human exposure to ETO is concerned.

One must also question the fact that in both studies the concentration of ETO was at least 20 times the OSHA "action level" (10 ppm vs. 0.5 ppm) for worker exposure, and as much as 200 times the level (100 ppm vs. 0.5). Also, the smallest dose level used in the Snellings study (10 ppm) is approximately 20,000 times the 51 ppt level in the model used by the California Air Resources Board Draft Report which amount needs to be lowered according to the facts presented in earlier portions of this response. Therefore, although these studies indicate further research is desirable, they do not prove adverse health effects at permitted worker-exposure levels, and especially at ambient levels stated in the ARB model.

The occupational exposure studies of Hogstedt, et.al., have been rebutted in Journal of the American Medical Association (Volume 256, No. 13-October 3, 1986). The Hogstedt studies from Plants #1 and #2 involved workers exposed to ETO and methyl formate at one plant, and ETO and several organic chemicals, including benzene, at the other. Where cancers were observed, the authors state they must have been due to ETO, since it was common to both plants. Carcinogenic effects of other chemicals the workers were exposed to were not considered. The rebuttal from Texaco (Attachment 3-printed in JAMA, reference above). points out that where no other carcinogenic materials were found (exposure groups A+B at plant #3), no leukemia was observed. The letter also points out that Morgan, et.al., observed no leukemia in their study, conducted in a plant similar to plant #3 (ethylene oxide exposure only). The Texaco letter is summarized by stating that Hogstedt, et.al., and Morgan, et.al., provide no convincing evidence that low exposures to ethylene oxide "cause any increased risk of death." We, therefore, must question the Draft Report conclusion (pg. 39-Part B) that these studies "provide substantial evidence of ethylene oxide's carcinogenicity in humans."

The Hemminki study on spontaneous abortion was admittedly questioned in the past (Draft Report reference to Gordon and Meinbandt, 1983), yet the conclusion is that the data suggest an association between ETO and spontaneous abortion even though OSHA agreed that only a qualitative risk was determined, not a quantitative one. A "Current Report" in Occupational Safety and

Health Report, points out that preliminary results in a State University of New York study of hospitals in western New York State (Attachment 4) showed "no statistically significant increase in spontaneous abortions when compared to a matched group of non-exposed workers." Therefore, the question of spontaneous abortion in exposed female workers remains unsolved, pending final results from the NY State Study.

A recent publication, Hazard Assessment of Ethylene Oxide, edited by Dr. Leon Golberg (CRC Press, 1986) summarizes many of the studies done on the hazards of ETO to laboratory animals and to human health. Dr. Golberg is currently a professor of Community and Occupational Medicine at Duke University. He was once Chairman of the Secretary of Health Education and Welfare's Committee on Pesticides. In Chapter 11 (Hazard Assessment), Section IV (A Biological Perspective on EO), he places the biological evidence on ETO effects in perspective. Neurotoxicity in mice was evident at 50 ppm, while other species tolerated 10 ppm or more, therefore, when combined with studies of ETO workers, it is unlikely that any neurologic effects will be seen in man "at or below atmospheric levels of 10 ppm EO." Teratogenicity (induction of birth defects) was not observed in rats until the females showed signs of toxic reaction (well above 100 ppm in the atmosphere). Reproductive effects on rats were not seen at levels of 33 ppm or below. Dr. Golberg noted one study showing spontaneous abortion in women workers exposed to EO, but this study (Hemminki, referred to earlier as the "Hemminki Study") has been shown to be flawed, and a more recent preliminary report (also cited earlier) gives rise to questions about the effects of ETO on pregnant female workers occupationally exposed to ETO. Dr. Golberg's conclusion is that EO exposure at or below 10 ppm would not give rise to reproductive effects. Effects on genetic material, according to Dr. Golberg, are only expressed at atmospheric levels above 10 ppm. The carcinogenic nature of EO is such that it "falls within the accepted definition of an animal carcinogen." However, Dr. Golberg points out that the studies which have been done are "subject to various criticisms." In Chapter 11, Section VI, Dr. Golberg summarized by stating that "exposure at or below 1 ppm Time-Weighted Average(TWA) may be considered as presenting no

apparent hazard (to man)." A value of 1 ppm TWA8 would be over 2,000 times the value used in the ARB Draft Report model. The exposure an individual would receive as a result of ETO emissions according to the ARB model would, therefore, be at least 3 orders of magnitude below any level where biological effects have been shown.

Further assessment of the risk of ETO exposure to human health comes directly from OSHA. In "OSHA's Summary Judgement Memorandum" at 19, Public Citizens Health Research Group v. Auchter (554 F. Supp. 242 [D.D.C. 1983]), OSHA conceded that the epidemiological evidence "contained no direct evidence of an excess risk of cancer at chronic exposure levels below approximately 14 ppm." Only later did OSHA decide to ignore available data and presume that a threshold value for exposure does not exist. This presumption has been ruled inappropriate by the U.S. Supreme Court (448 U.S. at 653-54), which had ruled that it is OSHA's responsibility to prove that no threshold value exists -- they may not shift the burden of proof that one exists on employers. Therefore, the OSHA statement that there is no excess cancer risk at levels below approximately 14 ppm must stand unless, and until, another value can be proven by the agency.

Ethylene oxide has been used as a sterilant for over 40 years now, often at exposures exceeding 50 ppm. OSHA's risk assessment (29 CFR Part 1910 pg. 25762) of 634-1,093 excess cancer deaths per 10,000 workers (about 1 in 10) would almost certainly have resulted in a noticeable rise in cancer rates amongst ETO workers if their risk assessment was completely valid. This has not been the case; and all prior information was at 50 ppm (the "legal" limit for years) and above. Today, at 1 ppm, the reality of the risk assessment is out of line with the observed effects.

Gerald A. Emison, Director of The Office of Air Quality Planning and Standards (OAQPS) in the Office of Air and Radiation of the EPA, has stated that the EPA has no direct evidence that concentrations of ETO in the ambient air due to stationary sources cause cancer. Projects are underway to further evaluate data already available. He further stated the 1985 EPA Health

Assessment Document on ETO did not incorporate comments by the Science Advisory Board concerning analyses of the estimate of cancer potency, that the estimate of cancer potency relies on the results of only one study and ignores the rest of the data available. He believes the EPA's estimate of public exposure to be unrealistic and that it should be re-evaluated.

Up to this point, all discussion has been directed at rebutting the potential hazards of ETO. A few comments concerning the benefits of ETO will now be presented.

Ethylene oxide's role as a sterilant and fumigant arises from the special differences between ETO sterilization and available alternative methods. In medical device/hospital applications, autoclaving can be and is used for applications where the high heat (about 250 degrees Fahrenheit, 120 degrees Centigrade) does not degrade the material being sterilized. Items such as metal surgical tools, bacteriological culture media and cloth gowns can be autoclaved. Items such as disposable syringes, plastic medical devices, pacemakers, heart valves, heart-lung machines, kidney dialysis machines, fiber optic devices, etc., cannot be autoclaved. As an alternative method of sterilization, irradiation can be used for some devices, however, it is expensive, requires highly complex machinery, controls and highly trained technicians, and some plastics which are the materials of choice for certain applications are degraded by embrittlement, discoloration and/or loss of tensile strength. (HIMA Report, 78-3, 1978 Submission to the EPA; excerpt included as Attachment 5). According to the HIMA Report 78-3, the total number of items sterilized by ETO in all U.S. hospitals would be approximately 200,000,000. This does not include items sterilized by hospital suppliers, private clinics, research institutions, etc. When these are included, the number rises to the billions. Some 18,000,000 surgical procedures are performed each year, virtually all requiring some items which must be sterilized with ETO. Appendices A-9 and A-10 list over a hundred items which are of necessity sterilized by ETO. Appendices B-7 and B-8 are depositions to the EPA which point out the absolute necessity of ETO sterilization in the health care industry, and the human suffering impact which would result from the loss of ETO as a sterilizing agent.

One example of public harm already caused by the removal of ETO sterilization occurred in 1984 at the University Hospital in Baltimore (Newspaper clipping, Attachment 6). The hospital had switched from ETO sterilization to pasteurizing of infant respirator parts. Bacterial growth in the breathing device was able to infect, and ultimately cause the death, of two infants. The hospital has returned to the use of ETO sterilization for all devices requiring in-hospital sterilization by ETO.

To summarize, we suggest that the original data on emissions offered in the Draft Report are gross distortions, both for reasons of assumptions made to arrive at them, and because facilities in the State of California will shortly introduce further emission controls to reduce present emission levels. Also, we suggest that, although there is cause to study the biological effects of ETO on humans in greater detail, the studies relied on in the Draft Report leave sufficient question as to the actual effect of ETO concentrations on occupationally exposed workers (approximately 0.5-1.0 ppm TWA8). Therefore, effects at the calculated ambient air value of 51 ppt. must be of much less significance, if any at all.

Industry has moved in a responsible direction to eliminate or greatly reduce the emissions of ETO to the atmosphere, as has the Industry moved to eliminate or reduce worker exposure to ETO. In our opinion, it serves no purpose to the Health Industry to put further restrictions and red flags onto an industry that is already exhibiting responsibility, that emits material far below any harmful levels. Further restrictions and red flags tend to move people away from a desirable method of sterilization (such as the Maryland baby deaths) to a condition where the cure would cause more harm than good.

Sincerely,



Paul Lewandowski
Ass't. Product Mgr.

PL/brs
Attachments

List of Attachments

1 - "Compliance Problems solved by Ethylene Oxide scrubber at specialty gas plant," Chemical Processing. January, 1986.

2 - Buffalo Health Appraisal Project, Johnson & Johnson Co. May, 1986.

3 - Rebuttal letter to the Editor of the Journal of the American Medical Association, Texaco. May, 1986.

4 - "Preliminary Results on ETO, Mercury Indicate Opposite Miscarriage Risks," Occupational Safety & Health Reporter. May, 1986.

5 - HIMA Report 78-3 (extract) with Appendices. "Ethylene Oxide Technical Report - 1978 Submission to the Environmental Protection Agency," Health Industry Manufacturers Association, pp. 156-201, A59-A65 and B167-B184. May, 1978.

6 - "Infant Deaths Linked to Poor Sterilization," The Baltimore Sun. August 29, 1984.

Compliance problems solved by ethylene oxide scrubber at specialty gas plant

Attachment 1

CP Staff

Problem

A specialty gas producer was confronted with an EPA compliance problem in dealing with ethylene oxide (EtO). The chemical had been added to the toxicity lists of the U.S. EPA and the Occupational Safety and Health Administration (OSHA). Effective August 21, 1984, the OSHA standard for EtO limited exposure to a 1 ppm, eight-hour time weighted average.

Ethylene oxide is used to sterilize many pharmaceutical and hospital supplies. Typically, EtO is supplied in cylinders as a mixture with Freon-12 or carbon dioxide. A standard cylinder contains 135 lb of product, of which about 16 lb is EtO.

When a customer is finished with an EtO cylinder, it is returned to the specialty gas producer. Before recharging a cylinder, it must be purged of any remaining EtO and then cleaned. The purged EtO presented a problem in removal and disposal.

Solution

An ethylene oxide scrubbing system was designed for the gas cylinder area. It consists of a specially designed 28 ft packed tower, a 400 gal holding tank, valves, and recirculation pump.

Gas purged from returned EtO cylinders is directed to the scrubber and is channelled upward through the packed bed as scrubbing liquid flows countercurrently over the packing. A mist eliminator at the top of the packed bed prevents entrained liquids from escaping with the vent gas. The water soluble EtO is hydrolyzed to ethylene alcohol and then to ethylene glycol, a relatively inert and harmless chemical.

The conversion of EtO to ethylene glycol involves first breaking the EtO bond to release oxygen and ethylene radicals before the ethylene radicals in turn form ethylene glycol. Because mass

transfer and hydrolyzation factors are critical in this two-part reaction, the system was designed to ensure adequate dwell time. The conversion reaction is also hastened by using an acid catalyst.

Results

The EPA evaluated the scrubbing system and monitored its operation after installation and found it to meet all compliance criteria. The scrubber is rated at up to 99% efficiency depending on the amount

of EtO introduced. Periodic reevaluations are made by the EPA and state environmental authorities to ensure proper operation.

The system was rated at 150 cfm, a case of design overkill intended to act as a safety cushion. In a worst case scenario, if an EtO cylinder were returned completely full, only 4 cfm of EtO would reach the scrubber. Typically, only residual EtO is introduced to the scrubber.

The ethylene oxide scrubber system has been on-stream about six years. About once a month, the scrubbing media is checked for volatility, flammability and pH—to determine how effectively the EtO is being hydrolyzed into ethylene glycol.

After the EtO is converted to glycol, it functions as an antifreeze to keep the outdoor system operational throughout the winter. When the holding tank shows evidence of excess glycol, a disposal company is called to remove the by-products. Content analysis typically finds the material to be non-volatile with a pH of 7.1.

Once a year, the scrubber is subjected to more radical maintenance. The system is taken apart to check the screens and make sure that they are not clogged with polymer and that there is still a good dispersion rate of the EtO.

In the six years of operation, scrubber performance has been highly satisfactory. The unit performs to spec with minimum maintenance, and that maintenance is easily done by staff personnel without need to call in the manufacturer's service team. After observing the success of the unit, the company added similar ethylene oxide scrubbers to its other facilities.

Ethylene oxide scrubber system is manufactured by Croll-Reynolds Co., Inc., 751 Central Ave., Westfield, NJ 07091. Circle 789



The ethylene glycol produced in the ethylene oxide scrubbing operation acts as an antifreeze to allow year-round operation

Johnson & Johnson

Attachment 2

OFFICE OF
GENERAL COUNSEL

ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, N. J. 08903 1002

May 13, 1986

Mr. George L. Henschel
Office of the Solicitor
Department of Labor, S-4004
200 Constitution Avenue, N.W.
Washington, DC 20210

Re: BUFFALO HEALTH APPRAISAL PROJECT,
April 25, 1986 Preliminary Report
of Cancer Incidence in a Group of
Workers Potentially Exposed to
Ethylene Oxide

Dear Mr. Henschel:

We are enclosing a copy of the above Preliminary Report which is the ninth report to OSHA on the continuing ethylene oxide studies of Johnson & Johnson.

This Preliminary Report deals with cancer incidence in workers previously employed at the Buffalo, New York plant, formerly operated by Extracorporeal (Plant III in previous Johnson & Johnson reports to OSHA) and was prepared under the general supervision of Paul Stolley, M.D. of the Clinical Epidemiology Unit of the University of Pennsylvania School of Medicine.

The report is based on data developed during the course of the Health Appraisal Project being conducted for Johnson & Johnson at the Millard Fillmore Hospital in Buffalo. The Health Appraisal Project was established in March 1982 to provide health evaluation for workers formerly employed during the period ethylene oxide was used at this Buffalo plant.

Sincerely,


Charles A. Harris

PP
Encl.

cc: w/encl. -- Dr. R. Lenen, NIOSH
Mr. J. A. Moore, EPA

UNIVERSITY of PENNSYLVANIA

SCHOOL OF MEDICINE

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PAUL D. STOLLEY, M.D., M.P.H.
Herbert C. Rorer Professor of Medical Sciences
Co-Director, Clinical Epidemiology Unit

April 25, 1986

Anthony A. Herrmann, M.D.
Director, Employee Health & Safety Affairs
One Johnson & Johnson Plaza
WH-6G38
New Brunswick, N.J. 08933

Dear Dr. Herrmann:

I have enclosed a report prepared by the Clinical Epidemiology Unit of the University of Pennsylvania School of Medicine. This report presents results of the employee health study being conducted in Buffalo, New York. The title of the report is "A Preliminary Report of Cancer Incidence in a Group of Workers Potentially Exposed to Ethylene Oxide".

Yours truly,



Paul D. Stolley, M.D., M.P.H.

FDS:mgb.
Enclosure

**A Preliminary Report of
Cancer Incidence in a Group of Workers
Potentially Exposed to Ethylene Oxide**

**Clinical Epidemiology Unit
University of Pennsylvania
School of Medicine**

April 25, 1986

I. INTRODUCTION

In March of 1982, a preliminary report of a pilot research chromosome study of workers at sites where ethylene oxide (ETO) gas was utilized as a sterilant was forwarded to the Occupational Safety and Health Administration by Johnson & Johnson. In the letter of transmittal, it was stated that "all previous employees at the Plant III (HRE)* location (see Preliminary Report for description), dating back to the initiation there of ETO sterilization, will be contacted and invited to participate in a prospective program of health evaluation...". The following preliminary report is the first report of this health evaluation analysis of the above mentioned Plant III (Worksite III) cohort. Hereinafter, in this report, this health evaluation activity will be referred to as the Health Appraisal Project (HAP).

The HAP cohort is defined as all persons who worked at Worksite III at any time during the interval July 1, 1974 to September 30, 1980, the period during which ethylene oxide was used at the plant. The present report relates to cancer incidence in that cohort up to the present. Specifically, observed numbers of cancers are compared with those expected in this cohort based on age- and sex-specific cancer incidence rates from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program (Horn et al., 1984).

Because data collection is ongoing, an follow-up of the cohort to the present is not complete, these preliminary analyses have been performed in several ways, with different assumptions about completeness of follow-up entering into each computation. In this way, a range of possible results can be examined. As with all epidemiological work, there are limitations inherent to the methods employed. The type of approach described below may suggest possible associations, but cause and effect conclusions do not necessarily follow.

* High Relative Exposure

II. METHODS

A. The HAP Cohort

The HAP cohort consists of all individuals who were employed at Worksite III at some time during the period July 1, 1974 to September 30, 1980. It can be further subdivided along two dimensions:

1. whether an employee was a regular employee or a temporary employee, or, in some cases, held both classifications at different times.
2. whether an employee participated in an HAP medical examination or interview (participant) or did not participate (non-participant).

In general, regular employees tended to remain employed at the plant for longer periods than temporary employees, and thus as a group may be thought to have had more potential for exposure to ETO than did the group of temporary employees. Employees who held both classifications at different times are considered to be regular employees in the analysis.

B. Observed Cancers in the HAP Cohort

At present, all of the observed cancers in the HAP study have come either from participants in HAP examination or interview, or from death certificates, or from the New York State Cancer Registry. Since about 95% of the non-participants are thought to reside in New York State, the New York State Cancer Registry data was considered to be instrumental in identifying additional cases of cancer among living non-participants. The names of all non-participants as of July, 1985, were submitted to the New York State Cancer Registry on July 9, 1985. Approval for access to the New York State Cancer Registry data was granted on December 9, 1985, and initial Registry reports on the non-participants were received on December 23, 1985. The Registry has been most cooperative, and two cancers in non-participants were discovered through the Registry search. However, the Registry has indicated that its computerized records are not

complete for 1985 or 1984, and the records for 1983 are considered preliminary. Until the information on the non-participants is current, all preliminary analyses in which non-participants are included may underestimate the incidence of cancer in the HAP cohort.

The analyses report below are based upon incident cancers occurring after July 1, 1974 (start of ETO use). No latency period has been assumed for these analyses, nor a minimum exposure period.

C. Comparing Observed and Expected Rates of Disease

1. Incidence

An incidence rate is the "number of new cases of disease per unit of population per unit of time" (Monson, 1980). In the HAP study, incidence is calculated from the number of observed events in the numerator and the number of person-years of follow-up in the denominator. Incidence rates are based on the assumption that the risks of developing disease in each of the years contributed by an individual are independent of each other.

2. Person-Years

Person-years of follow-up for a given individual in a cohort study refers to the number of years from start of exposure to either death, occurrence of the event of interest, to the end of the study or until the most recent contact with that individual. The total person-years for a study consist of the sum of the person-years over all individuals, and will increase over time as follow-up continues. In computing person-years, one person followed for 5 years contributes the same number of person-years as five people who are followed for one year (Monson, 1980).

Person-year calculations are further refined to give the number of person-years of follow-up within a certain age range, say, 40-44. A given person in a cohort study usually contributes person-years to more than one age

range. For diseases such as cancer, in which incidence rates vary greatly with age, it is important to know the total number of person-years of follow-up within narrow age ranges.

3. Expected Number of Cancers in Cohort

Cancer rates from a comparison population are applied to the number of person-years of observation in the HAP cohort. This provides an estimate of the number of expected cancers in the HAP group, assuming that risk of disease in the HAP cohort is the same as that in the comparison population.

Since cancer rates differ by age and sex, age- and sex-specific rates are applied to the appropriate number of person-years in that age-sex stratum in the HAP cohort. The total expected number of cancers in the cohort is obtained by summing the stratum-specific expected numbers.

For this series of analyses, the average annual age- and sex-specific SEER cancer incidence rates for the period 1978-1981 were used to calculate expected numbers of cancers. Data from the Western New York Tumor Registry and the New York State Cancer Registry are also available and give approximately the same results as the SEER data used.

A community control group was considered and rejected because the incidence rates are too low for the diseases under consideration for such a community control group to provide reliable comparative rates.

4. Relative Rates of Disease in the HAP and Comparison Groups

Of interest is the ratio of the observed cancer incidence rate in the HAP cohort to the expected cancer incidence rate in that cohort, or the relative rate of disease. The observed incidence rate is given by:

$$I_0 = \frac{\text{number of observed cancers}}{\text{total number of person-years of observation}} = \frac{O}{PY_{\text{total}}}$$

The expected incidence rate is:

$$I_E = \frac{\text{number of expected cancers based on SEER rates}}{\text{total number of person-years of observation}} = \frac{E}{PY_{\text{total}}}$$

By definition, the total number of person-years is the same in both cases. Therefore, the relative rate of disease is D/E .

Because the outcomes of interest are rare and the number of person-years is relatively large, the number of observed and expected events can be compared by means of the Poisson probability distribution.

D. Alternative Methods of Computing Observed and Expected Rates of Disease

A health-tracking project of this type usually employs several different alternative methods of computing the expected number of cancers or other diseases. In addition, various assumptions about periods of exposure, latency period, and closeout dates enter into the analyses. Thus it is customary to present several analyses using different assumptions to help clarify relationships and to facilitate a better understanding of the data. The assumptions for various analyses are as follows:

1. Analysis Confined to Participants

Definitions:

- a) Observed numbers of cancers are based on data obtained only from participants in HAP medical examination or interview.
- b) Follow-up begins at start of employment or July 1, 1974 (start of ETO use), whichever is later.
- c) Follow-up ends at latest examination or interview date, at death, or at the first occurrence of the diagnosis of interest.
- d) Person-years of observation begin at start of follow-up (start of potential exposure), continue to end of follow-up, and include participants only.

2. Analysis Includes Participants and Non-Participants: End of Follow-up Different for Participants and Non-Participants

Definitions:

a) Observed numbers of cancers are based either on data obtained from HAP medical examination or interview, from death certificates, or from New York State Cancer Registry data.

b) Follow-up begins at start of employment or July 1, 1974 (start of ETO use), whichever is later.

c) Follow-up ends at latest examination or interview date, at death, or at the first occurrence of the diagnosis of interest for participants. For non-participants, follow-up ends at death, at the first occurrence of the diagnosis of interest, or at December 31, 1985.

d) Person-years of observation begin at start of follow-up (start of potential exposure) and continue to end of follow-up.

3. Analysis Includes Participants and Non-Participants with End of Follow-up Same for Both Groups

Definitions:

a) Observed numbers of cancers are based either on data obtained from HAP medical examination or interview, from death certificates, or from the New York State Cancer Registry data.

b) Follow-up begins at start of employment or July 1, 1974 (start of ETO use), whichever is later.

c) Follow-up ends at death, at the first occurrence of the diagnosis of interest, or at December 31, 1985, for participants and non-participants alike.

E. Implications of the Methods of Analysis

Theoretically, when comparing observed and expected events, the period over which cancers are observed should coincide with the follow-up period used to

compute person-years. The first method of analysis is the only one satisfying this criterion, and is the conventional method used for an initial analysis of this type of data. However, it is limited to participants only (about 77% of the cohort) and follow-up could have ended as early as 1982. It thus will underestimate the total person-years for the cohort and produce the fewest expected numbers of cancers. The first method, as a result, may overestimate the relative rate of disease.

The second method of analysis includes both participants and non-participants for calculation of person-years but requires the unlikely assumption that there are no unknown cases of cancer among the non-participants. The above bias in calculating person-years is addressed, but the number of cancer cases may be incomplete, which would result in an underestimate of the relative rate of disease.

The third method of analysis takes into account that follow-up is on-going, and uses an end - of - follow-up date of 12/31/85 for both participants and non-participants. This represents the largest possible number of person-years for the study. For the third method of analysis, it is assumed that no cancers in addition to those discovered thusfar from death certificates or the New York State Cancer Registry exist in the non-participant group or in participants who were last examined or interviewed up to several years previously. This assumption may lead to underestimation of the number of cancers, since HAP experience has shown that the majority of the cancers were reported only when persons were contacted for routine follow-up of the cohort.

Together these three methods of analysis provide a range for calculation of person-years and relative rate of disease under a variety of assumptions. As data from the New York State Cancer Registry become complete, the distinction between participants and non-participants will become less critical.

F. Cancers Included in Analysis

There are 26 individuals with cancer known to date in the HAP cohort. Four of the cancers are skin cancers, specified as basal cell carcinoma in three. Since basal cell carcinomas are not reportable cancers for the SEER Program, and thus do not enter into calculations of expected numbers of cancers, the HAP skin cancers have been excluded from the analysis. One of the cancers was an in situ cancer of the cervix. It is included in the analysis, although its classification as a cancer is debatable. Ten of the 26 cancers were breast cancers. The analyses described below focus on observed and expected numbers of breast cancers, cancers of all sites, and cancers of all sites except breast.

III. RESULTS

Table 1 presents the number of persons and person-years entering into the computation of expected cancer rates. The data are subdivided by employment category - regular or temporary - and by participant status at the time this analysis was begun. Because the HAP is ongoing, with continual efforts to follow the cohort, some non-participants have recently become participants. The change in status is not reflected in this report, due to the time necessary to carry out the analysis. The close-out date for the determination of participants' status assignment for this preliminary report was December 31, 1985.

Females comprise the majority (82%) of the HAP cohort of 1132 persons. Forty-two percent of the eligible females were regular employees, and 58% were temporary employees. The participation rate among females was higher for regular employees than for temporary employees (86% vs 71%).

Sixty percent of the males were regular employees, and 40% were temporary. As was the case with the females, the participation rate was higher among regular employees than among temporary employees (85% vs 63%).

Information needed for the calculation of person-years of follow-up, and thus of expected numbers of cancers, was available for all of the participants and for 91% of the non-participants.

Table 2 lists the 26 cancers observed to date in the HAP cohort. Site of the cancer, sex, year and age at diagnosis, prior cancers and dates, and participation status are shown. Twenty-one of the cancers occurred in the regular employees, and 5 in the temporary employees. A description of the pathology study designed to verify the diagnoses of cancer is provided in the appendix.

Ten of the twenty-six cancers were breast cancers. For each of the individuals with breast cancer, Table 3 diagrams the date of diagnosis in relation to the length of employment and the period of ETO use. Table 4 contains additional information about these ten breast cancer cases. Rough estimates of duration of potential exposure to ETO and latency of breast cancer diagnosis from start of potential exposure can be made from these tables. As discussed in previous communications, ETO monitoring at the plant during the period of ETO use was intermittent. Thus, more accurate statements about dose or duration of exposure cannot be made (Stolley et al., 1984).

Tables 5 and 6 provide information on person-years of follow-up as a function of age for regular and temporary employees, respectively. The regular female employees were, on the whole, older during the follow-up period than the regular male employees. These women were also older than the male or female temporary employees.

The age distribution of non-participant person-years did not appear to differ substantially from that of the participant person-years, except, perhaps, for the male regular employees. For this group, the participants are somewhat younger than the non-participants. When follow-up to last interview and

follow-up to 12/31/85 are compared, it can be seen that with the longer follow-up (to 12/31/85) the number of person-years of follow-up increases, thus increasing the number of expected cancers with longer follow-up.

Observed and expected numbers of cancers are compared in Tables 7, 8 and 9. The analysis in Table 7 relates to participants only, with follow-up to either date of last interview, date of the diagnosis of interest, or death. Expected numbers of cancers in Tables 8 and 9 derive from follow-up of both participants and non-participants. For Table 8, follow-up for participants ends at date of last interview, at the diagnosis of interest, or death. For non-participants, follow-up ends either at the date of the diagnosis of interest, at death, or at 12/31/85. For Table 9, follow-up ends at the date of the diagnosis of interest, at death, or at 12/31/85 for all individuals and assumes the longest follow-up for the cohort. In all cases the date of the diagnosis of interest refers to the first occurrence of that diagnosis within the follow-up period.

For Tables 7, 8 and 9, data are presented for regular and temporary employees and for the two groups combined (Total). For females, observed and expected numbers of breast cancers, all cancers except breast cancer, and all cancers are compared. There were only 2 cancers in males; thus the analysis for males is presented for all cancers.

The observed number of breast cancers was significantly greater than expected for the regular female employees in all three analyses. The ratio of observed to expected breast cancers varied from 2.55 (Table 7) to 2.31 (Table 8) to 2.11 (Table 9), depending on the definition of the study group and the length of follow-up. The corresponding P-values associated with the comparisons of observed and expected breast cancers were 0.02 (Table 7), 0.03 (Table 8) and 0.04 (Table 9). P-values remained statistically significant for the total group of

regular and temporary females combined. Observed breast cancers were not significantly elevated above expected in the temporary group.

In none of the comparisons of observed and expected numbers of all cancers as a group was the observed number of cancers significantly greater than expected. The results for all other cancers except breast cancer in females were obtained by subtracting the observed and expected breast cancers from the corresponding values for all cancers. The observed number of all other cancers except breast cancer was approximately equal to or lower than expected in all comparisons.

Considered together, the two cancers in males were not significantly different from expected in any analysis. Tables 10 and 11 compare observed and expected cancers for males and females respectively for all of the sites described in the SEER report. As can be seen in Tables 10 and 11, at the time this preliminary report was prepared, no statistically significant increase was observed in males or females for any of the neoplasms suggested as associated with ETO based on previous animal and human published studies (leukemias, stomach cancer, and brain neoplasms) (Lynch et al., 1984; Hogstedt et al., 1979 a and b, 1986; Morgan et al., 1981; Snellings et al., 1984).

The two cases of cancer not included in Table 10 and 11 were identified by the initial report of the New York State Cancer Registry. They were both in women. One was an in situ cancer of the cervix and the other was a multiple myeloma. Cases received at the New York State Cancer Registry through March of 1985 have been computerized, but because of delays in reporting, the 1984 and 1985 files are incomplete.

IV. DISCUSSION

Comparison of observed numbers of cancers to date with those expected in the HAP cohort has demonstrated a statistically significant elevation of breast

cancer cases over the number expected in the regular female employees. This finding was obtained with several different methods of computing the expected numbers of cancers. No statistically significant excess of breast cancer was noted for the temporary female employees. Until data from the New York State Cancer Registry on cancers in the non-participant group are complete, all of the analyses must be considered preliminary.

No minimum time period for the development of detectable cancer after onset of potential ETO exposure (latency period) has been assumed for the calculations presented in this report. Studies of cancer cell growth and radiological evidence suggest that the time from tumor initiation to detection can sometimes be lengthy, but this is highly variable (Buchanan et al., 1983). With specific reference to breast cancer, it has been stated that the average breast carcinoma takes about ten years to become one centimeter in diameter (Hall, 1986). That is the size generally accepted as clinically detectable. A review of the literature on this subject suggests that approximately 30 doublings of the number of cells occur between the time a cell turns cancerous and the time a clinically detectable size of one centimeter is reached. The estimated doubling times for breast cancer cells have been reported to range from 30 to more than 200 days (Fisher, 1984). Thus, the estimated range around the above mentioned ten year estimated average could be from approximately 2.5 to 20 years for a cancer to develop to a clinically detectable size from the onset of abnormal growth.

Reviewing the ten observed breast cancers, the date of onset of ethylene oxide exposure and their date of diagnosis, and applying the estimated average of ten years to achieve a clinically detectable size of one centimeter suggests that the onset of each of these ten cases could have predated the onset of their ethylene oxide exposure. The application of a latency period utilizing the concept of a doubling time that relies on extrapolation and mathematical modeling

and which results in such a broad range (2.5-20 years) of possibilities for the estimated time of tumor detection has obvious limitations. If one assumes that there is a causal relationship between ETO exposure and breast cancer and that there is a minimum latency period, for example, two years, between exposure and the diagnosis of breast cancer, then it would be appropriate not to count cases of breast cancer until two years after the start of potential exposure. If this assumption is correct, analyses that use a latency period will be more sensitive than analyses that assume no latency period. The time elapsed from presumed exposure to breast cancer diagnosis in at least one of the cases is too brief (12 months) to be consistent with a possible ETO etiology in all probability. An exploratory analysis incorporating a two-year latency period deleted this case while reducing the total person-years at risk, and produced similar results to those reported above.

An association between ethylene oxide exposure and breast cancer was not hypothesized in advance of this study. Thus, information on the standard risk factors for breast cancer was examined for the ten individuals with breast cancer in the HAP cohort to see if other factors might account for the findings (Kelsey, 1979). No unusual distribution of risk factors for breast cancer was noted and, in fact, the group as a whole appeared to be largely free of the known risk factors for breast cancer. There was no increase in all other cancers except breast cancer as a group in either the regular or temporary female employees.

At the time this preliminary report was prepared, no statistically significant increase was observed in either males or females for any of the neoplasms suggested as associated with ethylene oxide based on previous animal and human published studies (leukemias, stomach cancer, and brain neoplasms). The New York State Cancer Registry has identified one case of multiple myeloma.

V. CONCLUSIONS

The finding of an increase of observed breast cancer cases over expected in the females classified as regular employees at Worksite III requires further investigation. Because the data are preliminary and because information about presumed ETO exposure is sparse, one must carefully evaluate this finding and consider it inconclusive at this time.

The question as to whether or not there is a causal relationship between ethylene oxide exposure and these breast cancers is a difficult one. The answer is unknown at present. The histopathological appearance of the tumors is not unique, nor is there an appearance common to all tumors. The data have a variety of limitations related to latency period, length of follow-up, lack of accurate historical exposure information and statistical considerations. The possibility of a statistically significant finding arising by chance must always be considered, particularly when statistical tests are done for many types of cancers. The cases have, by and large, no other important risk factors for this particular tumor, such as a strong family history, nulliparity, etc.

Regarding the cancers previously hypothesized as associated with ETO exposure - leukemia, stomach cancer, and brain cancer - it is noteworthy that no significant increase in leukemia has been found and no cases of stomach or brain cancer have been observed to date in this cohort.

Steps to pursue this initial observation will include continuing searches for any possible additional cancer cases using the New York State Cancer Registry; continuing ascertainment of cases through interview and examination of former Worksite III employees; continuing efforts to recruit non-participants; and continuing death certificate searches. In addition, cytogenetic data on sister-chromatid exchange and aberration rates for the individuals with breast cancer, where available, will be examined to determine whether there is any

relationship between cytogenetic factors and these cases. Numbers of observed and expected cases of cancer will be projected over time. Finally, studies such as the NIOSH cohort mortality study of workers exposed to ETO at sites throughout the United States may shed some additional information about the possible relationship of ETO to breast cancer among populations thought to be occupationally exposed to ETO in the past.

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TABLE 1
HEALTH APPRAISAL PROJECT
NUMBER OF PERSONS AND PERSON-YEARS ENTERING INTO COMPUTATION OF EXPECTED CANCER RATES

	Regular Employees			Temporary Employees			Overall Totals
	Participants	Non-Participants	Total	Participants	Non-Participants	Total	
Eligible Males	104	18	122	51	30	81	203
Eligible Females	338	53	391	383	155	538	929
Total Number Eligible for Study ^a	442	71	513	434	185	619	1132
Number of Employees Entering into Computation ^{b,c}	442	49	491	434	183	617	1108
Number of Person-Years Entering into Computation, Assuming Follow-up to Death, or to Diagnosis of Cancer, or to 12/31/85	4150	309	4559	2951	1192	4143	8682

^a 8 persons in the HAP study were not eligible for this analysis because they were not employed between 7/1/74 and 9/30/80, the period of LTD use.

^b 24 non-participants were excluded from person-year calculations because birthdate was not available.

^c Exact start of employment dates were unavailable for 16 persons. An estimated start date was used.

TABLE 2

MAP CANCERS DIAGNOSED AFTER JULY 1, 1970

	Sex	Year of Diagnosis	Site of Cancer	Age at Diagnosis	Prior Cancers/Date	Participant or Non-Participant
Regular Employees	F	1975	Breast	57	Cervix/1961	P
	F	1978	Breast	48		P
	M	1978	Skin	42		P
	F	1978	Colon	50		P
	F	1978	Colon	45		P
	F	1980 (1983 recurrent)	Skin	59	Skin/1973	P
	F	1980	Breast	55		P
	F	1985	Skin	56		P
	F	1981	Cervix	57		P
	F	1981 ^a	Multiple Myeloma	56		P
	F	1982	Breast	53		NP
	F	1982	Bladder	30		P
	F	1982 (1984 recurrent)	Skin	54	Skin/1971	P
	F	1977 ^b	Corpus Uteri ^b	58		P
	F	1983 (1985 Skin)	Breast	67		NP
	F	1983 ^b	Pancreas ^b	54		P
	F	1983	Renal Pelvis	57		P
	F	1983	Breast	59		P
	F	1984	Breast	59		P
	F	1984	Breast	47		P
M	1983 ^b	Lung	57		NP	
Temporary Employees	F	1981	Acute myelogenous leukemia	37		NP
	M	1981 ^b	Pancreas	41		NP
	F	1983 ^a	In Situ Cervix Uteri	31		NP
	F	1984	Breast	47		NP
	F	1985	Breast	41		P

^a Identified through New York State Cancer Registry

^b Information on primary site and/or date of diagnosis was obtained from the New York State Cancer Registry.

TABLE 3
EMPLOYMENT PERIOD, EMPLOYMENT DURATION, AND DIAGNOSIS OF BREAST CANCER IN COMBINED EMPLOYEE GROUP

PERIOD OF USE OF ETO AT WORKSITE III

Employees listed to agree with data in TABLE #2.	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	85	
1.	—————											X				
2.			—————													
3.				—									X			
4.								—————						X		
5.					—————						X					
6.					—————							X				
7.					—————											
8.	—————															
9.								○						X		
10.										○					X	

————— = EMPLOYMENT DURATION
 ○ = VERY BRIEF EMPLOYMENT DURATION
 X = TIME OF CA DIAGNOSIS

TABLE 4
HEALTH APPRAISAL PROJECT - PRELIMINARY REPORT ON BREAST CANCER CASES

	<u>Age at Diagnosis</u>	<u>Date Diagnosed</u>	<u>Date Reported</u>	<u>Months of Employment During ETO Use</u>	<u>Latency Period #</u>	<u>Smoking History</u>	<u>Number of Pregnancies</u>	<u>History of Breast Cancer</u>
1.	67	8/83	Oct. 15/84	74 months	109 months	+	5	
2.	57	7/75	June 2/84	12 months	12 months	-	2	
3.	59	3/83	June 23/83	3 months	100 months	-	4	
4.	59	7/84	July 84	10 months	78 months	-	5	
5.	55	11/80	Nov. 9/87	81 months	83 months	+	5	
6.	53	7/82	Oct. 18/83	6 months	85 months	+	2	None
7.	48	5/78	Oct. 4/82	32 months	32 months	+	5	
8.	47	8/84	Dec. 4/84	74 months	121 months	+	3	
9.	47	6/84	Aug. 24/84	.75 months	77 months	-	5	
10.	41	5/85	May 30/85	.58 months	56 months	+	6	

Latency Period - Number of months between date of employment and diagnosis, or, if employed prior to the start of ETO, from 1/01/74 to diagnosis.

TABLE 5
 PERSON-YEARS BY AGE^a AS A PERCENTAGE OF PERSON-YEARS OBSERVED
Regular Employees

Age During Follow-up	Participants				Non-Participants	
	Males To Last Interview %	Males To 12/31/85 %	Females To Last Interview %	Females To 12/31/85 %	Males To 12/31/85 %	Females To 12/31/85 %
15-19	2	2	2	2	1	2
20-24	16	14	14	13	6	11
25-29	25	25	17	17	13	15
30-34	17	19	9	9	9	12
35-39	10	11	8	8	15	9
40-44	5	6	9	9	19	7
45-49	5	5	10	10	4	12
50-54	8	8	11	11	6	14
55-59	6	6	11	11	9	14
60-64	3	3	8	8	9	4
65-69	1	1	7	3	6	0
70-74	.1	.1	.3	.4	3	0
Total ^b	100	100	100	100	100	100
Total Number of Person-Years	894	994	2888	3156	79	310

^a Age for each subject is age during follow-up, so a person may contribute person-years to more than one age category.

^b Percentages may not add to 100 due to rounding.

TABLE 6
 PERSON-YEARS BY AGE^a AS A PERCENTAGE OF PERSON-YEARS OBSERVED
Temporary Employees

Age During Follow-up	Participants				Non-Participants	
	Males To Last Interview %	Males To 12/31/85 %	Females To Last Interview %	Females To 12/31/85 %	Males To 12/31/85 %	Females To 12/31/85 %
15-19	1	1	4	4	0	4
20-24	10	16	21	29	16	20
25-29	31	31	25	27	28	27
30-34	10	20	11	12	20	16
35-39	6	7	0	0	13	7
40-44	7	7	7	7	13	7
45-49	4	4	5	5	4	5
50-54	5	4	4	4	4	7
55-59	6	5	3	3	2	3
60-64	5	5	2	2	0	2
65-69	1	1	1	1	0	0
70-74	0	0	0	0	0	0
Total ^b	100	100	100	100	100	100
Total Number of Person-Years	327	369	2312	2582	700	992

^a Age for each subject is age during follow-up, so a person may contribute person-years to more than one age category.

^b Percentages may not add to 100 due to rounding.

TABLE 7
OBSERVED AND EXPECTED NUMBER OF CANCERS
PARTICIPANTS

FOLLOW-UP TO DATE OF LAST INTERVIEW, TO DEATH, OR TO THE FIRST OCCURRENCE OF THE DIAGNOSIS OF INTEREST

		Breast Cancers Females	All Cancers Except Breast Cancer Females	All Cancers Females	All Cancers Males
Regular Employees	Observed	0	6	14	0
	Expected	3.14	6.74	9.00	1.74
	P-Value ^a	0.02	0.66	0.13	1.00
	O/E	2.55 (1.31 to 4.90) ^b	0.89	1.42	0
Temporary Employees	Observed	2	0	2	0
	Expected	1.02	2.30	3.32	0.50
	P-Value ^a	0.27	1.00	0.04	1.00
	O/E	1.96	0	0.60	0
Total	Observed	10	6	16	0
	Expected	4.16	9.04	13.20	2.32
	P-Value ^a	0.01	0.09	0.25	1.00
	O/E	2.40 (1.32 to 4.37) ^b	0.66	1.21	0

^a P-values are one-sided tests based upon the Poisson distribution.

^b Confidence intervals for the relative rate are 95% two-sided intervals calculated by the method described by Monson (1980).

TABLE 8

OBSERVED AND EXPECTED NUMBER OF CANCERS

PARTICIPANTS AND NON-PARTICIPANTS

PARTICIPANTS: FOLLOW-UP TO DATE OF LAST INTERVIEW, TO DEATH, OR TO THE FIRST OCCURRENCE OF THE DIAGNOSIS OF INTEREST

NON-PARTICIPANTS: FOLLOW-UP TO DEATH, TO THE FIRST OCCURRENCE OF THE DIAGNOSIS OF INTEREST, OR TO 12/31/85

		Breast Cancers Females	All Cancers Except Breast Cancer Females	All Cancers Females	All Cancers Males
Regular Employees	Observed	0	0	16	1
	Expected	3.47	7.37	10.04	2.09
	P-Value ^a	0.03	0.46	0.00	0.00
	O/E	2.31	1.09	1.40	0.40
		(1.10 to 4.54) ^b			
Temporary Employees	Observed	2	2	4	1
	Expected	1.40	3.11	4.51	0.70
	P-Value ^a	0.41	0.02	0.66	0.54
	O/E	1.43	0.64	0.89	1.20
Total	Observed	10	10	20	2
	Expected	4.87	10.48	15.35	2.87
	P-Value ^a	0.03	0.60	0.15	0.70
	O/E	2.05	0.95	1.30	0.70
		(1.12 to 3.75) ^b			

^a P-values are one-sided tests based upon the Poisson distribution.^b Confidence intervals for the relative rate are 95% two-sided intervals calculated by the method described by Monson (1980).

TABLE 9
OBSERVED AND EXPECTED NUMBER OF CANCERS
PARTICIPANTS AND NON-PARTICIPANTS
FOLLOW-UP TO DEATH, OR TO THE FIRST OCCURRENCE OF THE DIAGNOSIS OF INTEREST, OR TO 12/31/85 FOR ALL

		Breast Cancers Females	All Cancers Except Breast Cancer Females	All Cancers Females	All Cancers Males
Regular Employees	Observed	8 ✓	8	16	1
	Expected	3.79	0.07	11.06	2.32
	P-Value ^a	0.04	0.56	0.15	0.90
	O/E	2.11	0.99	1.35	0.43
		(1.07 to 4.15) ^b			
Temporary Employees	Observed	2	2	4	1
	Expected	1.53	3.44	4.97	0.85
	P-Value ^a	0.45	0.86	0.73	0.57
	O/E	1.31	0.58	0.80	1.18
Total	Observed	10	10	20	2
	Expected	5.32	11.51	16.03	3.17
	P-Value ^a	0.04	0.71	0.25	0.82
	O/E	1.88	0.87	1.19	0.63
		(1.02 to 3.46) ^b			

^a P-values are one-sided tests based upon the Poisson distribution.

^b Confidence intervals for the relative rate are 95% two-sided intervals calculated by the method described by Monson (1980).

TABLE 10

OBSERVED AND EXPECTED NUMBER OF CANCERS BY SITE

MALES
PARTICIPANTS AND NON-PARTICIPANTS^a

<u>SITE</u>	<u>OBSERVED</u>	<u>EXPECTED</u>	<u>P-VALUE^b</u>
Buccal cavity and pharynx	0	0.17	1.0
Stomach	0	0.08	1.0
Colon	0	0.23	1.0
Rectum	0	0.13	1.0
Pancreas	1	0.07	0.07
Larynx	0	0.08	1.0
Lung and bronchus	1	0.62	0.46
Melanoma of skin	0	0.14	1.0
Breast	0	0.006	1.0
Prostate gland	0	0.27	1.0
Urinary bladder	0	0.16	1.0
Kidney and renal pelvis	0	0.08	1.0
Brain and CNS	0	0.08	1.0
Hodgkin's disease	0	0.06	1.0
Non-Hodgkin's lymphomas	0	0.12	1.0
Leukemias	0	0.09	1.0

^a The follow-up period is the same as that specified in Table 8. For participants, follow-up ends at the date of last interview, or at death, or at the first occurrence of the diagnosis of interest. For non-participants, follow-up ends at death, or at the first occurrence of the diagnosis of interest, or at 12/31/85.

^b P-values are one-sided tests based upon the Poisson distribution.

TABLE 11

OBSERVED AND EXPECTED NUMBER OF CANCERS BY SITE

FEMALES
PARTICIPANTS AND NON-PARTICIPANTS^a

<u>SITE</u>	<u>OBSERVED</u>	<u>EXPECTED</u>	<u>P-VALUE^b</u>
Buccal cavity and pharynx	0	0.37	1.0
Stomach	0	0.19	1.0
Colon	2	1.06	0.29
Rectum	0	0.45	1.0
Pancreas	1 ^c	0.26	0.23
Larynx	0	0.10	1.0
Lung and bronchus	0	1.49	1.0
Melanoma of skin	0	0.63	1.0
Breast ^d	10	4.87	0.03
Cervix uteri	1	0.78	0.54
Corpus uteri	1 ^c	1.36	0.74
Ovary	0	0.80	1.0
Urinary bladder	1	0.24	0.21
Kidney and renal pelvis	1	0.20	0.18
Brain and CNS	0	0.26	1.0
Hodgkin's disease	0	0.19	1.0
Non-Hodgkin's lymphomas	0	0.40	1.0
Leukemias	1	0.28	0.24

^a The follow-up period is the same as that specified in Table 8. For participants, follow-up ends at the date of last interview, or at death, or at the first occurrence of the diagnosis of interest. For non-participants, follow-up ends at death, or at the first occurrence of the diagnosis of interest, or at 12/31/85.

^b P-values are one-sided tests based upon the Poisson distribution.

^c Confirmation of the primary site came from the initial report of the New York State Cancer Registry.

^d See Table 8 for a more detailed analysis of the breast cancers.

APPENDIX

Pathology Review

Health Appraisal Project

I. Objectives

The objective of this study was to obtain an independent pathology review of the cancers arising in the Health Appraisal Project (HAP) cohort after July 1, 1974, the start of ETO use at Worksite III.

Of the 24 known cancers in this cohort at the time the pathology study was conducted*, 10 were cancers of the breast. Thus, two separate studies were initiated - a breast cancer study and a review of the other cancers.

The objectives of the breast cancer study were to:

- 1) Verify the diagnosis of breast cancer.
- 2) Examine the distribution of histologic types to determine whether an unusual grouping of cell types was present.

* The New York State Cancer Registry data, received after the pathology review was completed, identified 2 additional cancers, one multiple myeloma and one in situ cervical cancer.

The objective of the review of the remaining 14 cancers was to verify the diagnosis of cancer.

II. Breast Cancer Study

A. Method

Dr. Virginia LiVolsi, Director, Department of Surgical Pathology, Hospital of the University of Pennsylvania, performed the slide review.

Upon receiving written consent from each of the individuals, the pathology reports and slides for all ten of the HAP breast cancers were requested by the HAP office and sent to the Clinical Epidemiology Unit at the University of Pennsylvania. Ten sets of control breast cancer slides, along with pathology reports, were obtained from a Philadelphia hospital. The control series was chosen to be similar in age distribution and in diagnosis to the breast cancers from the HAP cohort. The purpose of the control series was to mask the origin of the slides to prevent overreading of slides from the HAP.

Each set of slides was randomly assigned a code number from 1 to 20. Identifying hospital information on each slide was covered, and the slides were identified only by the randomly assigned code number, along with a letter of the alphabet to indicate the order of slides within a set.

The protocol used by Dr. LiVolsi to describe the pathology is attached (Attachment A). After all of the slides were read, the code was

broken. The hospital diagnoses, as obtained from the pathology reports, and Dr. LiVolsi's readings were compared.

B. Results

Table 1 shows the source of the slides, the hospital diagnoses and the results of the pathology review. The diagnosis of cancer was confirmed in each case. For all individuals except Code #11, the results of the pathology review and the original diagnosis were in agreement. Terminology differences for Code #13 and Code #18 were considered by Dr. LiVolsi inconsequential for this review. No unusual clustering of atypical cells or tissue suggestive of a particular action of a toxin was found.

Dr. LiVolsi reviewed the slides for Code #11 after they had been unmasked and, in addition, requested the autopsy report and slides. Upon review of the complete set of autopsy slides, she concluded that Code #11's cancer was a breast primary. This diagnosis was in agreement with the autopsy report.

Receptor assays were available for five of the ten HAP breast cancers. Three were positive and two were negative.

Dr. LiVolsi's report is attached (Attachment B).

Table 1Breast Cancer Pathology Review

<u>Code #</u>	<u>Source</u>	<u>Hospital Diagnosis</u>	<u>Pathology Review</u>
1	Control	Infiltrating duct carcinoma	Infiltrating duct carcinoma
2	HAP	Infiltrating lobular carcinoma	Infiltrating lobular carcinoma
3	Control	Infiltrating ductal carcinoma	Infiltrating duct carcinoma
4	HAP	Infiltrating duct adenocarcinoma growing in medullary pattern	Infiltrating carcinoma with features of atypical medullary carcinoma
5	HAP	Moderately differentiated ductal carcinoma of right breast	Infiltrating duct carcinoma
6	Control	Infiltrating duct carcinoma	Infiltrating duct and intraductal carcinoma
7	Control	Infiltrating duct carcinoma	Infiltrating duct carcinoma
8	HAP	Infiltrating duct cell carcinoma of breast	Infiltrating duct carcinoma
9	HAP	Infiltrating duct carcinoma	Infiltrating duct carcinoma
10	Control	Infiltrating ductal carcinoma of breast	Infiltrating duct carcinoma
11	HAP	No malignancy in breast. Metastatic poorly differentiated adenocarcinoma in axillary lymph nodes	Infiltrating duct carcinoma all over nodes and perinodal soft tissue. Only focal intraductal in breast
12	Control	Infiltrating duct carcinoma	Infiltrating duct carcinoma
13	Control	Carcinoid tumor of breast	Infiltrating duct carcinoma with funny trabecular pattern

Table 1 (continued)

Breast Cancer Pathology Review

<u>Code #</u>	<u>Source</u>	<u>Hospital Diagnosis</u>	<u>Pathology Review</u>
14	HAP	Infiltrating duct carcinoma, of mixed medullary and scirrhous type	Infiltrating duct carcinoma
15	Control	Massive infiltrating ductal carcinoma of breast	Infiltrating duct carcinoma
16	Control	Infiltrating ductal carcinoma of breast	Infiltrating duct carcinoma
17	Control	Infiltrating carcinoma, predominantly ductal, with lobular features	Infiltrating duct carcinoma
18	HAP	Carcinoma, undifferentiated	Infiltrating duct carcinoma
19	HAP	Infiltrating duct carcinoma	Infiltrating duct carcinoma
20	HAP	Infiltrating duct carcinoma	Infiltrating duct carcinoma

III. Review of Other Cancers

A. Method

There were 14 cancers other than breast cancer. Pathology reports were available for nine of these, and slides for eight. The one cancer with a pathology report but no slide was a basal cell epithelioma of the skin of the nose.

Of the five individuals with no pathology reports, four were deceased. The cancer sites, as stated on the death certificate, for these four were lungs and liver; lung; pancreas; and acute myelogenous leukemia. At present, no decision has been made about contacting next-of-kin for permission to access medical records. From information obtained from the New York State Cancer Registry, it was determined that, for the person whose death certificate stated lungs and liver, the primary site was corpus uteri. For the other three deceased individuals, the sites stated on the death certificate agreed with the New York State Cancer Registry report. The fifth individual with no pathology report did not sign a release of information because the cancer (skin) was first diagnosed before start of employment at Worksite III.

The available slides were not masked and were given to Dr. LiVolsi along with information on the site of the biopsy or the assumed primary.*

* At the time of writing this report, a slide for another basal cell carcinoma was received. This was a second cancer for one of the individuals with breast cancer. Dr. LiVolsi confirmed the diagnosis of basal cell carcinoma. Thus, her report refers to nine patients with non-mammary cancers, while this report states that slides were reviewed for 8 persons.

B. Results

Table 2 shows the site of each of the eight cancers reviewed, the hospital diagnosis and the results of the pathology review. The diagnosis of cancer was confirmed in each case.

Table 2

Review of Other HAP Cancers

<u>Code #</u>	<u>Site*</u>	<u>Hospital Diagnosis</u>	<u>Pathology Review</u>
21	Bladder	Papillary transitional cell carcinoma	Papillary transitional cell carcinoma
22	Colon	Carcinoid of colon	Adenocarcinoma compatible with colonic primary but there was no evidence of pre-existing lesions or colonic mucosa in the four slides
23	Colon	Markedly infiltrating moderately differentiated primary papillary adenocarcinoma	Moderately differentiated adenocarcinoma
24	Skin (lower right eyelid)	Basal cell carcinoma	Basal cell carcinoma
25	> Skin (face)	Basal cell carcinoma	Basal cell carcinoma
26	Liver	Metastatic moderately differentiated adenocarcinoma	Moderate to poorly differentiated adenocarcinoma, compatible with pancreatic or biliary origin or possibly stomach or other sites
27	Renal pelvis	Papillary transitional cell cancer of renal pelvis	Transitional cell carcinoma, partially papillary
28	Cervix (primary)	Undifferentiated carcinoma of vaginal apex, undifferentiated carcinoma of trigone of urinary bladder, and poorly differentiated adenosquamous carcinoma of omentum, appendix vermiformis and abdominal wall following adenosquamous carcinoma of cervix	Poorly differentiated squamous cell carcinoma; can't tell exact site of primary from slides. Compatible with cervical primary

*Site of the biopsy or the assumed primary

Proposed Protocol for Pathologic Variables - Breast Cancer slides
(Johnson & Johnson study)

Gross features

1. Size
2. Borders (circumscribed, infiltrative)

Histologic features

1. Tumor type (or types if combined features)
2. Tumor border (circumscribed, infiltrative)
3. Cell reaction to tumor
 - slight - none
 - moderate
 - marked
4. Tumor necrosis
 - present
 - absent
5. Tumor stroma
 - slight
 - moderate
 - marked
6. Histologic grade
 - 1, 2, 3
7. Nuclear grade
 - 1, 2, 3
8. Lymphatic involvement
9. Perineural involvement
10. Skin involvement
11. Fascial involvement
12. Nipple involvement
13. Intraductal carcinoma
 - in tumor
 - away from tumor
14. Lobular carcinoma-in-situ
 - present
 - absent
15. Associated lesions
 - cysts - yes or no
 - apocrine change - yes or no
 - sclerosing adenosis - yes or no
 - papillary duct changes - yes or no
 - lobular hyperplasia - yes or no
 - intraductal papilloma - yes or no
 - fibrosis - yes or no
 - atrophy - yes or no
16. Lymph nodes
 - not available
 - available
 - number
 - metastasis - yes or no
 - sinus histiocytosis
 - follicular hyperplasia
 - fatty replacement



UNIVERSITY of PENNSYLVANIA
MEDICAL CENTER

PATHOLOGY AND LABORATORY MEDICINE
CLINICAL PRACTICE

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November 12, 1985

TO: Paul D. Stolley, M.D., M.P.H.
Professor of Medicine and Research Medicine
229L Nursing Education Building/S2

FROM: V. A. Livolsi, M.D.
Director, Surgical Pathology

SUBJECT: Johnson & Johnson Study

I examined coded microscopic slides from ten cases from the Johnson & Johnson exposed population interspersed with ten cases of controls from Pennsylvania Hospital obtained via the auspices of Dr. Miles M. McFarland. Before the onset of the study and during my review of the slides I had no idea which cases were the controls and which were the Johnson & Johnson patients.

I examined the slides and filled out a form on each of them (this form listed many gross and especially microscopic parameters which were evaluated; copy enclosed). Except for case #11 in which the primary site was not obviously present in the breast, I confirmed the cancer diagnosis in all cases and in most cases agreed exactly with the original diagnosis. (One exception was the case that had been called carcinoid tumor of the breast by Pennsylvania Hospital which I thought was an unusual trabecular tumor of the breast, but since I don't make the diagnosis of carcinoid tumor I just included it as an infiltrating carcinoma.)

The difficult case was case #11 in which the patient presented apparently with an axillary node which was biopsied and felt to be consistent with a breast primary. She then underwent a mastectomy and had numerous lymph nodes positive in the axilla and, in the numerous sections of breast which were thought was probably diagnosable as intraductal carcinoma; however, there was no invasive cancer. My question was, on the initial review of the slides, whether or not the lesion represented in slide K of the coded slides was indeed the biopsy site and had been the primary or whether the patient had had cancer on the opposite side. I felt that this tumor represented a breast cancer since this is statistically most likely in a woman who presents with an axillary metastasis. I rereviewed the case on October 19, 1985, after decoding of slides: initial biopsy shows metastatic poorly differentiated carcinoma in node (really a node). Mastectomy of no help; no definite primary. In one

Paul D. Stolley, M.D., M.P.H.

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slide of axillary nodes S83-2751C an extranodal focus is present, but no breast tissue is present. It is possible the primary was high in the axilla, and very small. Autopsy slides were obtained (54 slides Roswell Park #A15259) and reviewed. Widespread tumor similar to that in axillary nodes was found in bones, lungs, brain, etc.; no other obvious primary site was found. Hence, I conclude this was a breast primary.

The second important finding to my mind was that despite the fact that I had the opportunity to look at varying numbers of slides on each of these cases, it appeared to me that I could not detect (either from the grade of the tumor, the type of the tumor, or the surrounding breast tissue) any changes which were out of the ordinary and would have made me suspect that these were in fact the cases which had come from individuals who had been exposed patients. But this is true in the ordinary day-to-day practice of surgical pathology and there was nothing unusual that indicated to me that I could tell the difference between the test and the control cases.

I subsequently examined unmarked slides from nine patients with nonmammary cancers of various sites. In each instance, the carcinoma diagnosis was confirmed.

nb
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ENVIRONMENTAL
HEALTH & SAFETY

JUN 20 1986

Attachment 3

May 16, 1986

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In the March 28, 1986 article by C. Hogstedt, L. Aringer and A. Gustavsson entitled "Epidemiology Support for Ethylene Oxide as a Cancer-Causing Agent" ¹, the authors assert that there is a strong indication that ethylene oxide is a carcinogen even at low-level exposures. The evidence presented in the article to substantiate this claim is very weak and certainly leads no credence to the authors' theory.

The major piece of supporting evidence for this claim appears to be the results of the study at plant 3, where there was one leukemia death versus 0.16 expected. The single case of leukemia for plant 3 occurred in group C, where workers had multiple chemical exposures and the lowest ethylene oxide exposures. What does stand out as significant is the fact that for all three plants the leukemia cases were observed in individuals with multiple chemical exposure and that no leukemia was observed in exposure groups A and B at plant 3, where exposure was limited to ethylene oxide. Further, if a true dose response relationship exists, then it would seem logical that cases for similar causes of death in the higher exposure categories for plant 3 would be observed. The authors offer as an explanation that "a strict application of experimentally well-defined single exposures would invalidate most epidemiologic studies." What is apparently overlooked is the lack of leukemia cases and overall mortality for workers in groups A and B at plant 3. Also overlooked in this study is the lack of leukemia and overall mortality at the plant studied by Morgan et al plant, which is similar to plant 3 in that exposures were generally limited to ethylene oxide.

There were other noteworthy inconsistencies and questionable methodologies in the article. The authors combined leukemia results from three very different plants. The exposures for plants 1 and 2 are considerably higher than plant 3, which would normally preclude comparisons between the plants for similar causes of adverse health. In addition, the types of exposure are extremely different due to the different chemicals and processes utilized at each location. Finally plants 1, 2, and 3 are not

CAM1/b

-1-

comparable from a method of operation standpoint. Plant 1 is a non-production facility, primarily involved in sterilization of equipment. Plants 2 and 3 utilize entirely different production methods, one process is based on epichlorohydrin and the other plant utilizes direct oxygenation. Yet, given these discrepancies and obvious differences the facilities are grouped together as analogous.

If comparisons are to be made between similar facilities then it would be appropriate to compare plant 3 and the ethylene oxide plant in the Morgan et al² study. If the leukemias from these two plants are combined, there is one leukemia death versus 0.86 expected. Although the small numbers prevent one from drawing any conclusions, this result does not indicate an excess. In contrast to plant 2, there were no stomach cancer deaths at either of these plants nor was there an increase of mortality overall. The authors have stated that the low overall mortality at the Morgan plant "indicates selective employment schemes." It is not clear what the statement implies other than to reference the brief preemployment physical examination required of all new employees.

In summary, the authors provide no evidence that exposures to ethylene oxide either at the production plants using the oxygenation process or at low exposure levels causes any increased risk of death.

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¹Hogstedt C, Aringer L, Gustavsson A.: Epidemiologic support for ethylene oxide as a cancer-causing agent. *JAMA* 1986;255:1575-1578.

²Morgan RW, Claxton KW, Divine BJ, et al: Mortality among ethylene oxide workers. *J Occup Med* 1981;23:767-770.

The study, which investigated exposure levels and reproductive outcomes in dental operatories in Georgia between 1978 and 1986, "should provide a basis for increased concern" about the health hazards of nitrous oxide, David Jacobs, an industrial hygienist with the Georgia Institute of Technology told the conference.

An examination of the reproductive outcomes experienced by the study population of 30,000 dentists, dental assistants, and dentists' wives revealed a statistically significant increase in spontaneous abortions when compared with the general population. Spontaneous abortions among dentists' wives were 52 percent above the normal rate. For female assistants, the rate was 230 percent above normal, Jacobs stated.

In addition, female assistants experienced a 58 percent increase in bearing children with congenital abnormalities, he said.

Exposures Above NIOSH Recommended PEL

Monitoring that was performed for the study demonstrated levels of nitrous oxide ranging from 64 parts per million to 659 ppm in the dentists' and assistants' breathing zones. Levels during peak excursion times exceeded 800 ppm, Jacobs added. The National Institute for Occupational Safety and Health recommends an eight-hour time-weighted average of 25 parts per million, he noted.

Levels of nitrous oxide in waiting room areas were found to range between 17 ppm and 533 ppm, according to the monitoring survey.

While a regular air monitoring program is necessary in dental operatories to identify high exposure levels, the best solution for the reduction of exposures is the use of substitutes, he concluded.

Reproductive Hazards

PRELIMINARY RESULTS ON EtO, MERCURY INDICATE OPPOSITE MISCARRIAGE RISKS

DALLAS — (By a BNA Staff Correspondent) — Preliminary results of two separate studies of workers indicated that those exposed to metallic mercury faced an increased risk of spontaneous abortion, but those exposed to ethylene oxide did not, occupational health physicians told an American Industrial Hygiene Conference session on reproductive hazards May 19.

Neither study is complete, nor are they without weaknesses, so interpretations should be made cautiously, the session was told.

A study of workers exposed to EtO at hospitals in western New York State between 1978 and 1984 found no statistically significant increase in spontaneous abortions, when exposed workers were compared with a matched group of non-exposed workers, John E. Vena, professor of social and preventive medicine at State University of New York at Buffalo, told the session.

The study observed a slightly higher average birth weight of live-born children of the exposed workers. On the other hand, he stated, two cancers, melanoma of the skin and lymphoma, were reported by members of the exposed group, while only cancer of the uterus was observed in the non-exposed group.

Vena emphasized that the results are only preliminary, and that the study has not been controlled for cigarette smoking or other confounding factors. In addition, analyses of effects were not conducted according to exposure levels experienced by the workers, he said.

The study may be further weakened, Vena added, because most of the pregnancies occurred prior to employment at the hospitals, which possibly may have reduced the occurrence of adverse reproductive effects.

Mercury Workers

An ongoing study of male workers exposed to metallic mercury from 1953 to 1960 at a uranium processing factory that produced thermonuclear weapons is demonstrating an increased rate of spontaneous abortions among the wives of workers, when exposed workers are compared with a similar group of non-exposed workers, according to Kelly Brix, assistant professor of occupational medicine in the department of environmental and industrial health at the University of Michigan's School of Public Health.

The exposed workers also are experiencing a higher incidence of infertility, according to Brix.

Wives of workers in the exposed group had a 15.1 percent miscarriage rate, while wives of the non-exposed workers reported an 8 percent rate. Mercury-exposed workers demonstrated a 15.6 percent infertility rate versus a 10 percent rate for the non-exposed group.

While Brix described the study as the largest and best-controlled study of mercury-exposed workers, she did acknowledge that the study has some problems. First, workers' recollections of their own exposure history as well as their wives' reproductive history need to be confirmed with employer records, she said.

Second, job titles and duties need to be more carefully analyzed to determine their effect on exposure levels, Brix stated. Finally, some consideration should be made to account for the imperfect recall of husbands in regard to their wives' pregnancies and miscarriages and children's birth weights and birth dates.

The non-exposed group, Brix noted, demonstrated a slightly higher rate of live-born children with congenital defects and serious childhood illnesses. The study has not to date found any statistically significant difference between the number of live-born children, as opposed to stillborn, in either group, although the exposed group did have slightly more live-born offspring, she said.

Enforcement

VOLUNTARY PROTECTION PROGRAMS EFFECTIVE IN REDUCING LOST WORKDAY RATES, OSHA SAYS

DALLAS — (By a BNA Staff Correspondent) — Companies have been able to reduce their lost workday rates by participating in the voluntary protection programs instituted by the Occupational Safety and Health Administration, Margaret Richardson, director of the program, told a session of the American Industrial Hygiene Conference May 21.

Workplaces operating any one of the agency's three voluntary programs consistently have demonstrated "outstandingly" low lost workday rates, which more than justifies operation of the program, she stated.

Statistics compiled by the agency indicate that participants in the "Try" program "can be expected to have lost workday rates 50 percent lower than the rate for their industry as a whole the first year, and 68 percent lower the second year," Richardson told the session.

"Star" program participants "can be expected to have lost workday rates 75 percent lower than the rates for their industry as a whole," she further stated.

Although enforcement may be the key to improving the safety and health records of employers that correct poten-

HIMA Report 78-3

Ethylene Oxide Technical Report
1978 Submission to the Environmental Protection Agency

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May 1978

VI. BENEFITS DERIVED FROM ETO STERILANT USE

A. INTRODUCTION

The arguments advanced in this section clearly establish that the economic, social, and environmental benefits of EtO use significantly outweigh the alleged risks. See 40 C.F.R. 162.11(a)(5)(iii). As fully discussed below, EtO is vital and often irreplaceable as a medical device sterilant. Many essential health care items cannot otherwise be sterilized, nor is it likely that new substitutes will be available in the near future. Additionally, direct and indirect economic costs to the public, the medical professions, and the industry mandate that no further restrictive regulatory controls be imposed. Furthermore, without EtO sterilized devices, it would be more difficult to treat illness and injury and countless lives would be lost that otherwise might have been saved.

The data and information contained in this section of our response establish EtO's indispensable role in maintenance of public health. Similarly, numerous government agencies and officials have attested to the essential nature of EtO sterilized products. For example, in the FDA notice regarding EtO residuals that appeared in the Federal Register, January 27, 1978 (43 Fed. Reg. 3800), the Commissioner of FDA stated that he "... believes that the current use of EtO as a sterilant for certain drug products and medical devices is necessary for the delivery of required health care..."

In 1976, Dr. Theodore Cooper, then the Assistant Secretary of Health of DHEW, in a letter to the Administrator of EPA, stated:

We know of no suitable alternate to ethylene oxide for a number of sterilizing procedures. (Cooper, 1976)

In 1977, Sherwin Gardner, then Acting Commissioner of FDA, stated in a memorandum:

I wish to stress that precipitous actions which would, in effect, severely limit the use of EtO for sterilizing devices or drugs could have a serious impact on the public's health. Many life-saving devices are sterilized by EtO both by industry, as well as individual hospitals or other similar facilities. The continuing availability of such devices is vital.

Acknowledgements similar to these may be found in a number of other recent publications (e.g. Falk et al., 1977 and Glaser, 1977).

B. MEDICAL DEVICES AND SUPPLIES STERILIZED WITH ETO

Pursuant to the requirements of the Medical Device Amendments of 1976 to the Food, Drug, and Cosmetic Act, more than 25,000 medical device products have thus far been registered by over 2100 medical device firms.

It may not be possible to identify every type of medical device sterilized with EtO in hospitals and industry. However, the Association believes that it is important to understand the number and range of medical products treated with EtO and the relationship of these products to the medical and allied health professions.

Attached to the testimony of Dr. Frank B. Engley (Appendix B-3) is a list of representative items treated with EtO in hospitals. This list of 91 items is representative of the significant types of products sterilized in hospitals for patient use. More importantly, the kinds of items listed are key to many critical medical/surgical procedures. In fact, Samuels (1978), estimated that 25 percent of items sterilized in his 300 bed hospital were processed with EtO.

The Association has surveyed its members and developed a list, shown in Appendix A-9, of 248 items that are industrially sterilized. The 248 high volume, essential products listed demonstrate the relative extent and importance of this sterilant's use to the medical device industry and the American public.

C. SUBSTITUTE METHODS OF STERILIZATION

No acceptable substitute methods exist for sterilization of heat-sensitive devices and supplies now sterilized with EtO. Alternative sterilization methods do not exist that can be used by the medical device industry without a major disruption of the health care system.

No substitute methods of sterilization are currently available to industry or to hospitals that would not create unacceptable adverse impacts on the quality of health care in the United States.

1. Industry

Industry's position with regard to substitute methods for EtO sterilization is somewhat different than that of hospitals, but no more hopeful because adequate alternative methods are not currently available.

To place the problem in proper perspective, one must realize that the health care system requires a constant flow of tens of billions of industry-sterilized items representing thousands of different product types. Even the threat of interrupting the flow of products has the potential to create a chaotic situation and endanger the lives of many people. The importance of EtO sterilization processes for industrially sterilized goods cannot be overemphasized. As much as 80% of industrially sterilized medical devices rely on EtO in the sterilization procedure. Finally, in evaluating methods to substitute for EtO, the factor of higher costs, for the public and industry, must be considered.

An evaluation of alternate sterilization methods and the reasons why each is not a viable replacement for EtO is presented below:

- Sterilization with steam under pressure

This method, also known as autoclaving, is a reliable and inexpensive sterilization procedure that is widely used for the sterilization of fluids and heat-stable items. Almost all products capable of being autoclaved are presently sterilized in this manner. However, as presently designed, virtually none of the products sterilized with EtO could withstand the conditions of autoclaving. This is also true of much of the packaging for these products. Redesign of products and packaging to allow autoclaving would require years to achieve, since the basic materials research necessary for development of an array of new, heat resistant and non-toxic materials would have to be conducted. Additionally, the following problems would still have to be overcome:

- Acceptability to the medical community.
- Preclinical and clinical studies to prove safety and efficacy.
- Possible FDA approval.
- Cost of retirement of capital equipment no longer useable.
- Cost and time for acquisition of new manufacturing and processing equipment.

It should be emphasized that in addition to the costs of retiring existing and acquiring new sterilization equipment, many types of molding, cutting, shaping, assembling and packaging machinery would also be involved. Obsolescence of a substantial portion of existing manufacturing equipment and purchase of new capital equipment could potentially bankrupt established firms and, at the very least, would create large cost increases for industry, some of which would necessarily be passed on to the public.

These cost considerations, combined with technological uncertainties and problems of new product approvals, lead to the conclusion that industry would be unable, except in rare instances, to convert to steam sterilization in place of EtO procedures.

- Sterilization with dry heat

Sterilization with dry heat is frequently used for production of sterile medical products. The temperatures required, however, are higher than for autoclaving and material degradation effects are even more severe. Conversion to dry heat processes, therefore, are not feasible for the same reasons applicable to autoclaving.

- Radiation sterilization

Sterilization by exposure to ionizing radiation has potential utility and will perhaps see expanded use in the future. However, substitution of radiation sterilization at this time for any more than a small fraction of products presently processed by EtO is not possible for the following reasons:

- Approval procedures and regulatory restrictions for the use of radiation sterilization will be severe and prohibitive for many products. Existing regulations, for example, require processing a new drug application if radiation sterilization is substituted for the present means of sterilizing a drug already on the market. For some products, the clinical studies required would be very extensive and would require years to complete.
- Many products presently treated with EtO will not withstand radiation treatment. Some polymers, for example, are degraded by embrittlement, discoloration, and loss of tensile strength. Other possible effects have been incompletely studied, including the formation of toxic substances that could exhibit long-term or chronic effects in certain materials.

- The same cost considerations and technological reasons applicable to steam sterilization apply to radiation.
- Even if radiation were a feasible alternate means of sterilization, sufficient radiation equipment will not be available in the near future. Preliminary estimates indicate that existing radiation sterilization plants have capacity to handle no more than two to five percent of the products presently processed with EtO.
- Finally, logistic problems exist which indicate that long lead times are needed to obtain permission to build radiation plants. Even if permission is obtained from Federal and state authorities, gaining permission of local community officials is often a lengthy and uncertain process.

Clearly, immediate and widescale substitution of radiation sterilization for EtO processing is not possible. It is expected that over time a greater array of sterilization methods will be used or become available to the health care system. However, until these methods can be shown to improve health care, lower risks, or lower costs to the American public, EtO use can and must be permitted for sterilization purposes.

2. Hospitals

U.S. hospitals utilize approximately 10,000 EtO sterilization devices and chambers of various sizes and types. An additional unknown number are employed in medical clinics, in practice of dentistry, and other situations related to health care. The principle use of these devices is to minimize infection through effective product sterilization.

Although alternate methods of sterilization exist, including radiation sterilization, formaldehyde gas treatment, and chemical solution treatment, none of these methods are currently available in hospital settings as feasible replacements for EtO.

The types of materials and devices sterilized are almost without exception items whose physical condition and/or composition is such that they would not withstand treatment by other available sterilization methods (primarily steam under pressure and dry heat). As previously discussed, such devices or materials would melt, warp, become brittle or dull, or otherwise be rendered unusable by heat treatment. In many instances, the useful life of very expensive instruments would be seriously reduced. Redesign of the vast array of items sterilized in hospitals by EtO would require many years, and would add tremendous costs to the health care system.

Therefore, steam under pressure, and dry heat sterilization are not practical substitutes for most materials presently treated with EtO.

Radiation sterilization, using Cobalt-60 or accelerated electrons, is not efficient for hospital use, since large processing plants must be built which continuously process products. Radiation sterilization installations of the size and type needed by hospitals are not available, and even if they were, the problems of certifying installations and control of public exposure to radiation sources render their use impractical. Installing them in thousands of hospitals would require many years and high increases in the annual cost of health care.

Formaldehyde gas exhibits sterilization properties and is used to a limited extent in other countries. Formaldehyde sterilization processes, however, are less efficient than EtO processes primarily because of reduced volatility and permeability. These deficiencies also create removal and accrual problems for formaldehyde. Irrespective of this, formaldehyde is not a viable EtO substitute for the following additional reasons:

- The lack of adequate instrumentation and processing.
- Its potential toxicity. Formaldehyde, like EtO, is an alkylating agent and exhibits toxic properties. It would require years for hospitals to learn how to deal with this agent in its gaseous form and to achieve the same level of safety as exists today with EtO. The final result might well be a hazard level of unacceptable magnitude with less efficiency in achieving sterility.

Chemical solution soaking is also unacceptable to hospitals for the following reasons:

- Chemical solution soaks lack the efficiency and the assurance of sterility provided by EtO. Many materials cannot be soaked without damage. Items "sterilized" by chemical soaks would probably be recontaminated by the packaging process.
- Widescale use of chemical soaks would probably create numerous toxic and other hazards since many chemical disinfectants are also alkylating agents and all have toxic properties. The problem with residuals on soaked products would be severe and widescale use would most certainly result in accumulation of persistent toxic chemicals.

A report by the Center for Disease Control (Spaulding, 1971) provides a review of potential substitute chemical disinfectants in relation to their toxicological activities. It is clear from this review, presented in Table 6.1, that all of the candidate chemical substitutes for EtO are less effective and are also toxic.

D. DEPENDENCE OF THE HEALTH CARE SYSTEM ON ETO STERILIZED PRODUCTS

I. General Health Care Statistics

The quality of U.S. health care is dependent on continued hospital and industrial use of EtO. The following is an analysis of the health care services provided in 7,082 U.S. hospitals, as reported by the American Hospital Association (1976). These hospitals have a total of 1,433,515 hospital beds and admit approximately 33,000,000 persons each year. The data presented in Table 6.2 helps in understanding the overall magnitude of patient care offered by hospitals. Table 6.3 presents a breakdown of those patient care procedures which heavily rely on the use of sterile materials.

TABLE 6.2

General Information on 7,082 U.S. Hospitals

1976

Beds	-	1,433,515
Admissions	-	36,775,770
Surgical Operations	-	17,603,529
Births	-	3,067,063
Outpatient visits	-	2,270,951,021

TABLE 6.3

<u>Facility or Service</u>	<u>% of Hospitals Having Facility or Service</u>
Operating Rooms with Recovery Units	76.7
Cardiac ICU's	32.6
Mixed ICU's	65.4
Open-heart Surgery Facilities	9.0
Organ Banks	2.5
Blood Banks	60.4
Respiratory Therapy Units	72.6
Hemodialysis Services - inpatient	13.4
- outpatient	10.7
Burn Care Units	2.7
Emergency Units	78.3
Abortion Services - inpatient	18.3
- outpatient	9.6
TB and Respiratory Disease Units	4.5
Neonatal ICU's	8.1

The above figures on facilities or services, as substantial as they are, do not include activities of private physicians, clinics, nursing homes, etc. which also depend heavily on sterile materials whose sterility is achieved and can only be achieved by EtO. (We have illustrated in Appendix A-10 specific lists of such materials.) They also do not indicate the magnitude of health care products resulting from direct purchase of sterile health care items by the American public (e.g. bandages, disposable syringes, medical cotton, pipettes, etc.)

2. Quantity Of EtO Sterilized Items

A basis for estimating the number of items sterilized by EtO in hospitals has been provided by Cobis (1977). From a survey conducted in 173 VA hospitals (90,000 beds), he determined that these hospitals sterilized approximately five million items for patient use per year. This amounts to an average of almost 29,000 items per hospital per year or 55 items per hospital bed per year. Another study in a private 300 bed hospital, reported EtO sterilization of approximately 60,000 items per year or 200 items per hospital bed per year (Samuels, 1978).

Using the lower VA estimates, the total number of items sterilized with EtO by all U.S. hospitals are:

55 items/hospital bed X 1,500,000 bed = 82,500,000
EtO sterilized items/year

The higher estimate yields a figure of 300,000,000
EtO sterilized items/year.

A conservative estimate would indicate the hospitals sterilize
at least 200 million items per year with EtO.

We further estimate that use of EtO sterilized items by
private clinics, physicians, dentists, veterinarians, research
institutions, and the public in direct purchases equals tens of
billions of items per year.

It must be reemphasized that of these billions of items
sterilized with EtO per year, most could not be sterilized by
other means.

3. Surgeons And Surgical Procedures

To understand the essential nature of EtO relative to medical
care, it is necessary to appreciate the effect EtO's unavail-
ability would have on surgeons and surgical procedures.

Table 6.4 shows the estimated number of U.S. board-certified
surgeons for identified specialties as of 1978.

TABLE 6.4

(Source: Surgery in the U.S., 1975)

<u>Specialty</u>	<u>Number of Surgeons</u>
General surgery	15,638
Neurosurgery	1,779
Obstetrics-gynecology	12,528
Ophthalmology	7,156
Orthopedic surgery	7,637
Otolaryngology	4,333
Plastic surgery	1,177
Thoracic surgery	2,624
Urology	3,959
Colon-rectal surgery	326
	<hr/>
TOTAL	57,151

Of course, operations are performed by physicians who are not certified surgeons. Therefore, the total number of licensed physicians who perform surgical procedures is estimated to be approximately 91,000, with each performing an average of 191 surgical procedures per year. An estimated total of almost 18 million operations are performed yearly in the U.S. All require sterile materials and sterile techniques, and virtually all depend, to some extent, on EtO sterilized products.

For example, open heart surgical procedures, a medical achievement impossible until relatively recently, has provided positive benefits to a significant proportion of the U.S. population. Approximately 50,000 to 60,000 of these procedures are performed each year. They significantly prolong the life span of infants born with heart defects and save the lives of adult citizens of all ages.

The open heart surgical operation is a result of expert and dedicated surgical training, but would not be possible without aseptic surgical techniques, life support instrumentation, and literally hundreds of sterile items. Illustrative of some of the EtO sterilized goods that must be readily available to the surgical team in predicted and reserve quantities are the following:

- Pharmaceuticals and drugs whose production depends on EtO
- Syringes
- Needles, hypodermic and specialty types
- Sponges
- Surgical drapes
- Surgical instruments
- Anesthesiology apparatus
- I.V. Infusion tubing and sets
- Suction apparatus
- Blood reservoirs and associated equipment
- Blood oxygenators
- Blood oxygenator tubing and accessory equipment

Open heart surgery is but one example from among hundreds of life-saving and important medical procedures that could not be performed without supplies and equipment rendered sterile by EtO.

Facts related to hemo (blood) dialysis provide a further example. Patients with renal failure are maintained by repetitive dialyzing procedures using instruments and equipment capable of performing the approximate physiological function of the human kidney. Approximately 30,000 U.S. citizens are able to survive and function in society in spite of inadequate renal functions. To do so, they rely on hemo dialysis several times each week. The success of this treatment depends absolutely on maintenance of sterile conditions and use of sterile equipment, including:

- dialyzers — various types such as coil, flat plate, etc.
- arterial/vein insertion equipment, such as various types of cannula and cannula systems.
- tubing sets to deliver blood to be purified from the patient to the machine and back to the patient.
- various monitors and control devices that provide assurances of safe conduct of the procedure.
- pumps of various types to deliver the blood from the body, through the dialysis unit and back to the body.

Virtually all of the above equipment is EtO sterilized. Any cessation, interruption, or restriction placed on artificial kidney service would pose an immediate threat to the increasing numbers of citizens whose health depends upon this life-sustaining procedure.

Although many other essential medical, surgical, and life sustaining procedures depend on EtO sterilized products, the above examples are sufficient to illustrate the absolutely essential and irreplaceable nature of EtO sterilized products in the health care system. We have listed below the 24 most frequently performed surgical procedures in the United States (Surgery in the U.S., 1975). Without EtO sterilized products, in ready and plentiful supply, few if any of these procedures would be possible. ^{*/}

^{*/} More specific information is presented in Appendix A-11 regarding estimates of 1976 operations and non-operative procedures requiring sterile devices, including patient survival estimates.

TABLE 6.5

The 24 Most Frequently Performed Surgical Procedures
(Source: Surgery in the U.S., 1975)

1. Delivery (vaginal)
2. Tonsillectomy with adenoidectomy
3. Dilation and curettage of uterus
4. Repair of inguinal hernia
5. Abdominal hysterectomy, total
6. Cystoscopy
7. Cholecystectomy
8. Appendectomy
9. Extraction of lens, intracapsular
10. Local excision of lesions, skin
11. Closed reduction without internal fixation
12. Ligation of fallopian tubes
13. Tonsillectomy without adenoidectomy
14. Prostatectomy, transurethral
15. Delivery, caesarean section
16. Mastectomy, partial
17. Vaginal hysterectomy, total and subtotal
18. Open reduction with internal fixation
19. Suture of skin
20. Hemorrhoidectomy
21. Excision and ligation of varicose veins
22. Biopsy of breast
23. Excision of intervertebral cartilage
24. Resection of colon, segmental

4. **Contributions Of EtO Sterilized Devices Used In Surgical Procedures: Mortality And Morbidity Data**

The unique benefits provided by EtO sterilized products may be further demonstrated by comparing mortality and morbidity data over the past 25 years (Table 6.6). Of course, EtO is not solely responsible for the improvements noted. Nevertheless, the diagnostic, treatment, and prosthetic devices that have contributed and continue to contribute to improved health care are dependent upon EtO for sterilization purposes.

TABLE 6.6

	<u>1945</u>	<u>1970</u>
U.S. Population	133.4 million	203.8 million
Deaths per 1,000 people	10.6	9.5
Life Expectancy at birth (years)		
males	63.6	67.1
females	67.9	74.6

Changes in mortality and morbidity rates over the past several decades, as related to selected surgical procedures, highlight the contributions made by EtO sterilized products.

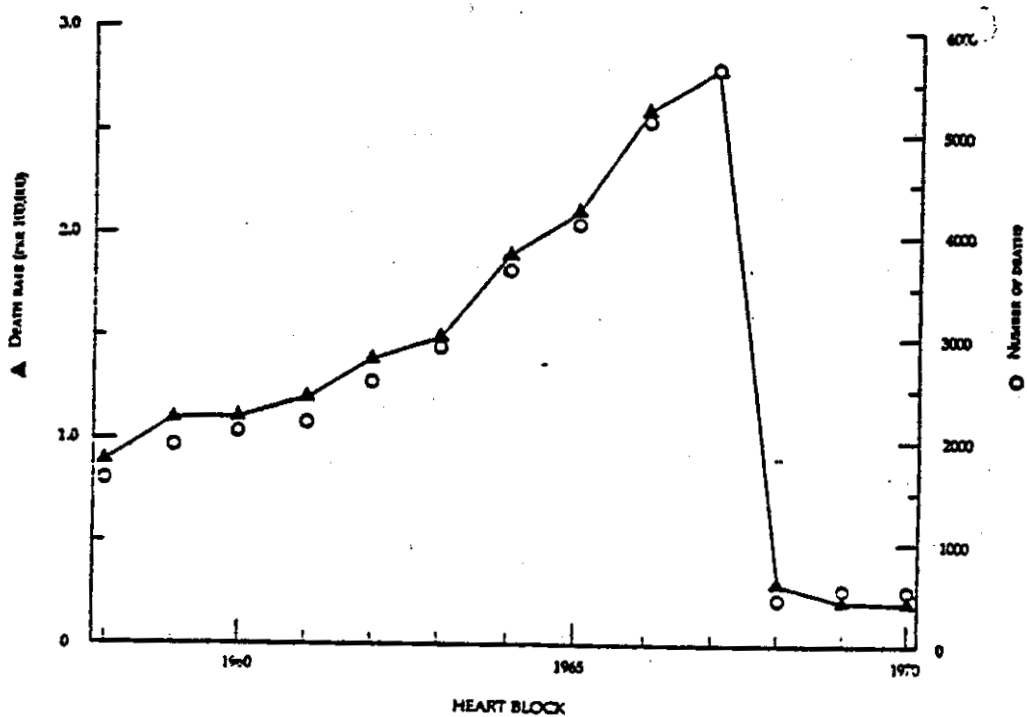
a. Mortality Data

Chronic Heart Blockage

During the period 1965 to 1970, a dramatic decrease in deaths from heart blockage occurred due to improved diagnosis and implantation in the body of sterile cardiac pacemakers. These devices were introduced in the early 1960's when the death rate from heart blockage was approximately one per 100,000 population. From 1960 to 1967, the death rates rose steadily to almost three per 100,000. However, as the medical profession became familiar with new monitoring techniques and as surgical implantation of pacemakers became more frequent, a dramatic drop in the death rate due to chronic heart blockage occurred. By 1970 the death rate was reduced to less than 0.25 deaths per 100,000. (Surgery in U.S., 1975). (See Figure 6-1)

FIGURE 6.1

Mortality rate and number of deaths from heart blockage between 1958 and 1970.
(Source: Surgery in the U.S., 1975)



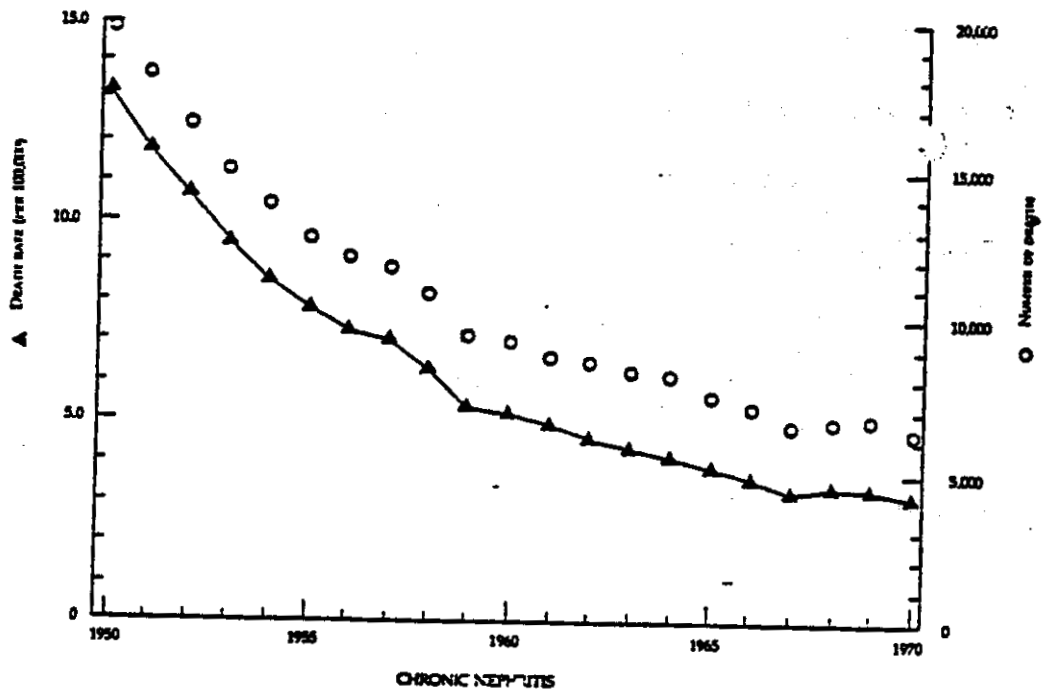
Chronic Renal Disease

In 1950, the death rate from kidney disease in the United States was approximately 13 per 100,000 or approximately 20,000 deaths per year. As shown in Figure 6.2, beginning in 1950 there was a steady decline in the death rate and by 1970 the rate dropped 75 percent to approximately 3.5 per 100,000 population. This reduction is due to a number of improvements in health care, but primarily to kidney transplantation and hemodialysis. The availability of low cost, reliable, and sterile "artificial kidneys" to those with chronic nephritis is made possible by EtO sterilization. Likewise, kidney transplant procedures utilize many types of EtO sterilized equipment. It has been estimated that in a single year, 1970, hemodialysis and kidney transplantation saved 31,911 lives in the United States (Surgery in U.S., 1975).

FIGURE 6.2

Mortality rate and number of deaths from chronic nephritis
between 1950 and 1970

(Source: Surgery in the U.S., 1975)



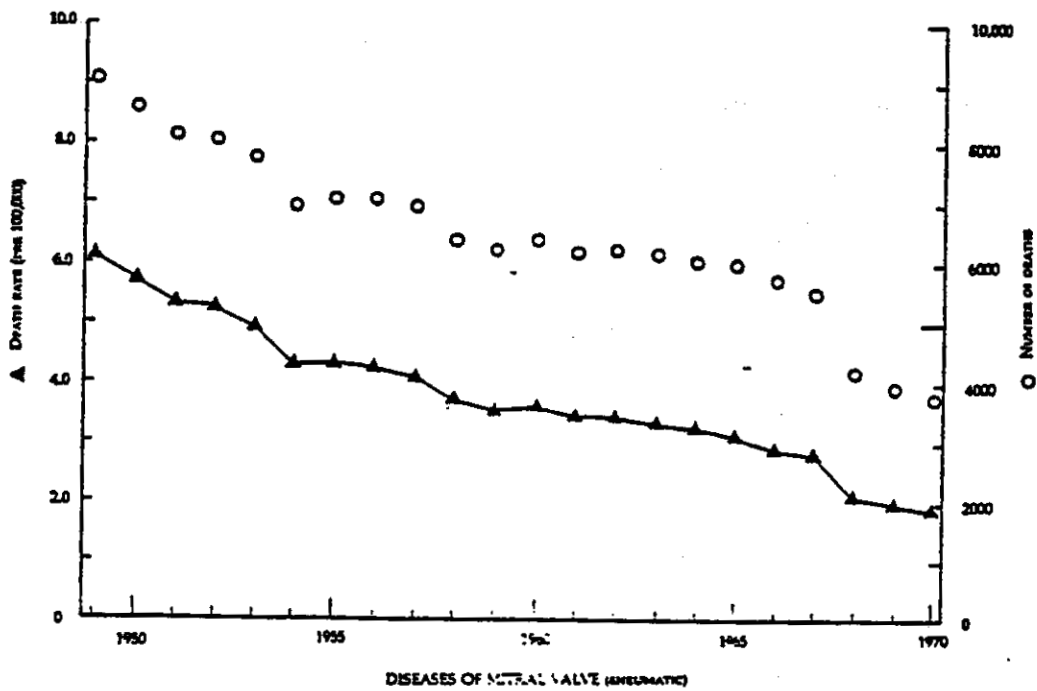
Rheumatic Mitral Valve Disease

Use of open heart surgery and placement of EtO sterilized artificial heart valves has yielded a significant reduction in rheumatic heart valve disease deaths. The "closed" surgical techniques used in the 1950's for correction of mitral and aortic stenosis were replaced in the 1960's by mitral and aortic prostheses used in "open heart" surgical techniques. As shown in Figure 6.3, the death rate due to this disease has steadily reduced since 1950. This has been possible not only because of availability of sterile heart valves, but also because of numerous other medical and surgical devices, such as blood oxygenators, that can only be sterilized with EtO.

FIGURE 6.3

Mortality rate and number of deaths from rheumatic mitral valve disease between 1949 and 1970

(Source: Surgery in the U.S., 1975)



Estimates of reduction in deaths due to a number of new or improved surgical techniques, all requiring EtO sterilized devices are significant. According to the data collected by the American College of Surgeons and the American Surgical Association (1975), 17 surgical research contributions helped save 78,538 lives in 1970 alone. (See Table 6.7) While it is not possible to exactly calculate the total number of lives saved through 1977 by surgical improvements made possible by EtO sterilized articles, estimates are that the procedures listed in Table 5.6 have saved over one million lives. In a society in which 50,000 surgical procedures are performed each day of the year, the advantages and essential nature of EtO sterilized materials is unquestionable.

TABLE 6.7

Estimated reduction in deaths in 1970 for diseases
from congenital heart diseases between 1950 and 1970
(Source: Surgery in the U.S., 1975)

<u>Disease</u>	<u>Base year for comparison</u>	<u>Total estimated reduction</u>
Tetralogy of Fallot	1960	260
Ventricular septal defect	1959	400
Atrial septal defect	1957	391
Patent ductus arteriosus	1957	271
Coarctation of aorta	1957	125
Acute nephritis	1950	1,930
Nephrotic syndrome	1950	1,568
Chronic nephritis, nephritis unqualified, renal sclerosis unqualified	1950	28,413
Arteriosclerosis	1950	19,620
Duodenal ulcer	1960	2,668
Disease of mitral valve (rheumatic)	1950	8,605
Disease of aortic valve (rheumatic)	1961	1,051
Accidents caused by fire, flames, hot substances	1950	3,011
Heart block	1967	5,503
Congenital hydrocephalus	1951	1,120
Ulcerative colitis	1950	246
Hypertensive renal disease	1950	3,352

b. Morbidity Data

Among the various indices of disease morbidity, available data relate mostly to length of hospital stay. Various factors influence this measure but major contributors to reduced morbidity include availability of better devices, and new surgical techniques. These have reduced the pain and suffering associated with many diseases and have returned many patients to their normal way of life faster and with a better assurance of complete recovery. A comparison of total hospital days from 1960 to 1972 for selected diseases establishes the contributions made by new surgical procedures and provision of sterile surgical equipment, supplies, and prostheses. Table 6.8 sets forth a list of reductions in hospital residence for selected diseases.

TABLE 6.8

Reductions in hospital stay days for selected diseases
 affected by surgical procedures, 1960 to 1972
 (Source: Surgery in the U.S., 1975)

<u>Diseases</u>	<u>Procedures</u>	<u>Reduced Hospital Days</u>
Tetralogy of fallot Artrial septal defect Ventricular septual defect Coarctation of aorta	cardiopulmonary bypass open correction procedures closed correction procedures	38,038
Acute nephritis Nephrotic syndrome Chronic nephritis Nephritis unqualified	Kidney transplantation Hemodialysis	905,301
Diseases of mitral valve Diseases of aortic valve	Prosthetic heart valves	19,852
Congenital hydrocephalus	Shunts for hydrocephalus	46,853
Retinal detachment	Photocoagulation and retinal surgery	16,516

In some cases where surgical intervention is possible statistics may be misleading because an increase in the prevalence or diagnosis of the disease may have resulted in increased hospital stays. The important point, however, is that increased chronicity and morbidity of disease, especially following surgical intervention, have been effective in significantly lowering mortalities and allowing persons to remain alive and useful. For example, replacement of arteries by surgical grafts for treatment of arteriosclerosis resulted in an increase in total patient hospital stay of more than one million days between 1960 and 1972. However, the mean stay per patient was reduced by 0.6 days and the benefits to improved health were enormous.

The use of cardiac pacemakers provides another example. Between 1960 and 1972, the prevalence of heart blockage increased by more than ten cases per 1,000 population and the total patient hospital days increased by 144,000. However, the mean stay per patient was reduced by 0.5 days and as a result of the device, thousands of lives were saved.

Another example is osteoarthritis, a painful and crippling disease whose correction in many instances has been made possible by the surgical techniques, equipment, and prostheses for total hip replacement. The prevalence of this disease has increased substantially over the past 25 years and total hip replacement procedures have raised the total patient hospital stay time by more than 66,000 days. However, without this surgical procedure and hip prostheses, thousands of individuals would be severely infirmed and bed-ridden for life.

Finally, in assessing the importance of EtO sterilized devices in surgery, it is appropriate to identify representative devices that have played an important role in making these health care advances possible. Consultation with surgical authorities indicates that almost all of the 18 million surgical procedures performed annually in this country require use of one or more items sterilized with EtO. Such items include drapes, sponges, needles, syringes, catheters, etc.

In their analysis of surgical research contributions between 1945 and 1970, the American College of Surgeons and the American Surgical Association (1975) listed a number of new and important procedures that depend upon various devices and prostheses, most of which are sterilized with EtO. (See Table 6.9)

TABLE 6.8

(Source: Surgery in the U.S., 1975)

Prosthetic heart valves
Arterial grafts
Hemodialysis apparatus
Cardiac pacemakers
Arterial blood gas and pH measuring apparatus
Shunts for hydrocephalus
Microneurosurgery equipment
Hip prostheses
Portocaval shunts
Silicone and silastic implants
Fogarty balloon catheters
Continuous suction drainage equipment
Indwelling intravenous catheters
Myringotomy and ventilation tubes
Abdominal wall prostheses

In summary, the practice of surgery in the United States today cannot be carried out without EtO sterilized devices and equipment. Development and availability of EtO sterilized surgical prostheses and life support equipment has been responsible for saving millions of lives and alleviating untold incapacitation and suffering.

5. The Role Of EtO Sterilization In Infection Control

EtO plays a vital role in the general quality of health care with regard to infectious disease control and control of hospital associated infections.

Elimination or restriction of EtO would add millions of dollars to national health expenditures and result in untold suffering, disability, and increased death rates from nosocomial infections. This statement is fully supported by the affidavit of Dr. Frank B. Engley, Jr., an expert in hospital infection control. (See Appendix B-3.) It is Dr. Engley's opinion that EtO is essential to control of hospital associated infections and there are no suitable alternate sterilization methods available.

In addition, Appendix B also contains statements by surgeons and physicians regarding the benefits and essential nature of EtO (see Appendices B-3, B-4, and B-5).

E. ECONOMIC IMPACTS OF ETO ELIMINATION OR RESTRICTION

1. Impact Of Removal

It is clear that EtO's removal from the market would have severe economic repercussions. One example of the possible impact of removal of EtO is illustrated by the analysis submitted to EPA by one relatively small medical device company which produces 83 EtO sterilized medical devices. The results predicted by this firm would occur with many similar companies that depend on EtO for production of sterile products.

The firm developed data showing the financial impact resulting from (1) substituting radiation sterilization where possible and (2) the situation in which no sterilization substitutes were possible.

TABLE 6.10

Impact From Using Substitute (Annual)

Increased Costs

Estimated Loss of Product (due to unadaptability)	\$1,000,000
Estimated Increase in Freight Cost	30,000
Estimated Increase in Labor to Handle Routing	20,000
Loss of Capital Equipment (Sterilizer) (\$90,000 (new in '78) over 5 years)	18,000
	<hr/>
DIRECT LOSS	\$1,068,000

TABLE 6.11

Economic Impact on Local Area

7 people directly involved in manufacturing (10% of work force) at \$9,000	\$63,000
Loss of 2 sterilizer operators at \$8,000	16,000
	<hr/>
	\$79,000

TABLE 6.12

Impact of Using No Substitute (Annual):

Company Loss of Product	10,000,000
Loss of Capital Equipment	25,000
Loss of Bldg. Utilization 13,000 sq. ft. at \$42/sq. ft. over 10-year cost	546,000
	<hr/>
SUBTOTAL	\$10,571,000

Economic Impact on Area (Annual)

70 people at \$9,000/ann. =	630,000
	<hr/>
ANNUAL TOTAL IMPACT =	\$11,201,000

Another larger company has estimated that elimination of EtO would result in loss to the health care system of 18% of their sterile products having a 1977 market value of almost \$25 million. Most of this firm's remaining EtO sterilized products would be unmarketable for one to four years for redevelopment, at an approximate cost of \$13.2 million. Disruptions and economic impacts of this nature, when multiplied by the hundreds of firms that use EtO, obviously would precipitate disastrous and unfavorable economic situations. Clearly there would be:

- Substantial increases in health care costs.
- A rapid rise in foreign-made EtO sterilized products to fill the gap left by U.S. products removed from the market.
- A significant rise in unemployment in the medical device industry.
- Financial hardships and/or bankruptcy for many American medical device firms.

It is obvious from this and other analyses that elimination of EtO would have a catastrophic effect on the economic well being of a large segment of the medical device industry, as well as significant corresponding economic effects on the American public.

2. Impact Of Severe Restrictions

The American Industrial Health Council (1978) recently estimated the cost to the health care industry of assuring a workplace EtO exposure level of ten ppm and attempting to reach levels of one ppm and less than one ppm. They estimated that although the selling price of EtO is approximately \$0.60/pound, the cost for the reductions would amount to nearly \$4.00/pound. The figures provided by the AIHC study are shown in Table 6.13.

TABLE 6.13

Equipment

Cost Increase Estimates (\$ millions)

	<u>Exposure Level</u>		
	<u>10 ppm</u>	<u>1 ppm (attempt)</u>	<u>Below 1 ppm (attempt)</u>
Capital Costs	18	20	20
Annual Costs	50	51	92
Differential First Year Operating Costs	16	16	16

We submit that, based on available data, this estimate is conservative and that an increase of from \$110 to \$125 million would be needed to attempt to achieve an exposure level below one ppm, while an increase of \$80 to \$100 million would be necessary to achieve the ten ppm level.

To reach exposure levels of ten ppm, industry would have to either: (1) double or triple its investment in large sterilizers; or (2) design and procure closed system aeration buildings and equipment capable of holding millions of cubic feet of EtO-treated products.

Currently, industry has available approximately 75,000 cubic feet of sterilizer capacity that is generally used on a "round-the-clock" basis. After treatment, the goods are removed and aerated in a quarantine area. If this procedure were no longer possible, aeration would have to be done in the chamber which would require purchase and installation of at least 75,000 sq. ft. more sterilizer space.

The cost to purchase new sterilizers would be \$10 million, while new facilities and controls would cost \$7 million. It might cost industry in excess of \$20 million to design and install large closed system aerators for EtO sterilized goods. The total economic impact of restrictions as low as ten ppm for both hospitals and industry would be approximately \$100 million for both capital and annual operating costs.

F. MEDICAL IMPACTS OF ETO ELIMINATION

A HIMA membership survey has identified the types of products that cannot presently be sterilized by any means other than EtO and those that would be removed from the market (as sterile items) by the manufacturer if EtO were not available.

Appendix A-10 contains a list of the 115 specific medical items manufactured by one or more HIMA member companies that can only be sterilized by EtO.

Elimination of EtO would presumably remove most of these items from the market. At the very least, most would be denied to the health care system until the long process of redesign, testing, and approval had been completed.

Table 6.14 lists those items which one or more companies have already determined would no longer be sold as sterile if EtO were not available as a sterilant.

We estimate that the overall effect of elimination of EtO would be immediate removal of at least 50% of the sterile products currently manufactured by the health care industry.

In conclusion, we submit that the unique and crucial benefits provided by EtO for use in sterilizing medical devices clearly outweigh any risks associated with its use and mandate reregistration.

TABLE 6.14

Items No Longer Provided Sterile By One Or More
Companies If EtO Were Eliminated

Adaptors
Bandage, adhesive, backed
Bandages, Spray adhesive (aerosol can)
Balloons, intra-aortic
Catheters, Foley
Catheters, intravascular subclavian
Collection systems, urinary
Connectors
Connectors, luer lock
Connectors, tubing
Containers, specimen
Cups, plastic urine collection
Dishes, petri
Drapes, OR, patient disposable
Drapes, surgical disposable
Gloves, examining
Gloves, procedural
Gloves, surgeons
Kits, anesthesia
Kits, anesthesia epidural
Kits, blood gas sampling
Kits, catheter care
Pad, pulsatile assist device
Sets, anesthesia extension
Sets, injection paracervical
Sets, blood, arterial/venous
Sets, douche
Sets, Foley catheterization
Sets, irrigation
Sets, mid-stream specimen collection
Sets, urethral catheterization
Support, heart
Syringes, unit dose products
Trays, procedural w/drugs
Trays, catheterization
Trays, plastic surgery, disposable
Tubes, endotracheal
Tubes, connecting I.V.
Tubes, urine
Tubing, drainage
Tubing, PVC
Valves, implantable

TOTAL OF ALL PRODUCTS: 42

VII.

CONCLUSIONS

The evidence, data, and information submitted in this response clearly warrant dismissal of the RPAR proceeding and reregistration of EtO.

It has been conclusively established that:

- EPA lacks jurisdiction under the Federal Environmental Pesticide Control Act of 1972 to control use of EtO as a medical device sterilant. Additionally, other agencies (FDA and OSHA) provide adequate assurance of the safe use of EtO in the health care field.
- Assuming EPA nevertheless asserts jurisdiction, this response, as supported by the attached materials and expert statements, conclusively rebuts the alleged human mutagenic and reproductive risks of EtO. Likewise, the fact that EtO does not accrue or persist in the environment makes the allegation of risk to non-target populations even more remote. Thus, only theoretical risks remain which are insufficient, based on current studies and data, to support further regulatory action.

A List of Items Sterilized by
Health Industry Manufacturers

Accessories, pacemaker	Bottles, lotion
Accessories, ventilator, respiratory care	Bridges, ostomy
Adaptors	Brushes, surgical scrub, germicidal
Adaptors, lead, implantable	Burrettes, chambers (cellulosic)
Adaptors, pacer to catheter	Cannula, extracorporeal
Adaptors, threshold	Cannula, flexible, aspiration
Airways, pharyngeal	Cannula, flexible w/PVC hose
Alarm, low level blood	Cannula, infusion
Apparatus, suction and drainage	Cannula, intravenous
Applicators, metal and cloth	Cannula, uterine aspirator
Assemblies, needle	Caps, bottle
Assembly, water safety	Caps, container
Bags, drainage	Catheter, central venous pressure
Bags, intestinal	Catheters, cut down
Bags, OR, plastic, drainage	Catheters, Foley
Bags, urinary, leg	Catheters, intravascular
Balls, cotton	Catheters, intravascular, subclavian
Balloons, intra-aortic	Catheters, suction
Bandages, adhesive	Catheters, urological
Bandages, adhesive, spray (aerosol can)	Centrifuges
Bandages, gauze	Circuits, breathing
Bells, circumcision	Clamps, cord, disposable
Bib, vaginal w/pouch	Clamps, flow control (plastic)
Blades, dermatome	Clamps, umbilical cord
Blades, knife, meniscus	Clamp, flow control (aluminum)

Appendix A-9 Continued

Clips, ligating, hemostatic	Drapes, surgical
Clips, Raney	Drapes, surgical, disposable
Clips, skin	Dressing, barrier, microporous
Clips, wound	Dressing, surgical
Closures, tape, skin	Droppers
Collection systems, urinary	Electrodes, scalp
Collectors, wound drainage	Electrodes, EKG
Components, blood pump	Electrodes, surgical
Components, oral feeding	Equipment, dialysis
Components, plastic, dispensing	Fabrics, cardiovascular
Connectors	Film, surgical
Connectors, luer lock	Filter, biologic, gas line
Connectors, tubing	Filter, blood
Connectors, urinary	Filter, blood, dialysers
Containers, specimen	Filters, industrial
Cover, Mayo stand	Filters, in-line, I.V.
Covers, burr hole	Filters, laboratory
Cups, plastic, urine collection	Filter, vena cava
Curvette, biopsy	Flashballs, latex
Devices, intrauterine	Generators, cardiac pacemakers
Dialyzers	Gloves, examining
Diapers, nursery	Gloves, procedural
Dilator, vessel	Gloves, surgeons
Dishes, petri	Gowns, OR, disposable
Domes, disposable, transducer, blood pressure	Gowns, uniform
Drape, aperture	Guidewires, catheterization
Drapes, OR patient, disposable	Handles, plastic, uterine, aspirator

Appendix A-9 Continued

Heartleads, pacemaker	Napkins, hospital, maternity
Heart valves, prosthetic, ball	Needles, dialysis
Heart valves, low profile	Needles, hypodermic
Hoses, gas-vacuum	Needles, spiral
Humidifiers, respiratory care	Needles, surgical
Incubators	Nebulizers, respiratory care
Indicators, pacemaker	Oxygenators, blood
Injection sites, rubber	Pacemakers
Implants, orthopedic	Packs, drape
Implants, orthopedic, plastic	Packs, gown
Instruments, suction	Packs, throat
Jelly, lubricating	Pads, maternity care
Kit, hyperalimentation care	Pads, cotton
Kit, I.V. care	Pads, foam
Kits, anesthesia	Pads, gauze
Kits, anesthesia, epidural	Pad, pulsatile assist device
Kits, blood gas sampling	Paks, instrument
Kits, catheter care	Paks, shave-prep
Kits, hand scrub and prep	Paks, transfer
Kits, intravenous placement	Pencil, electrosurgery
Kits, intubation, emergency	Perforators, amniotic membrane
Lancets, blood	Pins, safety
Leads, pacemaker	Pipettes
Leads, pacing, pacemaker	Pouch, cellophane
Magnets, test, pacemaker	Pouches, sterile products, hospital
Masks, surgical	Pouches, sterile product, industry
Mattresses, infant, incubator	Power, Soyaflof

Prostheses	Sheets, burn
Prostheses, middle ear	Sheets, nursery, basinet
Prostheses, vascular	Shunts, dialysis
Protectors, wound	Shunts, Thomas
Regulators, suction	Snares, nasal
Reservoirs, blood	Snares, tonsil
Reservoirs, cardiotomy	Sponges, eye
Samplers, microbiological	Sponges, cotton
Scalpels	Sponges, gauze
Screws, bone, disposable	Sponges, laparotomy
Sets, anesthesia, extension	Sponges, surgical
Sets, injection, paracervical	Stimulators, nerve
Sets, blood, arterial/venous	Stimulators, muscle
Sets, blood administration	Stimulators, neurologic
Sets, chest drainage, underwater	Stopcocks
Sets, douche	Stoplocks
Sets, Foley, catheterization	Stylers
Sets, irrigation	Sutures, stainless steel, surg
Sets, I.V. administration	Swabs, cotton
Sets, mid-stream specimen collection	Syringes, hypodermic
Sets, premature, gauge	Syringes, unit dose product
Sets, suture removal	Systems, autotransfusion, dis
Sets, tracheostomy care	Systems, contraceptive, intr progesterone
Sets, tubing	Systems, <u>in vivo</u> kidney perf
Sets, tubing, cardiovascular	Tape, skin
Sets, urethral, catheterization	Tips, electrode
Sheets, drape	

Tips, pipette, plastic	Tubing, PVC
Tips, surgical suction	Tubing, silastic
Tips, wound irrigation	Tubing, reusable
Towels, OR	Tubing, silicone rubber
Trays	Tubing, wound irrigation
Trays, catheterization	Valves, implantable
Trays, irrigation	Valves, one-way silicone
Trays, microdilution	Vessels, tissue culture
Trays, plastic surgery, disposable	Vials
Trays, premie gavage	Vials, plastic
Trays, surgical	Wrench, Allen, torque limited
Tubes, endotracheal	
Tubes, airways	<hr/>
Tubes, aspirating	<u>Total Products:</u> 248
Tubes, connecting	
Tubes, connecting I.V.	
Tubes, culture	
Tubes, infant feeding	
Tubes, sampling	
Tubes, tracheostomy	
Tubes, urine	
Tubes, ventilation, otological	
Tubing, blood	
Tubing, disposable	
Tubing, drainage	
Tubing, polyethylene	

APPENDIX A-10

Items Manufactured By One Or More Companies That Can Only Be Sterilized By EtO

Accessories, Pacemaker	Filter, vena cava
Adaptors	Generators, cardiac pacemaker
Adaptors, lead, implantable	Gloves, examining
Applicators, cotton	Gloves, surgeons
Assemblies, needle	Gowns, OR, disposable
Bags, drainage	Guidewires, catheterization
Bags, urinary, leg	Heart valves, prosthetic, Ball
Bags, OR, plastic, drainage	Heart leads, pacemaker
Balls, cotton	Heart valve, low profile
Bandages, adhesive	Humidifiers, respiratory care
Bandages, gauze	Instruments, suction
Bib, vaginal w/pouch	Kit, hyperalimentation care
Brushes, surgical scrub	Kit, I.V. care
Burrettes, Chambers (cellulosic)	Kits, anesthesia
Cannula, intravenous	Kits, anesthesia, epidural
Catheter, central venous pressure	Kits, blood gas sampling
Catheters, cut-down	Kits, catheter care
Catheters, Foley	Kits, intravenous placement
Catheter-introducer	Kits, hand scrub & prep
Catheters, intravascular	Leads, pacemaker
Catheters, suction	Leads, pacing, pacemaker
Catheters, urological	Nebulizers, respiratory care
Circuits, breathing	Oxygenators, blood
Clamp, flow control (plastic)	Packs, drape
Clips, wound	Pads, cotton
Collection systems, urinary	Pads, foam
Components, blood pump	Pads, gauze
Components, oral feeding	Paks, shave-prep
Components, plastic dispensing	Paks, transfer
Connectors	Prostheses, (heart valves)
Connectors, luer lock	Protectors, wound
Connectors, tubing	Reservoirs, blood
Containers, specimen	Reservoirs, cardiotomy
Cups, plastic urine collection	Scalpels
Dialyzers	Sets, anesthesia extension
Diapers, nursery	Sets, injection, paracervical
Drape, aperture	Sets, blood arterial/venous
Drapes, OR, disposable	Sets, blood administration
Drapes, surgical, disposable	Sets, chest drainage, underwater
	Sets, douche
Dressing, barrier, microporous	Sets, Foley catheterization
Dressings, surgical	Sets, irrigation
Electrodes, scalp	Sets, IV administration
Electrodes, EKG	Sets, mid-stream specimen collection
Film, surgical	Sets, tubing
Filter, blood, dialyzer	Sets, tubing, cardiovascular
Filters, industrial	Sponges, cotton
Filters, in-line, I.V.	Sponges, gauze

APPENDIX A-10 (Continued)

Sponges, surgical
Stimulators, muscle
Stimulators, nerve
Stimulators, neurologic
Stopcocks
Stoplocks
Syringes, hypodermic
Tape, skin
Trays, catheterization
Trays, plastic surgery, disposable
Trays, surgical
Tubes, endotracheal
Tubes, connecting
Tubes, connecting, I.V.
Tubes, infant feeding
Tubes, tracheostomy
Tubes, urine
Tubing, blood
Tubing, disposable
Tubing, PVC

TOTAL PRODUCTS: 115

FOR THE ADMINISTRATOR
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C.

In Re:

Rebuttable Presumption
Against Registration of
Ethylene Oxide

EPA DOCKET NO. OPP-30000

TESTIMONY OF

WILLIAM G. MALETTE, M.D., F.A.C.S., F.A.C.C., F.A.C.C.P.

1. I reside at 667 Parkwood Lane, Omaha, Nebraska 68132. I received my M.D. from Washington University St. Louis in 1953.
I am a Fellow of the American College of Surgeons, a Fellow of the American College of Cardiology, and a Fellow of the American College of Chest Physicians. I am licensed to practice medicine in the states of Missouri, Kentucky, Florida, California and Nebraska.
2. I have held professorships at the University of Kentucky School of Medicine and the University Hospital, Jacksonville, Florida. I am presently Professor of Surgery at the University of Nebraska College of Medicine and Creighton University School of Medicine, Omaha, Nebraska.
3. I am a past president of the Association for the Advancement of Medical Instrumentation, and have been active in the standards field for the past 12 years, both domestically and internationally.
4. I have done research in surgery and aerospace medicine, supported not only by the Armed Services but by the National Institutes of Health. I have had a number of surgical residents go on to productive careers in academic medicine, research and the military services.

Appendix B-7 Continued

5. I have been a Consultant to the United States Army and the United States Public Health Service. As can be seen by my attached curriculum vitae, I am a member of a number of other organizations, and I have published a number of papers and produced scientific motion pictures. I have been a consultant in medical facilities design for the past 15 years and have assisted in the design and construction of one complete hospital.
6. It is my opinion that a safe substitute for Ethylene Oxide sterilization has not been found. By the use of this mode, numerous advances in medical science have been possible. A glance at appendix A of the Federal Register, Friday January 27, 1978, Part III, (entitled Ethylene Oxide rebuttable presumption) will reveal that items listed include a wide spectrum of medical and surgical apparatus that is absolutely necessary to the practice of present day medicine and surgery. I make particular reference to implantable prosthetic devices. No examples are given in this particular appendix; however, these include such items as cardiac pacemakers. Without Ethylene Oxide sterilization the electronic components, lithium iodide batteries and connections to these pacemakers will not withstand any other form of sterilization. In this one item alone, many lives will be put in jeopardy since pacemakers will not then be available. One could go down the entire list to include all manner of surgical supplies developed by the plastics industry that will not stand heat or steam sterilization. I, furthermore, feel that the only constraints placed on Ethylene Oxide in the medical field should be in the form of guidelines in its use.
7. At the present time it is obvious that there is no substitute for this form of sterilization. I am certain that if all the items presently

sterilized by this means and not suitable for sterilization by any other means were to disappear from our armamentarium, we would have stepped back 30 years in the practice of medicine and surgery in this country. Such action would be the most retrogressive act that could be taken by any regulatory body.

8. It is recognized by all concerned that Ethylene Oxide is a dangerous chemical. However, numerous other dangerous chemicals are used every day without harm to the personnel using them, provided proper precautions are taken. Gasoline itself is an extremely hazardous substance that can quickly lead to loss of life. However, it is used every day with only the realization of all individuals that precautions must be taken in its handling.
9. Voluntary guidelines have been developed for the use of Ethylene Oxide and its removal from any material by proper aeration. With the education of personnel using this material and strict adherence to already known guidelines this should be a safe method of sterilization without undue risk considering the benefits gained from its use.
10. I, therefore, recommend that no federal regulation be designed or enacted which could interfere with the flow of surgical instrumentation to our operating rooms and to our wards. It would seem to me that the Environmental Protection Agency should exercise its regulatory powers no farther than to guarantee that equipment used in this method be properly constructed and that personnel using it be educated to its hazards. Under no circumstances should Ethylene Oxide sterilization be eliminated as a sterilant at this time.

Respectfully submitted,



WILLIAM G. MALETTE, M.D.
F.A.C.S., F.A.C.C., F.A.C.C.P.

CURRICULUM VITAE

William G. Malette, M. D.
Veterans Administration Hospital
4101 Woolworth Avenue, Omaha, Nebraska 68105

PERSONAL HISTORY:

Date of birth: March 27, 1922

Place of birth: Springfield, Missouri (Greene County)

EDUCATION:

Drury College, Springfield, Missouri	1940-1942
Fresno State College, Fresno, California	1947-1949
Washington University, St. Louis, Missouri	1953 (M.D.)

GRADUATE HOSPITAL CLINICAL EXPERIENCE:

Intern, Letterman Army Hospital	1953-1954
Assistant Resident, Denver VA Hospital	1954
Resident, Denver VA Hospital	1958

ACADEMIC APPOINTMENTS:

Chief, Experimental Surgery Department School of Aviation Medicine Brooks Air Force Base, Texas	1958-1961
Chief, Unit II, General Surgery Service Wilford Hall USAF Hospital Lackland Air Force Base, Texas	1961-1963
Associate Professor of Surgery University of Kentucky Medical Center Lexington, Kentucky	1963-1972
Chief, Surgical Service VA Hospital Lexington, Kentucky	1963-1973
Chief of Staff VA Hospital, Cooper Drive Division Lexington, Kentucky	1971-1973
Associate Dean for VA Affairs University of Kentucky Medical Center Lexington, Kentucky	1971-1973

Appendix B-7 Continued

Professor of Surgery University of Kentucky Medical Center Lexington, Kentucky	1972-1973
Chairman, Emergency Medical Services University Hospital of Jacksonville Jacksonville, Florida	1973-1974
Professor of Surgery University Hospital of Jacksonville Jacksonville, Florida	1973-1974
Thoracic and Cardiovascular Surgery Fort Myers, Florida	1974-1976
Director, Emergency Medical Services Kern Medical Center Bakersfield, California	1976
Chief, Surgical Service VA Hospital Omaha, Nebraska	1977-present
Professor of Surgery Creighton University School of Medicine Omaha, Nebraska	1977-present
Professor of Surgery University of Nebraska School of Medicine Omaha, Nebraska	1977-present

LICENSURE:

State of Missouri	1953
State of Kentucky	1963
State of California	1970
State of Florida	1973
State of Nebraska	1977

CERTIFICATION:

American Board of Surgery	1964
American Board of Thoracic Surgery	1966

Appendix B-7 Continued

COMMITTEES:

Vice Chairman, Biomedical Engineering Committee
American College of Chest Physicians

Member, Medical Devices Committee
American College of Surgeons

Chairman, AAMI Committee on Oxygenator Standards
(American College of Cardiology Representative)

Chairman, International Standards Organization Subcommittee
on Pacemaker Standards

MILITARY SERVICE:

U.S. Air Force Training Command	1942-1944
U.S. Air Force Transport Command	1944-1946
U.S. Air Force Medical Corps	1953-1963
U.S. Navy Reserve Medical Corps	1964-present

HOSPITAL APPOINTMENTS:

Wilford Hall USAF Hospital Lackland Air Force Base San Antonio, Texas	1961-1963
VA Hospital Lexington, Kentucky	1963-1973
University of Kentucky Medical Center Lexington, Kentucky	1963-1973
St. Joseph's Hospital Lexington, Kentucky	1963-1973
Central Baptist Hospital Lexington, Kentucky	1963-1973
Good Samaritan Hospital Lexington, Kentucky	1963-1973
University Hospital of Jacksonville Jacksonville, Florida	1973-1974
Fort Myers Community Hospital Fort Myers, Florida	1974-1976
Lee Memorial Hospital Fort Myers, Florida	1974-1976
Kern Medical Center Bakersfield, California	1976

HOSPITAL APPOINTMENTS (cont.):

VA Hospital Omaha, Nebraska	1977-present
University Hospital University of Nebraska Omaha, Nebraska	1977-present
Creighton Memorial - St. Joseph's Hospital Omaha, Nebraska	1977-present

SOCIETY MEMBERSHIPS:

Society for Thoracic Surgery
American Medical Association
Fellow, American College of Surgeons
International Cardiovascular Society
Central Surgical Society
American Association for Thoracic Surgery
Southern Thoracic Surgical Association
Fellow, American College of Cardiology
Pan-Pacific Surgical Association
Fellow, American College of Chest Physicians

OTHER:

Consultant, General and Thoracic Surgery Ireland Army Hospital Fort Knox, Kentucky	1963-1973
Consultant, General and Thoracic Surgery Public Health Service, Clinical Research Center Lexington, Kentucky	1963-1973
Consultant, Medical Systems Technical Services, Inc. Los Angeles, California	1963-present

HONORS:

Past President, Association of VA Surgeons
Past President, Association for the Advancement of Medical
Instrumentation

LISTED IN:

Who's Who in the South and Southwest	1973
American Men and Women of Science	1965

FOR THE ADMINISTRATOR
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C.

IN RE:

Rebuttable Presumption
Against Registration of
Ethylene Oxide

EPA DOCKET NO. OPP-30000

TESTIMONY OF

Kenneth L. Mattox, M.D, F.A.C.S.

1. I reside at 5142 Braesvalley, Houston, Texas 77096. I received my B.S. degree from Wayland College in Plainview, Texas in 1960 and my M.D. from Baylor College of Medicine in 1964. I finished my residency in General Surgery in 1971 and my residency in Thoracic Surgery in 1973, both at Baylor College of Medicine in Houston, Texas. In 1972 I was certified by the American Board of Surgery and in 1974 I was certified by the American Board of Thoracic Surgery.
I am a member of the American College of Surgeons, American College of Chest Physicians, American College of Cardiology, and the American College of Emergency Physicians. In addition, I am a member of multiple other professional organizations.
I am licensed to practice medicine in the state of Texas.
2. I am Assistant Professor of Surgery at Baylor College of Medicine, a position I have held since 1974. My responsibilities include being Director of the Emergency Surgical Service and Deputy Chief

For the Administrator
U.S. Environmental Protection Agency

of Surgery at the Ben Taub General Hospital where Doctor Michael E. DeBakey is Chief of Surgery. I am actively involved in the surgery of patients who have cardiovascular, thoracic and trauma problems.

3. I have been actively involved in the Association for the Advancement of Medical Instrumentation since 1973. This association, deeply involved in medical device legislation, in scientific sessions as they relate to patient safety, is a unique interface of physician users, paraphysician users, biomedical industry, biomedical engineering and representatives from F.D.A. The voluntary consensus standing committees of AAMI now number 28 and have been very active in working with multiple organizations as they relate to consumer safety. For the last three years I have been Chairman of the Blood Filter Standards Committee, and for the past year I have been Medical Co-chairman of the Board of Standards. Virtually all of the standards committees of AAMI have some piece of equipment or their entire device requiring sterilization. Many of these contain elements which make them unacceptable for steam sterilization or high temperatures.
5. I have been the author of multiple scientific publications and chapters in books and am on the editorial board of several journals (see curriculum vitae).
6. I have read the Federal Register, Friday, January 27, 1978, vol. 43, #19), pp 3800-3815. I am impressed with the extensive scientific material which is reported. As pointed

For the Administrator
U.S. Environmental Protection Agency

out on pp. 3811, there are a large number of classes of items that are presently sterilized with Ethylene Oxide within the hospital or health care facilities. Many of these items are of absolute necessity for both emergency and elective surgery. To remove these items from the available list of sterile equipment would cripple the health care industry and result in literally millions of unnecessary deaths or complications in patients annually. The non-availability of devices, equipment, and instruments which can only presently be sterilized with Ethylene Oxide would set medicine and surgery back to the pre-antibiotic era and would negate most of the advances which have been made in the last one-half century.

7. It is recognized that all advances in science carry a risk-benefit ratio. Regardless of the medication or instrument, a misuse of that equipment, device, drug, or chemical might result in some injury. This statement applies to medications as simple as aspirin or devices as complex as a totally implantable artificial heart. The tabulation of metabolic, oncogenic, teratogenic, hematologic, etc. effects of any medication, device or chemical is important from a safety standpoint and helps all of us develop standards for the protection of personnel and patients. The mere stipulation of a potential hazard should not, however, preclude its safe use. To remove an item, drug or chemical, merely because it might at some time be used unsafely is ingoring

For the Administrator
U.S. Environmental Protective Agency

the overwhelming evidence of its usefulness and efficacy when used within the safety and standard bounds which are set by consensus among federal agencies, users, and industry. Therefore, logic as it applies to the removal of Ethylene Oxide from the market, one must respond that yes, Ethylene Oxide is good in that it provides safe sterilization to items which are too delicate to be sterilized by heat; yes, Ethylene Oxide does have some hazards if used incorrectly; yes, there have been reports of some accidents or misuse. However, these latter two statements become true, true and unrelated in regard to conclusions in the Federal Registry that one must consider withdrawal of Ethylene Oxide in order to protect consumers, manufacturers and users from potential hazards.

8. I strongly support the contention that until a suitable, efficient reliable, safe substitute is found for Ethylene Oxide that we should continue to use Ethylene Oxide in our hospitals for the sterilization of equipment which cannot withstand the heat of steam sterilization. I further strongly recommend that the only constraints that should be placed upon the registration of Ethylene Oxide should be in the form of guidelines on how and by whom it should be used.
9. Guidelines have been developed for the use of Ethylene Oxide and require that products exposed to Ethylene Oxide have proper aeration, and these guidelines can be made mandatory.

For the Administrator
U.S. Environmental Protective Agency

Persons who are knowledgeable in these guidelines and have demonstrably approved education and training skills should be used for this method of sterilization.

10. I, therefore, conclude with the strong recommendation that absolutely NO federal regulation be designated or enacted which would limit the normal flow of surgical instruments to our operating rooms, the normal availability of implantable devices such as pacemakers, etc. or the normal availability of items such as micropore filters, catheters, and the like which are used in emergency centers around the country for the care of emergency and electively treated patients. It is recommended that the Environmental Protection Agency, the Department of Health, Education and Welfare, and the Food and Drug Administration work together to exercise in their regulatory powers no further limitations that to guarantee that equipment used in this sterilization method (Ethylene Oxide) be appropriately constructed to conform to the gas and to secure its proper venting. They could also responsibly require that voluntary consensus guidelines for the use of Ethylene Oxide become mandatory. Under absolutely no circumstances should the aforementioned agencies limit the present use of this tremendously important gas which is so vital to the present care of our patients.

Respectfully submitted



Kenneth L. Mattox, M.D., F.A.C.S.

CURRICULUM VITAE

KENNETH L. MATTOX, M.D.

NAME Kenneth Leon Mattox
 ADDRESS 5142 Braesvalley
 Houston, Texas 77096
 OFFICE ADDRESS 1200 Moursund Avenue
 Houston, Texas 77030
 BIRTHDATE October 25, 1938
 BIRTHPLACE Ozark, Arkansas
 CIVIL STATUS Married
 One Child

EDUCATION

College	Wayland College Plainview, Texas B.S. Degree	1956 - 1960
Medical School	Baylor College of Medicine Houston, Texas M.D. Degree	1960 - 1964
Internship	Ben Taub General Hospital Houston, Texas	1964 - 1965
Residency	Baylor College of Medicine Affiliated Hospitals Houston, Texas General Surgery Thoracic Surgery	1967 - 1971 1971 - 1973
MILITARY SERVICE	U.S. Army Medical Corps Flight Surgeon, Captain Assigned: U.S. Army Board for Aviation Accident Research	1965 - 1967
Special Appointment:	Aeromedical Consultant Department of Army Natick Laboratories	1967 - 1969

LICENSURE

Texas State Board of Medical Examiners, August, 1964
 American Board of Surgery, February, 1972
 American Board of Thoracic Surgery, January, 1974

HONORS AND AWARDS

Who's Who in American Colleges and Universities	1959 - 1960
Texas College Academy of Science Northwest Regional Director	1959 - 1960
Certificate of Proficiency Texas Academy of Science	1960
Alpha Chi National Collegiate Honorary Society	
Signa Tau Delta National Writer's Society	
Citizenship Award Outstanding Graduating Senior Wayland College	1960
Participant - NATO - Advisory Group for Aerospace Research and Development	1966 - 1967
Legion of Merit - Presidential Citation	1967
Outstanding Young Men of America	1968
Outstanding Personalities of the South	1969
Vice President, Baylor College of Medicine House Staff Association	1970
Citation of Achievement, Wayland College	1969
Two-Thousand Men of Achievement	1972
Dictionary of International Biography (England)	1972 - 1973
AMA Physician Recognition Award	1972
AMA Physician Recognition Award	1973
American College of Chest Physicians' Most Outstanding Motion Picture	1974
Certificate of Appreciation, American College of Emergency Physicians	1975

MEMBERSHIP - PROFESSIONAL ORGANIZATIONS

American College of Surgeons
American College of Emergency Physicians
Board of Directors, Texas Division
American Medical Association
American Trauma Society
Founding Member; Secretary (1974), Vice President (1975) - Harris Unit
President, Texas Division, 1975-76; State Board of Directors
National Board of Directors
American College of Chest Physicians
Association for Academic Surgery
Association for the Advancement of Medical Instrumentation
Harris County Medical Society
National Association of Residents and Interns 1964-1975
Student American Medical Association 1960-64
University Association for Emergency Medical Services
Program Chairman, 1976-79
International College of Angiology
Southwestern Surgical Congress
American College of Cardiology
International Cardiovascular Society, North American Chapter
Texas Medical Association
American Association for the Surgery of Trauma
Houston Surgical Association
Texas Surgical Society
Pan Pacific Surgical Association
Michael E. DeBakey International Cardiovascular Society
Society of Thoracic Surgery
Society of Vascular Surgery
Southern Thoracic Surgical Association
Pan American Medical Association

MEMBERSHIP IN OTHER ORGANIZATIONS

Texas Collegiate Academy of Science, 1956-60
Texas Academy of Science, 1959
Aerospace Medical Association
Disaster Physician, Harris County Sheriff's Department

TEACHING EXPERIENCE

Instructor	Wayland College Biology	1958-1960
Lecturer	Mechanisms of Crash Injury Flight Safety Foundation Crash Investigators School	1966-1967

Appendix B-8 Continued

Lecturer	U.S. Army, Aviation Safety Officer's Course	1965 - 1967
Lecturer	U.S. Army Aircraft Accident Investigator's School	1965 - 1967
	"Physiologic Aspects of Aircraft Accidents"	
	"The Flight Surgeon in Aircraft Accident Investigation"	
	"Crash Safety Concepts"	
	"Mechanism of Crash Injury"	
Lecturer	Flight Safety Foundations, Aviation Safety Engineering Research	1966 - 1967
	"Mechanism of Impact Injury"	
Assistant Instructor	General Surgery Department of Surgery Baylor College of Medicine	1967 - 1971
Assistant Instructor	Thoracic Surgery Department of Surgery Baylor College of Medicine	1971 - 1973
Instructor	Department of Surgery Baylor College of Medicine	1973 - 1974
Assistant Professor	Department of Surgery Baylor College of Medicine	1974 - present

HOSPITAL AFFILIATIONS

Ben Taub General Hospital
Deputy Surgeon-In-Chief
Director, Emergency Surgical Services

Texas Institute for Research and Rehabilitation, Houston, Texas
Surgical Consultant

Veterans Administration Hospital, Houston, Texas
Surgeon Attending

St. Luke's Hospital, Houston, Texas
Courtesy Staff

Methodist Hospital, Houston, Texas
Active Staff

ADDITIONAL BIOGRAPHICAL DATA

Member, Editorial Advisory Board for EMERGENCY MEDICINE	1976 - Present
Disaster Medical Care Zone One Coordinator, State of Texas, Governor's Division of Disaster Emergency Services	1976 - Present
Editorial Consultant, JOURNAL OF TRAUMA	1976 - Present
Editorial Consultant, CHEST	1976 - Present
Associate Editor- Thoracic Trauma, CURRENT CONCEPTS IN TRAUMA CARE	1977 - Present
North American Vice President of Pan American Medical Association's SECTION ON TRAUMATIC SURGERY	1978

COMMITTEES

Emergency Department Design and Function, The University Association for
Emergency Medical Services, 1974-75

Emergency Medical Services Committee, Harris County Medical Society

Chairman, Hospital Subcommittee, Emergency Medical Services,
Harris County Medical Society

Disaster Subcommittee, Emergency Medical Services Committee,
Harris County Medical Society

Emergency Care Committee, The Greater Houston Hospital Council

Medical Students Admission Committee, Baylor College of Medicine

Chairman, Emergency Room and Outpatient Committee,
Harris County Hospital District

Transfusion Committee, Harris County Hospital District

Chairman, Clinical Department Heads Committee, Harris County Hospital District

Utilization Review Committee, Harris County Hospital District 1974-75

Nurse-Physician Committee, Harris County Hospital District

Infectious Disease Committee, Harris County Hospital District

Research Committee, American College of Emergency Medicine

Chairman, Program Committee, University Association for Emergency Medical Services

Chairman, American College of Surgeons South Texas Committee on Trauma

Emergency Medical Services Committee, Texas Medical Association

Research Committee, University Association for Emergency Medical Services

Chairman, Long Range Planning Committee, American Trauma Society

Chairman, Community Services Committee, American Trauma Society, 1975-76

Robert Wood Johnson Grant ad hoc Committee, Baylor College of Medicine

Allied Health Manpower Development Committee, Baylor College of
Medicine

Program Committee, KOPPA Pulmonary Conference, 1974-present

Executive Committee, American Trauma Society, 1975 - present

COMMITTEES (CONTINUED)

AMROC Committee, Baylor College of Medicine

American Association of Medical College's Education Review Committee

Curriculum Committee, Baylor College of Medicine

Medical Advisory Board, Occupational Therapy, Texas Womens University

Chairman, Blood Filter Standards Committee, Association for the
Advancement of Medical Instrumentation

Committee on Pulmonary Surgery, American College of Chest Physicians

Chairman, Categorization Subcommittee, EMS Committee of Houston-Galveston
Area Council

Budget and Finance Committee, Southwestern Surgical Congress

Executive Committee, University Association for Emergency Medicine

Medical Co-Chairman, Board of Standards Committee for Association for
the Advancement of Medical Instrumentation

Utilization Review Committee, Texas Institute of Rehabilitation and
Research

Steering Committee, American College of Chest Physicians

PUBLICATIONS:

73 articles on surgical procedures, techniques, cardio-vascular devices and treatments, operative management of pathological conditions, and treatment of traumatic conditions through surgical intervention.

**Infant deaths
linked to poor
sterilization**

By Jane A. Smith 8/29/84
The Sun

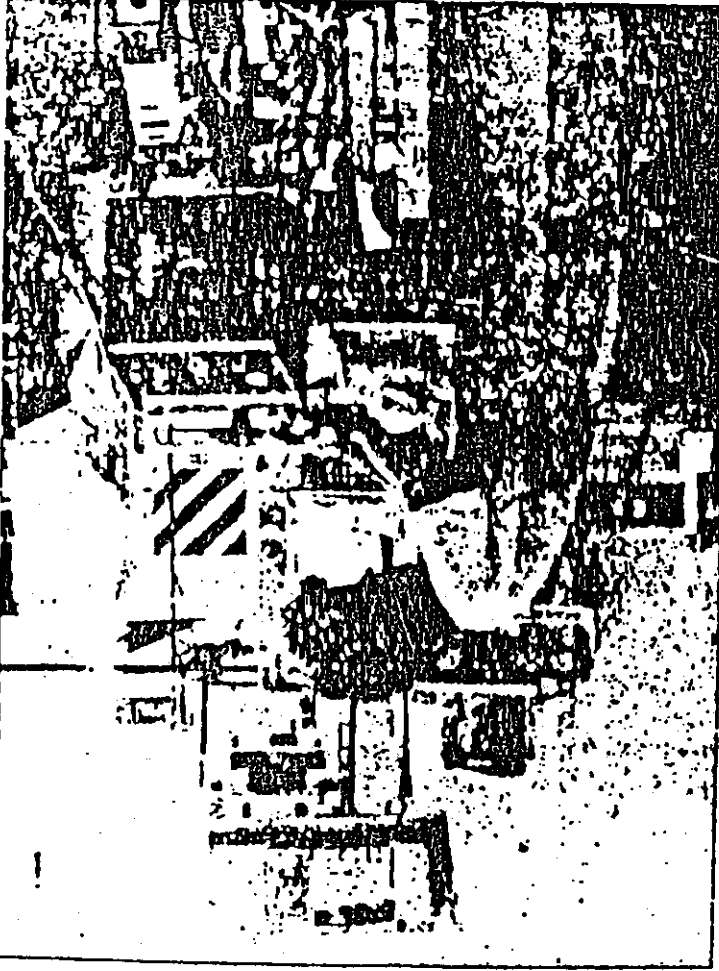
Doctors studying the outbreak of a bacterium at University Hospital expected to, that lactecture and frequent sterilization of respiratory equipment contributed to two of the three deaths of premature infants.

The infant who died on August 3 — the first death during the outbreak of "pseudomonas aeruginosa" in the hospital's intensive care nursery — was infected by his mother, doctors said at a news conference yesterday. That particular strain of the bacterium, contracted by the mother before she entered the hospital, was not spread to other babies, according to Dr. Feng-Ying Lin, the state epidemiologist, and two University Hospital doctors who aided in the investigation.

Evidence indicates that the two other babies who died were infected to the hospital because of a failure to follow standard, accepted sterilization procedures.

Doctors believe that the second baby, to die, on August 8, may have been infected by the respirator it was on during the six days of its life.

In June, the hospital switched from a gas method of sterilizing the respirators to a pasteurization method, which entails dunking the ap-



University Hospital respirator for premature babies is typical of the equipment involved in bacterial outbreak and deaths of patients.

Attachment 6

Infant deaths linked to inadequate sterilization

BABIES, from 1D

parates into hot water for 30 minutes. The electrical heating unit, which contains water and a heating rod so that the infants' air supply is warm and moist, could not be submerged, so it was wiped with disinfectant instead. While the pasteurization method is acceptable, washing the heating unit by hand is not, Dr. Lin said.

The bacterium could have traveled from the heating device through plastic tubing, the doctor said.

The second deficiency was found in the resuscitation room in the old labor and delivery suite. A baby born on August 8 to another woman

infected with *Pseudomonas* was given a resuscitation bag to pump oxygen into its lungs immediately after birth.

That same rubber air bag, about the size of a grapefruit, was used on three other infants who were born within the same 24 hours. Contrary to what is supposed to be standard procedure, the bag was not sterilized between uses.

The baby whose mother was carrying the bacteria survived. One of the three infants who used the same bag died on August 11.

"It [the sterilization] wasn't happening. It may have contributed to the outbreak, but we can't prove it," said Dr. Lillian M. Blackmon, direc-

tor of nurseries at the hospital.

She said "we have had a problem periodically in the past" with nurses forgetting to sterilize the bags.

Assured that all sterilization procedures had been corrected, however, the hospital yesterday resumed accepting infants into the neo-natal intensive care unit on the sixth floor.

The infants who were affected by the outbreak will be cared for in a separate section of the unit, however, Dr. Blackmon said.

Culture results completed yesterday turned up four different strains of the bacterium, but only three of them caused infection. In all, seven babies became sick, three of them dying. Six others carried the bacterium but did not become ill.

The different varieties of the bacterium — which caused pneumonia and blood poisoning — suggested there were several sources of it, the doctors said.

Pseudomonas aeruginosa is a common bacterium often found on fresh fruits and vegetables and in hospitals. It poses no problem to people with healthy immune systems, but has been known to cause infections in premature infants and patients suffering from burns, severe trauma and cancer.

The doctors' conclusions were drawn more from common sense than scientific proof. More than 300 cultures were taken in hopes of tracking down the sources, but positive cultures of *Pseudomonas* were obtained only from the tubing on respirators being used by infants carry-

ing the bacterium — not an unexpected finding.

The fact that *Pseudomonas* was not found on other equipment does not mean it never grew there, however.

While *Pseudomonas* was not found on the heating devices in the respirators, other bacteria was. Leading the doctors to speculate that *Pseudomonas* did exist at one time and traveled to the babies through the plastic tubing.

What turned up more conclusive evidence than the lab work was a review of sterilization procedures.

All the babies who died faced health risks to begin with, weighing less than 2 pounds and born at least 10 weeks premature.

Since the outbreak, the hospital has returned to the gas method of sterilizing the respirators. The hospital switched methods because it anticipated that new OSHA standards would make its use of ethylene oxide unacceptable, Barbara W. Cahn, a University Hospital spokeswoman said.

All other deficiencies have been corrected and frequent cultures will be taken to assure early detection if the bacterium resurfaces, Dr. Blackmon said.

She declined to speculate whether any personnel would be disciplined.

"There were gaps," she said. "Things were not as thorough as we would have liked them to be, but it is difficult to point to any one individual."

I. Environ Corp.

ENVIRON

ENVIRON Corporation
Counsel in Health and Environmental Science

January 13, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
California Air Resources Board
Attn: Ethylene Oxide
P.O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

ENVIRON Corporation is commenting on the "Draft Report to the Air Resources Board on Ethylene Oxide Submitted to the Scientific Review panel for Review" dated November 1986.

ENVIRON is a scientific and regulatory affairs firm that specializes in the evaluation of actual and potential risks to humans and their environment from exposures to substances in their environment. As such, ENVIRON serves both government and industry in providing expert and objective insight into complex scientific issues within a regulatory context. A brochure describing our firm is attached herewith.

Last year, ENVIRON was retained by McCormick and Company, Inc. to examine independently whether ethylene oxide (EtO) emissions from McCormick's Shilling plant in Salinas, California, present any threat to the health of individuals located in the vicinity of the plant, and, if so, the magnitude of those health risks. That evaluation was undertaken in several steps (with particular attention to exposure assessment including our own exposure modelling, and to risk estimation), the results of which were presented to the Monterey Bay Air Pollution Control District, the organization with regulatory jurisdiction over emissions from that plant.

Recently, McCormick made available to ENVIRON the November 1986 Draft Report on EtO and sought our impartial analysis of its contents, and asked that our comments be communicated directly to the Air Resources Board. Those comments follow. Because of the brevity of the time period for public comment, our comments are necessarily limited in scope.

1. We have performed for McCormick evaluations of ethylene oxide emissions and population exposure using two models widely-accepted by the scientific community and using the most dependable meteorological information for the Salinas area. We submit for the Air Resource Board's consideration, those reports which are as follows:

- o Modeling of Human Inhalation Exposures to Ethylene Oxide from Air Emissions at McCormick & Co.'s Schilling Plant (Salinas California). January 6, 1986.
- o Assessment of Possible Health Risks Associated with Exposure to Ethylene Oxide Released to the Atmosphere from the Salinas Plant of McCormick and Company, Inc. January 15, 1986.
- o Supplement to Assessment of Possible Health Risks Associated with Exposure to Ethylene Oxide Released to the Atmosphere from the Salinas Plant of McCormick and Company, Inc. (January 15, 1986), June 27, 1986.

While the Board may have seen these reports previously, they may not have been considered in the Draft Report with respect to comments related to McCormick's operation.

2. The Draft Report presents an estimate of emissions from McCormick's Shilling plant of 20 tons per year, a quantity that is at least a threefold exaggeration of actual emissions. We believe that estimate is erroneous. To model the concentrations of EtO surrounding the Shilling plant, ENVIRON requested and received the same analytic, and all inclusive, data that had been submitted to the Air Resources Board with which to carry out its exposure modelling. We were also provided detailed information about the operating conditions of the plant, which appear compatible with those referenced in the subject draft. Given this discrepancy, we recalculated the total emissions. During normal operation, McCormick measured average total emissions of EtO from all stacks and vents of 0.349 g/second. Based on a 17-hour operating day, and 260 operating days per year, this emission corresponds to a total annual emission of 6.1 tons, with a maximum of 8.6 tons per year if operation occurs 365 days/year. These emission data, which were developed by McCormick and submitted to the ARB and the local air authority, differ substantially from the data described in the ARB report (Appendix D, page D-10). The reason for this discrepancy is unclear and should be investigated before any final decisions are reached. Should the Board possess analytic information about emissions rates and concentrations other than those supplied by McCormick, we ask that they be provided to us so that we may evaluate them fully to establish their consequence on our original estimates of risk provided to the District and to McCormick.

3. The evaluation of risks presented in the draft contains several factors that are either incorrect or represent exaggerations of conventional interpretations of data. Those factors are:

- a. The exposure concentrations represent maximum rather than average concentrations. Since the cancer risk is related to the lifetime average daily dose (as influenced for EtO by the concentrations in inhaled air), the correct expression of inhaled concentration is the daily average and not the maximum concentration that represents only occasional excursions.
- b. The interpretation of data about peritoneal mesotheliomas in relation to the application of the trend test represents an over-interpretation of the results of a statistical test. A significant outcome in the Armitage trend test indicates that the slope of the best-fitting straight line through the data points is significantly different from zero. It says nothing about whether a straight line (i.e. a directly proportional increase with dose), or some other curve, best represents the dose-response relationship.
- c. The epidemiological evidence is exaggerated in importance with regard to establishing causation for EtO carcinogenesis in humans. In only two studies (not five) was the excess cancer incidence significantly different from controls. In two other studies, the "excess" was each based on a single case, and in no study was the excess based on more than three cases. Such studies are limited in establishing causation, particularly in light of the other chemicals to which the workers were exposed.
- d. The unit cancer risk (upper 95% confidence limit, UCL) cited in the draft is considerably (i.e., 8-fold) higher than that determined by McCormick. That difference is the result of the Board incorporating conservative assumptions that have little scientific foundation. We recommend strongly that the Board consider seriously the Risk Assessment for EtO submitted by McCormick, one that relies on all available information about the biological/carcinogenic properties of EtO (see attached report). The result of such unjustifiably inflated UCRs is to overestimate the risk, a condition that may lead to inappropriate public health actions.
- e. The draft report examines the application of the Gaylor-Kodell model, but does so by restricting the dose groups to which it is applied. The methodology developed by the authors of that procedure involves applying a computer model to the data from all of the dose groups to estimate the upper confidence limit on the response at the lowest dose level; it does not suggest using data from only the lowest dose group as was done in the Draft Report.

Mr. Loscutoff

-4-

January 13, 1987

We trust that these comments will be of assistance in subsequent revisions of the Board's draft. We would ask that future communications seeking comments be sent directly to us.

Should you have any questions about our comments, we would be pleased to respond to your inquiries by mail or by phone.

Sincerely,


Robert G. Tardiff, Ph.D.
Principal

RGT:wc

Attachments

cc: Dr. Richard Hall, McCormick & Company
Mr. James Schwefel of Noland, Hamerly, Etienne & Hoss

**MODELING OF HUMAN INHALATION EXPOSURES
TO ETHYLENE OXIDE FROM AIR EMISSIONS
AT McCORMICK & CO.'s SCHILLING PLANT
(SALINAS, CALIFORNIA)**

Prepared for

**McCormick and Company
Attn: Dr. Richard Hall
11350 McCormick Road
Hunt Valley, Maryland 21031-1066**

Prepared by

**Environ Corporation
1000 Potomac Street, NW
Washington, D.C. 20007**

January 6, 1986

**For further information, contact Dr. Robert G. Tardiff or Mr. Michael Scott at
(202) 337-7444.**

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I. INTRODUCTION

Presently McCormick and Company fumigates spices with ethylene oxide (EtO). McCormick's Schilling plant at Salinas, California, conducts such fumigations on a regular basis and, as such, releases into the ambient air approximately 57 pounds of ethylene oxide daily.

The Monterey Bay Unified Air Pollution Control District, which has regulatory jurisdiction over the plant, has proposed to limit ethylene oxide air emissions from that plant to approximately one-tenth of the present daily rate of release. The District's rationale for such action rests solely with the conclusion reached by the California Department of Health Services that the present emissions constitute an unacceptable cancer risk to humans. That conclusion, in turn, rests in part on an exposure evaluation performed by the California Air Resources Board.

In view of the importance of the regulatory proposal and with knowledge of the degree of uncertainty that often accompanies such assessments, McCormick sought assistance in the evaluation of the scientific soundness of the components of the State's risk assessment. McCormick retained Environ Corporation initially to review the State's exposure assessment which was based on dispersion modeling of air emissions from the plant. After review of the State's report, it became readily apparent that there was insufficient documentation of the State's modeling procedures and supporting data to permit a thoughtful and in-depth review. Subsequently, McCormick asked Environ to

conduct a state-of-the-art exposure assessment using the same general approach that the State had used.

Exposure was assessed for three scenarios: (1) under present operating conditions, (2) with the addition of a DEOXK scrubber, and (3) with the addition of a DEOXK scrubber and raising the height of the main stack to approximately 50 feet. This report presents in Section IV the results of ENVIRON's modeling of air concentrations in the areas surrounding the Schilling plant and estimates the concentrations anticipated in neighboring communities, with a description of the uncertainties that surround those estimates. The model used to derive these estimates is described in Section II; and the data used in the model are presented in Section III.

II. THE MODEL

The dispersion of EtO emissions from the plant was represented using a mathematical dispersion model developed for the Environmental Protection Agency (EPA). This is the Industrial Source Complex (ISC) model and was selected as a recognized and recent model capable of simulating the emission sources of interest in this study (Bowers, et al., 1979). It consists of two separate computer codes. The first (ISCST) is a short-term or sequential model which uses hourly meteorological data for the site under study to simulate hourly ambient air concentrations downwind of emission points. These hourly values can also be aggregated to form averages over longer periods. The second (ISCLT) is a long-term or climatological model which uses joint frequency data of wind speed, wind direction, and atmospheric stability class

to produce annual or seasonal ambient air concentrations around the emission points. Since the annual average exposures to EtO emissions were of primary importance in this study, the second long-term ISCLT code was used.

The ISC model treats the dispersion of each emission source as a Gaussian plume, in which the concentration of pollutants within the plume follows a normal distribution, or "bell" curve in the vertical and horizontal, crosswind directions. Volume sources, of interest here, are represented as virtual point sources, i.e., as if they are point sources emitting at some distance upwind of the actual point of emission. This distance depends on the dimensions of the volume sources and atmospheric stability conditions. Concentrations are calculated at specified points downwind as a function of meteorological parameters, i.e., wind speed, atmospheric stability class, mixing height, and as a function of downwind distance. In the long-term version, ISC calculates concentrations at a given receptor for a complete range of meteorological parameters and the results are then weighted according to the frequency of occurrence of these parameters at the location under study, thus forming an average concentration for the period of the frequency data, e.g., one year.

III. INPUT DATA

1. Meteorological and Topographic Data

The first set of input data required by the model are concerned with local meteorological and topographic conditions. The required meteorological

joint frequency data were obtained from the National Climatic Data Center. The best frequency data readily available were for Salinas Airport, derived from observations taken over the five year period 1960 to 1964, inclusive. Those data are attached to this report as Appendix A. An additional climatic variable required by the model is the annual average afternoon mixing height. A value of 700 m was used, based on published data for the area (Holzworth, 1972). Variations in mixing height with wind speed and atmospheric stability conditions were incorporated in the model simulation according to procedures set out in the model user's guide (Bowers, et al., 1979). No attempt was made to validate this approach with local measurements. However, considering the nature of the emission sources, i.e., close to the ground with little or no plume rise, the results are not expected to show significant sensitivity to this factor. Topographic relief was not considered in the simulation. Since the emissions are released close to ground level and there are no major elevation changes in the vicinity of the plant, this is not considered to be a significant limitation of the analysis.

2. Emissions Data

The emissions sources were treated conservatively as two separate volume sources, since the heights and locations of the various vents are such that emissions would likely be downwashed and mixed into the building wakes under some wind conditions. Exhaust from stacks 1 to 16 (Rice Mill, Mill Exhaust and Cinnamon Exhaust) was assumed to emanate from the first volume source of height 37 ft. and an average cross-sectional dimension of 27 ft. The effective release height for this source was 18.5 ft. The exhaust from all

other stacks was assumed to emanate from the second volume source of height 22 ft. and an average cross-sectional dimension of 95 ft. The effective release height in this case was 11 ft. These two sources were modeled separately, initially assuming a unit rate of emission (1 g/s) from each. In a third simulation, only emissions from stack 20 (aeration stack) were considered assuming the stack height as raised. In this case, emissions from the stack were treated as a single point source, i.e., unaffected by building downwash effects, at a height of 48 ft. above grade. It should be noted that, in all simulations, no credit has been taken for any plume rise due to buoyancy or momentum of the exhausts.

3. Receptor Data

The final set of input data concerns the locations of the receptor points at which ambient concentrations are to be calculated by the model. In ISC, these must be specified by the user. To cover the potential impact area of plant emissions, a polar grid of receptors was specified between 300 m (the distance to the closest residence) and 5 km from the plant. The distance increments used were 100 m between 300 m and 2 km, and 500 m between 2 km and 5 km. Receptors along each radial arc were regularly spaced at 22.5 degree intervals, corresponding to directions N, NNE, NE, ENE, E, etc. from the plant. In addition, an additional receptor was included at 60 m from the plant to represent the fenceline of the facility.

IV. ESTIMATED EXPOSURES

1. Dispersion Factors

Using the ISCLT model the annual average patterns of concentrations at ground level were estimated for a unit emission rate (1 g/s) from each of the three source groupings identified above, i.e., for stacks 1 through 16, 17 through 23, and for stack 20, if raised, respectively. The maximum estimated concentrations at distances of 60 m and 300 m from the plant and the critical receptors are identified below in terms of dispersion factor expressed in $\mu\text{g}/\text{m}^3$ per g/s:

<u>SOURCE GROUPING</u>	<u>DISPERSION FACTOR AT 60m ($\mu\text{g}/\text{m}^3/\text{g/s}$)</u>	<u>DISPERSION FACTOR AT 300m ($\mu\text{g}/\text{m}^3/\text{g/s}$)</u>	<u>DIRECTION TO CRITICAL RECEPTOR</u>
1. Stacks 1 - 16	120	22.9	E
2. Stacks 17 - 23	310	42.5	ESE
3. Stack 20 (if raised)	15	14.2	E

It should be emphasized that the estimated concentrations at 60 m from the plant are approximate only, since at such close distances the accuracy of the model becomes less precise.

The highest concentrations, which are estimated to occur to the E and ESE of the plant, reflect the predominance of W and WNW winds at Salinas. They occur 19.3% and 16.8% of the time, respectively. Relatively high levels also occur to the WNW, reflecting the 11.9% of the time when winds blow from the

ESE. However, it is important to note that these frequencies, and the frequency data available from input to the ISC model in this study, were based on round-the-clock observations. Since the McCormick plant operates only between the hours of 7 a.m. and midnight, the use of these meteorological data introduces the potential for bias in the modeling results.

The location of Salinas, in the Salinas River valley and only a few miles from Monterey Bay, suggests that winds with a westerly component would be more likely to occur in the day, and winds with easterly components would be more likely to occur at night. This is the expected consequence of sea breeze and valley flow effects in this area. Although the necessary wind direction frequency analysis for Salinas, stratified by time of day, was not readily available to confirm the presence of this phenomenon, such an analysis was obtained for Monterey. This was based on seven years (1973 through 1979) of observations at Monterey Peninsula Airport, about 15 miles WSW of Salinas. At Monterey, E and ESE winds were particularly prevalent during the night in all seasons except summer. Typical frequencies of occurrence were between 10% and 20% for both these directions, even though they occurred only 3.1% and 2.2% of the time, respectively, on an annual average, round-the-clock basis (compared with 15.3% and 22.5% of the time for WSW and W winds, respectively).

The above indicates that a significant correlation exists between wind direction and time of day at Salinas and, therefore, between wind direction and plant emissions. Since there are no emissions at times when a disproportionate frequency of easterly winds would occur, use of the round-the-clock wind data with the dispersion model would tend to overestimate

concentrations to the west of the plant and underestimate concentrations to the east. Thus, the maximum levels, which occur to the east, may be higher than given in the above table, although this is offset by the conservative idealization of the emission sources and the fact that better dispersion conditions (greater atmospheric instability) are generally associated with westerly winds. No attempt has yet been made to quantify the sensitivity of the results to bias in the meteorological data. However, it is expected that a factor of 1.5 applied to the maximum concentrations estimated by the model would provide reasonably conservative exposure estimates. Further examination of this question would be needed if exposures calculated on this basis approached or exceeded levels likely to have an adverse effect on human health.

2. Estimation of Ethylene Oxide Concentrations

To estimate the concentrations of ethylene oxide (EtO) resulting from actual plant emissions, a two step process was undertaken. First, for each source grouping, EtO concentrations were estimated at downwind receptor locations by multiplying the unit emission dispersion factors (calculated from the dispersion model) by the actual emissions from that source grouping. Second, the contributions from each source grouping were combined to arrive at a total EtO concentration.

The emissions of EtO were for two types considered in the modeling of plant operation: plant ventilation emissions and chamber emissions. Plant ventilation emissions are continuous over the 17 hour operating day and occur through stacks 1 through 19. Chamber emissions are associated with the

fumigation process and include four exhaust systems: primary exhaust emissions (stack 21); secondary exhaust (stack 23); auxiliary exhaust (stack 22); and aeration exhaust (stack 20). In addition, consideration was also given to changes in EtO chamber emissions that would occur with the addition of a DEOXX system. Down wind EtO concentrations were estimated based on three release cases.

The first case consisted of two source groupings: stacks 1-16 (effective release height of 18.5 ft.) and stacks 17-23 (effective release height of 11 ft.). Emissions in this first case did not include the reduction in emissions due to the DEOXX system.

The second release case included the same two source groupings as did case one, with modifications of the emissions due to the DEOXX system. The DEOXX system would be designed to handle the EtO load from the aqueous discharges generated in the fumigation process as well as the air emissions from the primary and auxiliary exhausts. The system will provide at least a 99.9% reduction in the EtO emissions from these sources.

The third release case consisted of three source groupings: stacks 1-16 (effective release height of 18.5 ft.); stacks 17-23 (effective release height of 18.5 ft.); stacks 17-23 (effective release height of 11 ft.) excluding stack 20; and stack 20 (effective release height of 48 ft.). Emission reductions due to the DEOXX system were also included in this case.

The actual emissions from the plant ventilation system were determined from hourly EtO emissions in lbs./hr. and extrapolated to lbs./day to reflect a 17-hour operating day. This emission rate was converted to g/s for multiplication by the appropriate unit emission factor. Aeration emissions through stack 20 were determined by multiplying the pounds of EtO emitted per chamber by four chamber emissions per day. Emission data for stacks 1 through 20 are presented in Appendix B.

Chamber emissions due to the fumigation process were calculated based on data obtained from a mass balance of EtO (conducted by McCormick and Company in 1985) during a complete fumigation cycle. As fumigation in the chamber occurs four times during the operating day, the results from this test were multiplied by 4 to obtain the pounds of EtO emitted per day. This amount was converted to g/s for multiplication by the appropriate unit emission factor. Emission results and mass balance data from this test are presented in Appendix B.

The results of the analysis are presented in Table 1 for downwind distances of 60 m and 300 m in the easterly direction (i.e., that of the highest concentrations). In addition, isopleths showing EtO concentrations out to 3.5 km from the plant are shown on Figures 1 through 3 for cases 1 through 3, respectively.

3. Population Exposures

In an effort to determine the significance of the predicted EtO exposures, the population in the vicinity of the plant was estimated. The

TABLE 1

EtO Concentrations

Downwind Distance

	60 m		300 m	
	$\mu\text{g}/\text{m}^3$	ppm	$\mu\text{g}/\text{m}^3$	ppm
Case 1	89.1	0.04	12.2	0.006
Case 2	17.0	0.008	2.34	0.001
Case 3	2.8	0.0013	1.0	0.0005

area of concern was chosen to be that within the $0.11 \mu\text{g}/\text{m}^3$ isopleth in Case 3. This is based on the belief that an EtO concentration of $0.11 \mu\text{g}/\text{m}^3$ translates into an estimated cancer risk which is acceptable in a regulatory context.

Based on a review of USGS topographic maps of the Salinas area and a visual inspection, it was estimated that there are no more than 50 residential homes within the area of concern. Based on an average of 3 persons per home, this corresponds to a population of 150. In addition, it was estimated that there are 140-150 industrial establishments in the area, which employ approximately 2,100 to 2,200 people. This estimate is based on a visual inspection and a review of the city's Industrial Guide.

A visual inspection of the area also indicated two inactive and five active migrant labor camps. Each of the five active camps contains 90 one-bedroom units. The two inactive camps each contain 80-100 one-bedroom units.

Based on the above, it is conservatively estimated that between 3,000 to 3,500 people may be exposed to concentrations of EtO in excess of $0.1 \mu\text{g}/\text{m}^3$ due to emissions from the McCormick facility. The industrial workers would be exposed for no more than 8 hours per day, 5 days per week. The migrant workers are likely to be exposed for only a fraction of the year and may not return in future years. Consequently, the number of individuals who might be exposed continuously for extended periods should be no greater than 100 to 200.

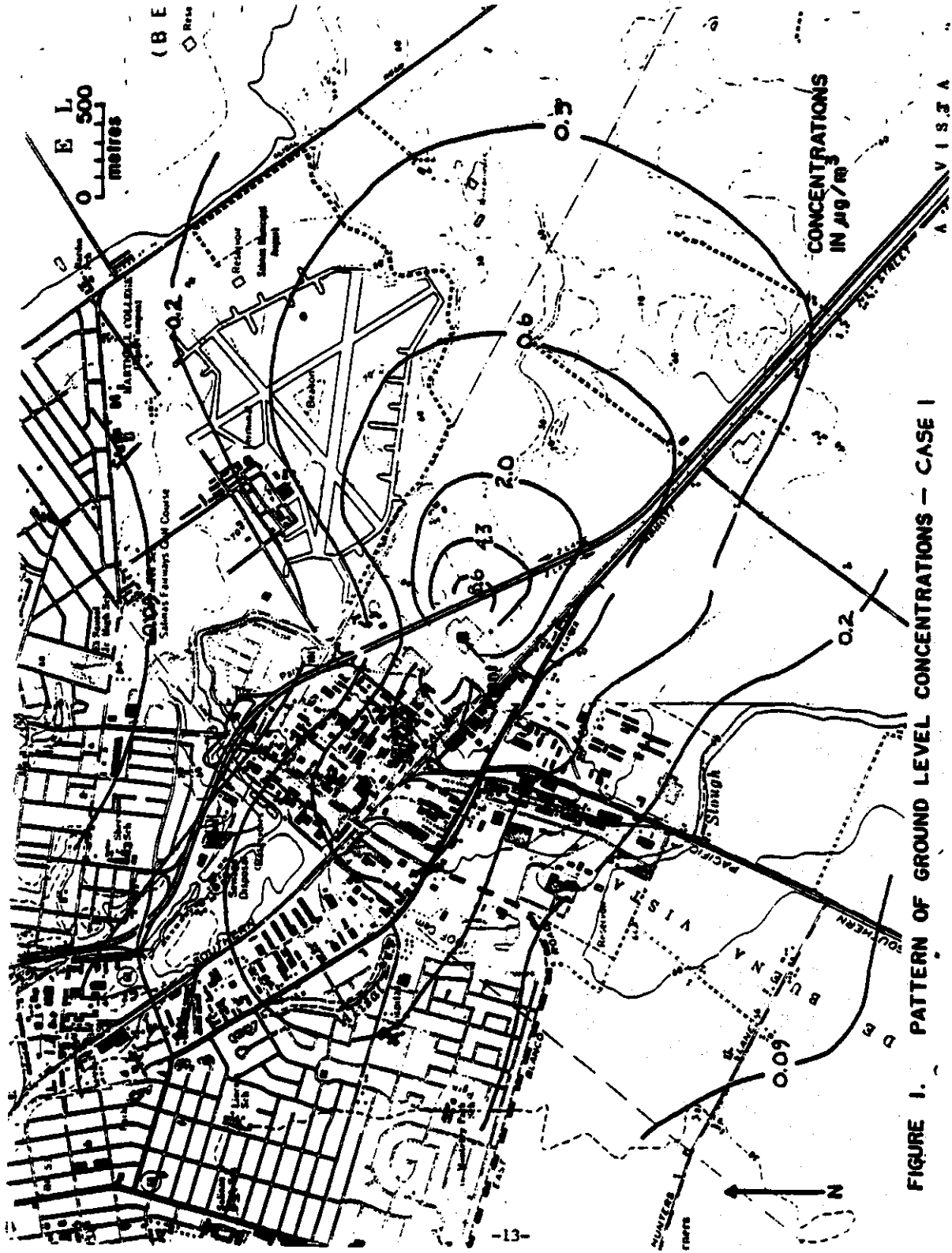


FIGURE 1. PATTERN OF GROUND LEVEL CONCENTRATIONS - CASE I

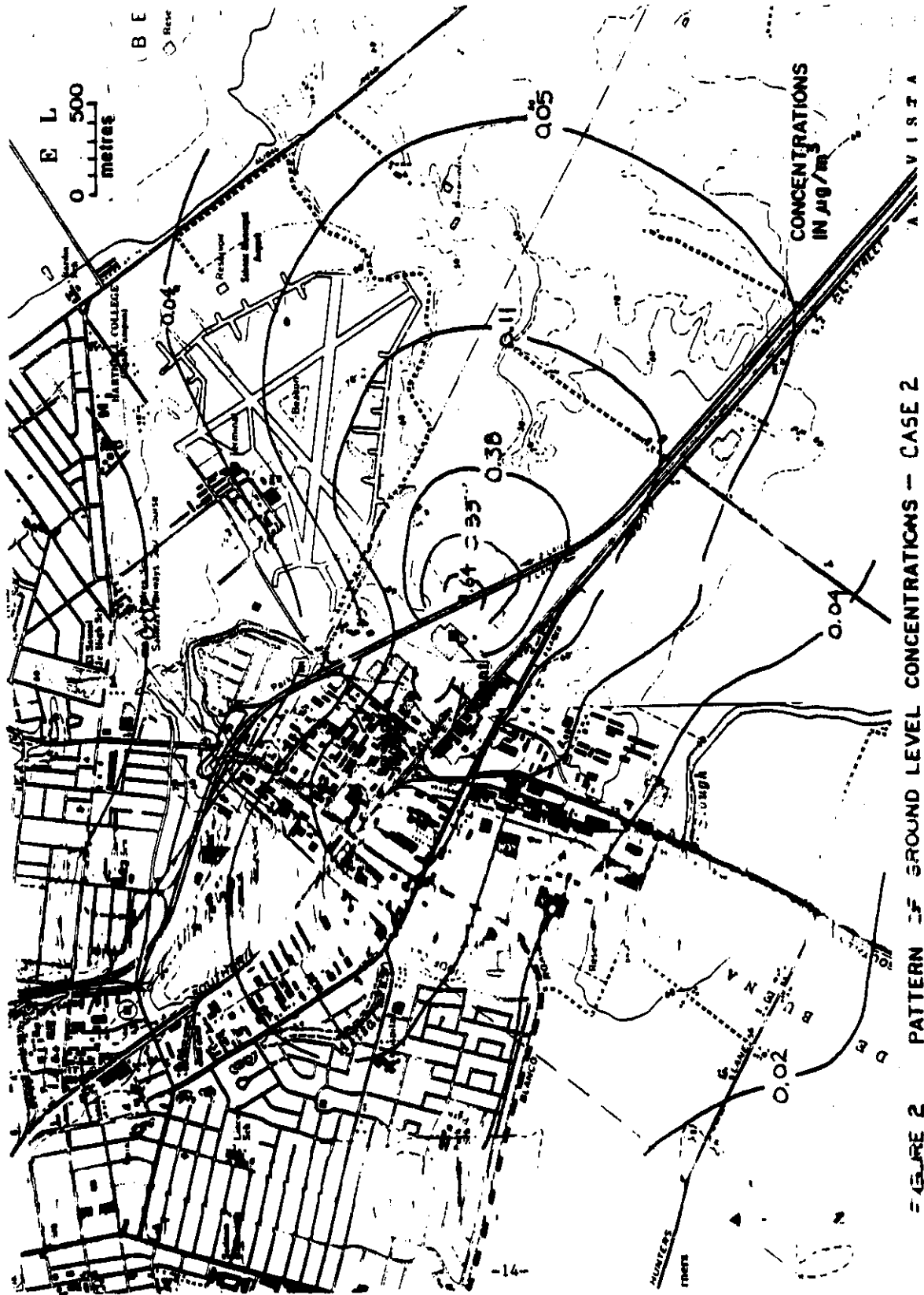


FIGURE 2 PATTERN OF GROUND LEVEL CONCENTRATIONS - CASE 2

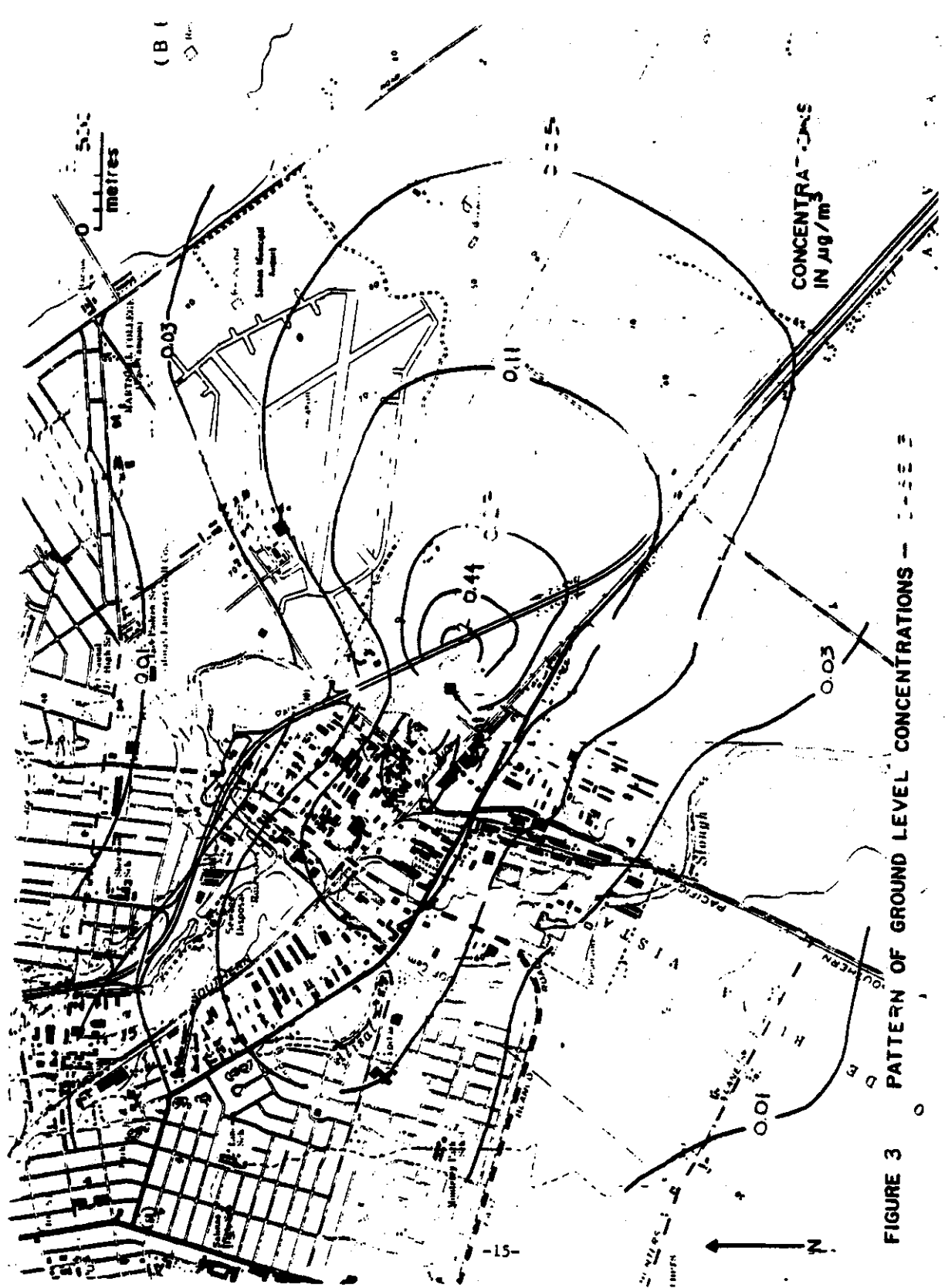


FIGURE 3 PATTERN OF GROUND LEVEL CONCENTRATIONS - CASE 3

V. CONCLUSIONS

As indicated in the discussion of unit emission rates, the pattern of highest concentrations predicted by the air modeling is predominantly to the E and ESE of the plant and to a lesser extent to the WNW. There is, however, very limited population to the east of the plant, so that, in general, population exposure would be more of concern to the WNW of the plant where the residential and commercial areas of Salinas are located. More specifically, the following conclusions can be reached:

1. The average annual concentration of EtO predicted at the nearest possible off-site receptor, i.e., the fence line of the facility under current operating conditions is $89 \mu\text{g}/\text{m}^3$ at the eastern boundary of the facility. Lower concentrations are predicted at the fence line for those points not located in the dominant wind direction.
2. The predicted annual average concentration at the nearest residence which is located approximately 300 m east of the plant, is $12 \mu\text{g}/\text{m}^3$ under current operating conditions.
3. Based on review of the USGS topographic map for the Salinas area, it would appear that under current operating conditions the maximum annual average EtO concentrations, to which the populated areas to the WNW of the plant are exposed, are in the range $1-2 \mu\text{g}/\text{m}^3$.
4. The installation of the DEOXX system has the effect of reducing exposures at a given point by approximately an order of magnitude.
5. The raising of the aeration stack after installation of the DEOXX system has a limited effect on annual average concentrations, except at distances very close to the plant. At 300 m from the plant, an additional reduction in average annual concentration by a factor of two is predicted, and this falls off rapidly with increasing distance from the plant.
6. With the installation of the DEOXX system and raising of the aeration stack, the exposed population within an area encompassed by the $0.11 \text{ mg}/\text{m}^3$ 150 isopleth was estimated to be no greater than 3,000-3,500, with most individuals exposed for only part of the day and some for only a few months in their life. At most, only a few hundred individuals might be exposed continuously for long periods of time.

VI. REFERENCES

Bowers, J.F., Bjorklund, J.R., and Cheney, C.S., Industrial Source Complex (ISC) Dispersion Model User's Guide, H.E. Cramer Inc., U.S. Environmental Protection Agency Report No. EPA-450/4-79-030 (NTIS Acc. No. PB80 133044), December 1979.

Holzworth, G.C., Mixing Heights, Wind Speeds, and Potential for Urban Air Pollution Throughout the Contiguous United States, U.S. Environmental Protection Agency Report No. AP-101, January 1972.

Acknowledgment: ENVIRON is grateful for the technical assistance in the air modeling provided by Dr. Colin Baynes, Georgetown, Ontario, Canada.

APPENDIX A
METEOROLOGICAL DATA

ANNUAL

RELATIVE FREQUENCY DISTRIBUTION

STATION #23233 SALINAS, CA

24 DRS

1960-64

SPEED(KTS)

DIRECTION	0 - 3	4 - 6	7 - 10	11 - 16	17 - 21	GREATER THAN 21	TOTAL
N	0.000337	0.000050	0.000000	0.000000	0.000000	0.000000	0.000387
NNE	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
NE	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
ENE	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
E	0.000168	0.000023	0.000000	0.000000	0.000000	0.000000	0.000191
ESE	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
SE	0.000191	0.000000	0.000000	0.000000	0.000000	0.000000	0.000191
SSE	0.000168	0.000023	0.000000	0.000000	0.000000	0.000000	0.000191
S	0.000168	0.000023	0.000000	0.000000	0.000000	0.000000	0.000191
SSW	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000	0.000000
SW	0.000168	0.000023	0.000000	0.000000	0.000000	0.000000	0.000191
WSW	0.001010	0.000157	0.000000	0.000000	0.000000	0.000000	0.001167
W	0.004063	0.000325	0.000000	0.000000	0.000000	0.000000	0.004388
WNW	0.002397	0.000320	0.000000	0.000000	0.000000	0.000000	0.002717
NW	0.001761	0.000160	0.000000	0.000000	0.000000	0.000000	0.001921
NNW	0.000337	0.000050	0.000000	0.000000	0.000000	0.000000	0.000387
TOTAL	0.010329	0.001325	0.000000	0.000000	0.000000	0.000000	

RELATIVE FREQUENCY OF OCCURRENCE OF A STABILITY = 0.010329

RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE WITH A STABILITY = 0.010329

1-7

ANNUAL		RELATIVE FREQUENCY DISTRIBUTION					STATION #23233 SALINAS, CA 24 PDS 1960-61	
		SPEED (kts)						
DIRECTION	0 - 3	4 - 6	7 - 10	11 - 14	17 - 21	GREATER THAN 21	TOTAL	
N	0.000072	0.000275	0.000099	0.000000	0.000000	0.000000	0.001013	
NNE	0.000179	0.000071	0.000073	0.000000	0.000000	0.000000	0.000273	
NE	0.000360	0.000291	0.000000	0.000000	0.000000	0.000000	0.000651	
ENE	0.000279	0.000228	0.000073	0.000000	0.000000	0.000000	0.000530	
E	0.000830	0.000558	0.000114	0.000000	0.000000	0.000000	0.001502	
ESE	0.001605	0.001302	0.000395	0.000000	0.000000	0.000000	0.003272	
SE	0.002230	0.001142	0.000291	0.000000	0.000000	0.000000	0.003663	
SSE	0.000379	0.000297	0.000000	0.000000	0.000000	0.000000	0.000676	
S	0.000236	0.000231	0.000000	0.000000	0.000000	0.000000	0.000467	
SSW	0.000132	0.000127	0.000000	0.000000	0.000000	0.000000	0.000270	
SW	0.000909	0.000358	0.000228	0.000000	0.000000	0.000000	0.001495	
WSW	0.001297	0.001276	0.000799	0.000000	0.000000	0.000000	0.003372	
W	0.002779	0.005322	0.004703	0.000000	0.000000	0.000000	0.012804	
WNW	0.003022	0.005682	0.005898	0.000000	0.000000	0.000000	0.014602	
W	0.002997	0.003015	0.001502	0.000000	0.000000	0.000000	0.007514	
WNW	0.000862	0.000822	0.000193	0.000000	0.000000	0.000000	0.001877	
TOTAL	0.018407	0.019600	0.013110	0.000000	0.000000	0.000000		
RELATIVE FREQUENCY OF OCCURRENCE OF θ STABILITY = 0.021304								
RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE WITH θ STABILITY = 0.012226								

A-2

A-3

ANNUAL RELATIVE FREQUENCY DISTRIBUTION STATION #23233 SALINAS CA 24 OBS 1960-65

SPEEDS (KTS)

DIRECTION	0 - 3	4 - 6	7 - 10	11 - 16	17 - 21	GREATER THAN 21	TOTAL
N	0.000250	0.000525	0.000365	0.000000	0.000000	0.000000	0.001140
NNE	0.000087	0.000114	0.000114	0.000023	0.000000	0.000000	0.000338
NE	0.000139	0.000206	0.000238	0.000000	0.000000	0.000000	0.000583
NNE	0.000123	0.000365	0.000274	0.000000	0.000000	0.000000	0.000762
E	0.000558	0.001941	0.002010	0.000089	0.000000	0.000000	0.004598
ESE	0.000998	0.003426	0.003989	0.000206	0.000000	0.000000	0.011619
SE	0.001025	0.003083	0.003132	0.000160	0.000000	0.000000	0.007400
SSE	0.000216	0.000617	0.000274	0.000000	0.000000	0.000000	0.001107
S	0.000128	0.000274	0.000046	0.000000	0.000000	0.000000	0.000448
SSW	0.000065	0.000137	0.000046	0.000000	0.000000	0.000000	0.000248
SW	0.000367	0.000868	0.000683	0.000297	0.000000	0.000000	0.002215
WSW	0.000431	0.001005	0.001705	0.002997	0.000297	0.000000	0.005635
W	0.000775	0.002672	0.010490	0.012920	0.000349	0.000000	0.033206
WNW	0.000853	0.002832	0.012439	0.012269	0.000297	0.000000	0.031678
W	0.000748	0.002010	0.003185	0.002672	0.000046	0.000000	0.010661
WNW	0.000234	0.000685	0.000982	0.000274	0.000023	0.000000	0.002198
TOTAL	0.006989	0.020761	0.056984	0.031907	0.001005	0.000000	

RELATIVE FREQUENCY OF OCCURRENCE OF C STABILITY = 0.117648

RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE WITH C STABILITY = 0.002607

ANNUAL

RELATIVE FREQUENCY DISTRIBUTION

STATION #23233 SALINAS, CA 24 OBS 1960-64

SPEEDS (KTS)

DIRECTION	0 - 3	4 - 6	7 - 10	11 - 16	17 - 21	GREATER THAN 21	TOTAL
N	0.000628	0.000868	0.000320	0.000220	0.000023	0.000000	0.002158
NNE	0.000363	0.000343	0.000091	0.000091	0.000000	0.000000	0.000888
NE	0.000372	0.000396	0.000091	0.000115	0.000000	0.000000	0.001774
ENE	0.000362	0.000480	0.000297	0.000200	0.000000	0.000023	0.001362
E	0.001146	0.002033	0.002704	0.003175	0.000434	0.000046	0.009598
ESE	0.001812	0.003860	0.004496	0.014303	0.003997	0.001730	0.034504
SE	0.002117	0.003586	0.003997	0.004477	0.001799	0.000571	0.016506
SSE	0.000287	0.001090	0.000390	0.000320	0.000137	0.000023	0.002351
S	0.000349	0.000822	0.000320	0.000137	0.000046	0.000000	0.001674
SSW	0.000358	0.000640	0.000320	0.000137	0.000023	0.000000	0.001477
SW	0.001303	0.002078	0.002320	0.002129	0.000617	0.000049	0.007728
WSW	0.001652	0.003677	0.000610	0.013999	0.002078	0.000091	0.030064
W	0.002712	0.003733	0.017701	0.033391	0.002991	0.000343	0.062560
WNW	0.001824	0.000665	0.012447	0.020321	0.000914	0.000069	0.047649
NW	0.001999	0.003317	0.004993	0.000062	0.000343	0.000000	0.019060
NNW	0.000628	0.001119	0.000708	0.001142	0.000200	0.000000	0.003801
TOTAL	0.018591	0.034510	0.063813	0.111479	0.013361	0.002969	

RELATIVE FREQUENCY OF OCCURRENCE OF 0 STABILITY = 0.244724

RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE WITH 0 STABILITY = 0.014103

(NEUTRAL / DAY)

ANNUAL

RELATIVE FREQUENCY DISTRIBUTION

STATION #2323 SALINAS, CA 24 DBS 1950-64

SPEED(KTS)

DIRECTION	0 - 3	4 - 6	7 - 10	11 - 16	17 - 21	GREATER THAN 21	TOTAL
N	0.001656	0.002078	0.001195	0.000228	0.000000	0.000000	0.003127
NNE	0.000573	0.000799	0.000308	0.000046	0.000000	0.000000	0.001616
NE	0.001616	0.001516	0.000137	0.000000	0.000000	0.000000	0.003169
ENE	0.000823	0.001073	0.000395	0.000228	0.000023	0.000000	0.002544
E	0.001918	0.003380	0.003339	0.003253	0.000320	0.000000	0.015210
ESE	0.003076	0.005573	0.009410	0.012767	0.002627	0.001188	0.034640
SE	0.003561	0.005703	0.004317	0.003408	0.002078	0.000822	0.019891
SSE	0.000791	0.001152	0.000617	0.000320	0.000137	0.000000	0.002920
S	0.001024	0.000891	0.000231	0.000137	0.000000	0.000000	0.002283
SSW	0.000828	0.001119	0.000411	0.000411	0.000069	0.000000	0.002828
SW	0.003789	0.005956	0.006098	0.003801	0.000274	0.000023	0.020021
WSW	0.005111	0.008017	0.014320	0.010232	0.000320	0.000046	0.037046
W	0.007248	0.013430	0.020190	0.007720	0.000777	0.000049	0.049232
WNW	0.003701	0.011236	0.018317	0.005618	0.000160	0.000000	0.041230
W	0.006556	0.009912	0.011280	0.004248	0.000091	0.000000	0.032200
WNW	0.001277	0.002923	0.002786	0.001233	0.000023	0.000000	0.008242
TOTAL	0.045940	0.072949	0.094692	0.058632	0.006877	0.002157	

RELATIVE FREQUENCY OF OCCURRENCE OF E STABILITY = 0.280209

RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE WITH E STABILITY = 0.023928

(NEUTRAL / NIGHT)

ANNUAL

RELATIVE FREQUENCY DISTRIBUTION

STATION #23233 SALINAS, CA 25 OBS 1960-64

SPEED (KTS)

DIRECTION	0 - 3	4 - 6	7 - 10	11 - 16	17 - 21	GREATER THAN 21	TOTAL
N	0.007136	0.008365	0.002581	0.000000	0.000000	0.000000	0.018082
NNE	0.002760	0.003015	0.002297	0.000000	0.000000	0.000000	0.008072
NE	0.005268	0.003791	0.000320	0.000000	0.000000	0.000000	0.009379
ENE	0.003339	0.003700	0.000558	0.000000	0.000000	0.000000	0.007607
E	0.007918	0.010348	0.008886	0.000000	0.000000	0.000000	0.027152
ESE	0.009532	0.013552	0.010737	0.000000	0.000000	0.000000	0.033821
SE	0.008203	0.007354	0.002421	0.000000	0.000000	0.000000	0.017978
SSE	0.001445	0.001370	0.000114	0.000000	0.000000	0.000000	0.002929
S	0.001327	0.001516	0.000069	0.000000	0.000000	0.000000	0.002912
SSW	0.000995	0.001028	0.000437	0.000000	0.000000	0.000000	0.002460
SW	0.004700	0.002299	0.003139	0.000000	0.000000	0.000000	0.010138
WSW	0.004519	0.007720	0.002331	0.000000	0.000000	0.000000	0.014570
W	0.009522	0.012379	0.010735	0.000000	0.000000	0.000000	0.032636
WNW	0.009500	0.013087	0.009661	0.000000	0.000000	0.000000	0.032248
W	0.016105	0.018980	0.011351	0.000000	0.000000	0.000000	0.046435
NNW	0.006302	0.009230	0.008090	0.000000	0.000000	0.000000	0.023622
TOTAL	0.099169	0.120532	0.076089	0.000000	0.000000	0.000000	

RELATIVE FREQUENCY OF OCCURRENCE OF F STABILITY = 0.294200

RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE WITH F STABILITY = 0.000640

ANNUAL

RELATIVE FREQUENCY DISTRIBUTION

STATION #23233 SALINAS, CA 24 OBS 1960-64

SPEED (KTS)

DIRECTION	0 - 3	4 - 6	7 - 10	11 - 16	17 - 21	GREATER THAN 21	TOTAL
N	0.010205	0.012356	0.004499	0.000348	0.000023	0.000000	0.027322
NNE	0.003879	0.004362	0.000914	0.000160	0.000000	0.000000	0.009315
NE	0.007925	0.000258	0.000777	0.000114	0.000000	0.000000	0.015073
ENE	0.004970	0.005847	0.001507	0.000434	0.000023	0.000023	0.012804
E	0.012738	0.018272	0.019033	0.008496	0.000734	0.000046	0.058338
ESE	0.017947	0.027613	0.036018	0.027576	0.006623	0.002723	0.118610
SE	0.018488	0.019870	0.015138	0.009044	0.003637	0.001393	0.066170
SSE	0.003731	0.004344	0.001393	0.000640	0.000274	0.000023	0.010006
S	0.003534	0.003677	0.000689	0.000274	0.000046	0.000000	0.008216
SSW	0.002371	0.003000	0.001233	0.000348	0.000091	0.000000	0.007303
SW	0.012086	0.013772	0.014486	0.009227	0.000891	0.000091	0.050348
WSW	0.014132	0.022131	0.035766	0.027179	0.002695	0.000137	0.102041
W	0.025505	0.039261	0.069820	0.054061	0.003700	0.000411	0.192758
WNW	0.022814	0.030320	0.060793	0.040204	0.001370	0.000069	0.167230
W	0.028009	0.037294	0.035210	0.014903	0.000689	0.000000	0.116001
WNW	0.009409	0.014326	0.010797	0.002949	0.000291	0.000000	0.037593
TOTAL	0.198634	0.269604	0.303284	0.202037	0.021263	0.002116	

TOTAL RELATIVE FREQUENCY OF OBSERVATIONS = 1.000001

TOTAL RELATIVE FREQUENCY OF CALMS DISTRIBUTED ABOVE = 0.198630

APPENDIX B
EMISSIONS DATA

SUMMARY
ETHYLENE OXIDE FATE

<u>SUBSTRATE</u>	<u>ETHYLENE OXIDE ACCOUNTED FOR</u> <u>(AS POUNDS OF EtO)</u>	
	<u>INITIAL</u>	<u>AFTER STORAGE</u>
WATER	24.79	
AIR	11.48	
SPICE PRODUCTS (64900)		
Post Treatment	13.03	
24 Hours		4.93
1 Week		1.53
DRUMS (34)	0.16	
PALLETS (9)	2.91	
Total EtO Accounted for	52.37	
TOTAL CHARGE	56	
% OF TOTAL CHARGE ACCOUNTED FOR	93.5%	

0777I

AIR EMISSION DATA

STACK NUMBER	SOURCE	VOLUMETRIC AIR FLOW (ft ³ /min)	SO ₂ CONC (mg/m ³)	SO ₂ EMISSIONS		STACK HEIGHT ABOVE ROOF (inches)
				lb/hr	lb/day (16 hr operation)	
RICE MILL						
1	0 1	548	0.21	0.0004	0.007	24
2	2	548	0.17	0.0003	0.005	24
3	3	548	0.06	0.0001	0.002	24
4	4	548	0.10	0.0002	0.003	24
5	5	275	0.30	0.0003	0.004	24
6	6	275	0.60	0.0006	0.009	24
7	7	636	0.33	0.0007	0.012	24
8	8	733	N. D.	0	0	24
9	10	672	0.22	0.0005	0.008	24
10	11	601	0.19	0.0005	0.007	24
11	12	275	N. D.	0	0	24
12	13	596	0.28	0.0006	0.010	24
MILL EXHAUST						
13	1	1,130	0.55	0.002	0.037	30
14	2	1,130	0.26	0.001	0.017	30
15	3	1,040	0.41	0.002	0.025	30
16	3	1,130	0.34	0.001	0.023	30
CINNAMON EXHAUST						
BOYOCLOSURE						
17	Foil/Cans	7,385	N. D.	0	0	36
18	Bottle/Cans	7,225	N. D.	0	0	36
19	Mills	8,170	0.26	0.007	0.12	36
20	AREATION			<u>g/chamber</u>	<u>g/day</u>	36
	1st 30 min.	7,070	67.33	0.89	3.57	
	2nd 30 min.	7,070	38.72	0.51	2.05	
	3rd 30 min.	7,070	37.15	0.49	1.97	
	4th 30 min.	7,070	38.88	0.41	1.63	
PROCESSING EXHAUST				0.018	0.28	
AREATION EXHAUST				2.38	9.22	

B-2

ETHYLENE OXIDE AIR EMISSION DATA

<u>STACK NUMBER</u>	<u>SAMPLE</u>	<u>H₂O CONC. (mg/m³)</u>	<u>VOLUMETRIC AIR FLOW (ft³)</u>	<u>H₂O DISCHARGED (lbs)</u>	<u>STACK HEIGHT ABOVE ROOF (ft.)</u>
21	(PRIMARY EXHAUST VENT)				72
	<u>CYCLE 1</u> - 1	165,385	66.74	0.69	
	- 2	592,165	72.34	2.67	
	- 3	224,597	102.61	2.56	
	TOTAL	294,758*	321.69	5.92	
	<u>CYCLE 2</u> - 1	49,903	256.42	0.80	
	- 2	10,812	237.87	0.16	
	- 3	47,450	82.20	0.24	
	- 4	41,407	92.20	0.24	
	- 5	37,987	92.20	0.22	
	TOTAL	34,942*	760.91	1.66	
	<u>CYCLE 3</u> - 1	38,789	335.67	0.82	
	- 2	44,023	47.85	0.13	
	- 3	14,935	217.16	0.21	
	- 4	7,355	90.10	0.05	
	- 5	6,380	169.06	0.07	
	TOTAL	23,657*	859.84	1.27	
	<u>CYCLE 4</u> - 1	6,966	358.98	0.15	
	- 2	5,170	188.45	0.07	
	- 3	7,210	110.71	0.05	
	- 4	3,778	83.03	0.02	
	- 5	1,696	23.56	0.02	
	TOTAL	6,493*	764.73	0.31	
22	(AUXILIARY AIR VENT)				4
	CYCLE 1	5,212	5,055	1.64	
	CYCLE 2	233.3	8,594	0.13	
	CYCLE 3	65.96	6,572	0.03	
	CYCLE 4	106.8	8,089	0.05	
	DURING RUN	14.65	76,843	0.07	
23	(SECONDARY AIR VENT)				4
	0-6 min.	296.9	3,448	0.06	
	6-18 min.	154.4	6,896	0.07	
	18-30 min.	350.8	6,896	0.15	
	30-42 min.	146.3	6,896	0.06	
	42-57 min.	48.29	20,114	0.06	

*Calculated Average

Assessment of Possible Health Risks
Associated with Exposure to Ethylene Oxide
Released to the Atmosphere from the
Salinas Plant of McCormick and Company, Inc.

Prepared by:

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January 15, 1986

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ACKNOWLEDGMENT

McCormick and Company gratefully acknowledges the technical assistance of some of the Nation's technical leaders in toxicology, biostatistics, exposure modelling, and health risk assessment. Those contributors include Mr. Carrol Weil (retired from the Carnegie-Mellon Institute), Dr. Robert Sielken (Texas A&M University), Dr. Leon Golberg (Duke University), and the professional staff of ENVIRON Corporation particularly Dr. Robert G. Tardiff, Dr. Catherine St. Hilaire, Dr. Duncan Turnbull, and Mr. Michael Scott.

McCormick is also indebted to Dr. Norman Gravitz of the California Department of Health Services and Peter Ventorini of the California Air Resources Board for providing details of their own evaluation of the exposures and estimated health risks from ethylene oxide at the Salinas Plant.

I. INTRODUCTION

The Monterey Bay United Air Pollution Control District, using an assessment performed by the California Department of Health Services, has proposed to limit ethylene oxide air emissions from the Schilling plant of McCormick and Company, Inc., which is located in Salinas, California. This assessment was made following the proposal by the federal EPA to list ethylene oxide as a hazardous air pollutant (USEPA 1985a). In view of the regulatory proposal and with knowledge of the degree of uncertainty that is inherent in the performance of risk assessments for possible human carcinogens such as ethylene oxide, McCormick and Company, Inc. has evaluated the scientific soundness of the State's risk assessment and has prepared a parallel assessment which is presented in this document. We note that our health assessment contains numerous scientific and methodologic considerations beyond those incorporated in the State's. The limitations in the State's assessment were no doubt occasioned in part by restrictions on time and resources. We are confident that our evaluation encompasses the most scientifically supportable conclusions and that these should form the basis for the District's risk management decisions. Uncertainties remain as to the degree of estimated risk from the air emissions of ethylene oxide. They derive from our general scientific ignorance and are typical of those encountered in estimates of cancer risk from virtually all compounds.

During the years that McCormick has operated the Salinas plant, it is convinced that, based on prevailing scientific information, the air emissions

of ethylene oxide have caused no harm or unreasonable risk to the health of the surrounding population, and in fact that the risk is highly likely to have been zero. As additional information about any possible health risks of ethylene oxide exposures becomes manifest, and to the extent that technological processes are available to mitigate such exposures, McCormick is committed to incorporate all reasonable processes to reduce air emissions to lower even the appearance of unacceptably high health risks.

Despite differences in professional judgment as to the magnitude of estimated risks from defined concentrations of ethylene oxide, McCormick has identified technology to reduce air emissions of ethylene oxide by approximately ten-fold and to incorporate those processes at the Salinas plant in 1986. In light of such an initiative, one might reasonably question the utility of our analysis of the possible health risks. The main objective of such an analysis is, in our view, to instill public confidence that the District's regulatory initiative and the firm's technological modifications were not in response to any real or imagined imminent threats to health and that the descriptions of the health impacts were based on the soundest scientific analysis that our country has to offer. In that spirit, we offer our detailed and documented evaluation of the health impact of ethylene oxide air emissions on the community surrounding the Salinas plant.

Throughout our comprehensive risk assessment for ethylene oxide released from the Salinas plant, we highlight the differences between our approach to assessing the risks of ethylene oxide and those used previously by the State of California Department of Health Services and indicate the bases for those

differences. We follow the general outline and procedures for risk assessment developed by the National Academy of Sciences (1983), because these procedures have become the accepted standard approach most appropriate for developing and presenting risk assessments. We begin with a description of the risk assessment process and then apply it to the assessment of potential risks to human health associated with ethylene oxide emissions from the Salinas plant.

II. OVERVIEW OF THE RISK ASSESSMENT PROCESS

The capacity of a substance to cause harm under specified conditions of exposure is a function of several variables: the toxicity of the substance, the relationship between dose and toxic response, and the extent of human exposure. Risk assessment integrates these factors to estimate the likelihood that a substance will cause toxic effects within the exposed human population. Risk assessment is distinct from risk management which is the process of evaluating alternative management actions (e.g. regulations) and selecting among them (NAS, 1983).

A recent study of risk assessment in the federal government conducted by a committee of the National Academy of Sciences (1983) describes risk assessment as having four basic steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization.

Hazard Identification. All chemical substances, whether natural or man-made, have the potential to cause some form of toxicity -- biological injury, disease, or death -- under some conditions of exposure. The purpose of the hazard identification phase of risk assessment is to collect and evaluate information on the inherent toxic properties of chemicals of interest. It should be noted that identifying the toxic properties of a substance is not equivalent to identifying its possible risk, because the conditions of exposure -- dose and duration -- are important determinants of whether or not an adverse effect will occur. Thus, all of the steps of risk assessment must be completed before any statement can be made about risk.

The two principal sources of information about the toxic properties of chemical substances are: investigations of exposed human populations or individuals (epidemiological or clinical investigations), and experimental studies involving laboratory animals or other biological systems. In addition, knowledge of the molecular structure of a substance may be of value in predicting certain of its toxic properties.

Dose-Response Assessment. After identifying the types of toxicity associated with a substance, the next step is to describe dose-response relationships. For an exposure of a given duration, the risk (the frequency with which toxic effects appear in an exposed population and often the rapidity with which they appear), increases with increasing exposure (or dose). In many cases the types of toxic effects change as exposure increases, becoming more severe and involving additional organs with increasing exposure.

The dose-response relationship is critical to risk assessment, and so must be well-defined. Generally, well-defined dose-response relationships for toxic effects are not obtainable from epidemiological studies because of uncertainty regarding the amount of exposure associated with a given response. Thus, experimental animal data are the primary sources of dose-response information for risk assessment.

For non-carcinogenic effects, the dose-response data from an animal study are used to identify a no-observed-effect level (NOEL); i.e., under appropriate experimental design, the highest dose at which no adverse effect is observed among the animals being tested. For carcinogens, because the induction of cancer by some carcinogens is thought to have no threshold,

mathematical models are used to estimate the probability, or risk, of cancer per unit of dose (unit carcinogenic risk, UCR) for the laboratory animals under investigation. For both carcinogens and noncarcinogens, the unit carcinogenic risks and NOEL values determined in experimental animals must be converted to similar measures of toxic potential in humans.

Exposure Assessment. Two tasks are undertaken in an exposure assessment: first, the determination of the amount, duration, and route of exposure to a substance which a population is likely to receive, and second, characterization of the population as to the distribution of susceptibility to the toxic properties of the substance.

Knowledge of the magnitude, duration, and route of human exposure to environmental agents and, most importantly, the dose that results from this exposure, is an essential component of risk assessment. If the concentrations of contaminants in each of the media through which exposure can occur and the magnitude and frequency of human contact with, and intake of, the various media are known, the human dose of each of the contaminants can be estimated. In addition, when systemic toxicity is of concern, absorption rates into the bloodstream may also be considered.

Characterization of the exposed population will usually result in identification of the number of people who will be exposed. In some cases, population groups with unique sensitivity to the substance of interest may be identified (e.g., pregnant women in the case of a teratogen). Because a single exposure level may injure different organs or have different potencies

in individuals of different susceptibilities, more than one NOEL or UCR may be derived.

Risk Characterization. Risk characterization for non-carcinogens takes the form of determining the margin-of-safety (MOS): the numerical value derived when the human NOEL is divided by the anticipated human dose. A judgment is needed to determine whether the MOS is sufficiently large to protect most members of the exposed population. (This judgment, because it usually involves more than a scientific interpretation, is largely a component of risk management.) With this approach, the smaller the MOS, the larger the probability that injury may occur. The actual degree of risk associated with a given MOS is, however, not quantifiable and there is no currently known method for making this determination. Provided the toxicity of a noncarcinogen is well studied, a very large MOS provides virtually complete assurance that adverse effects will not occur.

Risk characterization for carcinogens provides an estimate of risk for a population by combining the estimated daily lifetime dose for the population with the unit carcinogenic risk calculated for humans. Thus, risk is estimated and takes a value between 0 (certainty that adverse effects will not occur) and 1 (certainty that they will). Even for well-studied carcinogens, this estimate of risk is uncertain, and the estimate can not be asserted to be the true risk.

III. RISK ASSESSMENT FOR ETHYLENE OXIDE

A. Hazard Identification

Ethylene oxide is released from the Salinas plant as a consequence of its use as a sterilizer/fumigant for spice products produced at the plant. According to the EPA "[s]ignificant public health benefits are derived from the use of ethylene oxide as a sterilizing agent" (USEPA 1985a).

Ethylene oxide has been associated with several adverse health effects based on studies in animals and on data collected in humans: "[r]espiratory, ocular, dermal, systemic and neurological effects in humans have been associated with acute and subchronic exposure to ethylene oxide" (USEPA 1985a). Ethylene oxide tested positive in two long-term animal bioassays; and, in humans, three epidemiologic studies have suggested a possible association between exposure to ethylene oxide and subsequent development of cancer.

Because the regulatory emphasis concerning the adverse effects of ethylene oxide has focused on its cancer-producing properties, we shall concentrate on the evidence for carcinogenicity of this compound in this risk assessment.

Animal Data. Two lifetime inhalation studies in rats demonstrated that ethylene oxide can cause cancer in laboratory animals (Snellings et al. 1981; Lynch et al. 1982).

In the study by Snellings et al. (1981), Fischer 344 rats were exposed to 100, 33, or 10 ppm ethylene oxide vapor, 6 hours/day, 5 days/week, for approximately two years. Ethylene oxide produced significant increases in the incidences of several tumor types -- mononuclear cell leukemia (female rats), peritoneal mesothelioma (male rats), subcutaneous fibromas (male rats) and brain tumors (male and female rats). In addition, EPA has suggested that development of pituitary adenomas "appear[s] to be accelerated in female rats exposed to 100 ppm, although there was no statistically increased incidence of these tumors."

In the study by Lynch et al. (1982), male Fischer 344 rats were exposed to ethylene oxide at either 50 or 100 ppm for 7 hours/day, 5 days/week, for 24 months. These authors reported, in a preliminary analysis of the data, that ethylene oxide appeared to increase the incidence of mononuclear cell leukemia. When only animals examined at terminal sacrifice were included in the analysis, there was a statistically significant linear trend in the incidence of this type of leukemia. In addition, ethylene oxide significantly increased the incidence of peritoneal mesotheliomas, and mixed cell gliomas were observed in low incidence in treated animals but not in untreated controls.

Human Data. Three epidemiologic studies of persons exposed to ethylene oxide in the workplace reported an association between ethylene oxide exposure and cancer incidence or mortality. Significantly increased mortality for stomach cancer and leukemia, and significantly increased incidences of cancers of all sites were observed in ethylene oxide production workers (Hogstedt et al. 1979a, 1984). Hogstedt et al. (1979b, 1984) also reported significantly

increased incidences of leukemia and cancer of all sites and significantly increased mortality from leukemia among workers exposed to ethylene oxide as a sterilizing agent. A major shortcoming of the epidemiology studies described above is that the cohorts were exposed to other chemicals in addition to ethylene oxide including methyl formate and two animal carcinogens, ethylene dichloride and bis(2-chloroethyl) ether. Consequently, it is not possible to determine which if any of those substances was causally related to the observed increase in cancer incidence. In the third positive human study, Morgan et al. (1981) reported increased mortality from pancreatic cancer and Hodgkin's disease among workers exposed to ethylene oxide.

Conclusion

There is sufficient evidence to conclude that ethylene oxide is an animal carcinogen. The direct evidence in humans is equivocal; however, it is reasonable to infer from the animal studies that ethylene oxide might cause cancer in humans exposed to sufficiently high dose levels. According to the EPA, "ethylene oxide is probably carcinogenic in humans" based on positive chronic animal bioassays and limited human evidence (USEPA 1985a).

B. Dose-Response Assessment

The risk estimate developed by the State of California was based on the Hogstedt et al. (1979b, 1984) study showing an increased mortality from leukemia in individuals exposed to ethylene oxide in the workplace. On this basis, the lifetime probability of dying from leukemia due to ethylene oxide exposure was estimated by the State to be 3.6×10^{-4} for lifetime inhalation

exposure to ethylene oxide at $1 \mu\text{g}/\text{m}^3$. That is, the UCR was estimated to be $3.6 \times 10^{-4} (\mu\text{g}/\text{m}^3)^{-1}$.

There are, however, a number of defects with this approach:

- The mortality rate among exposed females in Sweden was compared to the lifetime probability of dying of cancer with no or negligible ethylene oxide exposure for U.S. males (USEPA 1985b).
- There was a general lack of exposure information in the epidemiology studies.
- The Hogstedt investigation was based on a study population that was exposed to a gas containing 50% ethylene oxide and 50% methyl formate. Little is known about the adverse health effects of methyl formate or the combination of ethylene oxide and methyl formate.
- Extrapolation from the human leukemia data results in a highly uncertain risk estimate due to the small numbers of leukemia cases that were observed and expected.

Several of the above-mentioned limitations were highlighted in EPA's Final Report of the Health Assessment Document for Ethylene Oxide (EPA 1985b). In that document, the human evidence for carcinogenicity of ethylene oxide was categorized as "limited bordering on inadequate." Similarly, we conclude that the epidemiologic data are inadequate to derive an estimate of cancer risk from exposure to ethylene oxide.

EPA developed an incremental UCR estimate for ethylene oxide of $1.0 \times 10^{-4} (\mu\text{g}/\text{m}^3)^{-1}$. This UCR indicates that if a person was continuously exposed to 1 microgram of ethylene oxide per cubic meter of air for 70 years, the 95% upper confidence limit on the increased probability of getting cancer as a result of ethylene oxide exposure would be 1 in 10,000 (i.e., the probability in addition to the probability of developing cancer due to all other causes).

EPA's risk estimate was developed using a linearized multistage model applied to incidence data on total mononuclear cell leukemias and brain gliomas in female Fisher 344 rats from the Snellings et al. (1981) study. The procedures for deriving this risk estimate were generally consistent with the EPA's carcinogen assessment guidelines (USEPA 1984) including:

- The 95% upper confidence limit on the extra risk (due to exposure to test substance) is used to give an upper bound on risk.
- The data set (tumor dose-response information) that gives the highest estimate of the lifetime carcinogenic risk, q_1^* , is used to develop the risk estimates. In cases where two or more significant tumor sites are observed in the same study, the number of animals with at least one of the specific tumor sites is used as incidence data. (In fact, EPA erred in deriving these incidence data and double-counted several animals that had both leukemia and glioma.)
- The interspecies scaling factor used to adjust doses used in animal studies to equivalent doses in humans is relative body surface area or dose expressed per (body weight)^{2/3}.

The methods used by EPA's Carcinogen Assessment Group (CAG) are extremely conservative and tend to result in high estimates of risk which likely greatly overestimate the true risk. Several factors contribute to this overestimation: 1) the selection of a linear, nonthreshold extrapolation model (the linearized multistage model); 2) the use of tumor incidence data from the most sensitive but not necessarily most relevant, animal species/strain/sex; and 3) the use of body surface area as an interspecies scaling factor which increases the risk estimate by a factor of between 5 and 10 (for ethylene oxide, EPA's risk estimates were increased by a factor of 5.5 for the males and 6.8 for the females). Also, ignoring time-to-tumor information and relying on total incidence data may distort the estimate of risk.

We have performed a sensitivity analysis to determine the cumulative impact of various combinations of assumptions made by EPA in its assessment. We estimated UCR's and 95% upper confidence limits using two different models, four sets of tumor incidence data, and four assumptions regarding interspecies equivalence in sensitivity, using data from the Snellings et al. (1981) study. In all cases, the high-dose group was deleted because inclusion of this group generally gave a poorer fit of the low-dose extrapolation models than when the high dose group was included due to the flattening out of the dose-response curve at high-dose levels. By excluding the highest dose group, the fitted model more closely reflects the shape of the dose-response curve in the low-dose region of the animal study. A wide range of UCR values is obtained just by varying the following four choices:

1. The Response of Concern:
 - 1.1) Brain Neoplasia in Male Rat
 - 1.2) Peritoneal Mesothelioma in a Male Rat
 - 1.3) Brain Neoplasia in Female Rat
 - 1.4) Mononuclear Cell Leukemia in Female Rat
2. The Mathematical Model:
 - 2.1) Multistage Model
 - 2.2) Probit Model
3. The Value Representing the Mathematical Model:
 - 3.1) Fitted Model Value (Maximum likelihood estimate)
 - 3.2) Upper Bound (95%)

4. Assumed Basis for Species Equivalence:

- 4.1) Air Concentration
- 4.2) Exposure Days per Week
- 4.3) Body Weight
- 4.4) Body Surface Area

The value of the UCR for each of the corresponding 64 combinations of choices is shown in Table 1. The ratio of the largest to the smallest UCR is approximately 32,000. Thus the UCR for ethylene oxide vapor inhalation varies over four orders of magnitude depending on those four choices alone. Even if the mathematical model is limited to the multistage model, the UCR value varies 2,000-fold over the three remaining choices. Furthermore, those variations exclude the negative lower bounds on the UCR.

Unfortunately, the discussion of unit risks in the EPA Health Assessment Document for Ethylene Oxide (USEPA 1985b) reports only the UCR values associated with the upper bounds of the multistage model. The Health Assessment Document does not report the UCRs estimated from the best fits of the multistage model, nor those associated with the lower bounds on the multistage model. Nor does it report UCR values for other models. Furthermore, the Health Assessment Document refers to UCR values based on the upper bounds as UCR estimates instead of bounds on the UCR. This terminology is misleading and should not be used; a careful distinction should be made between an estimate of a UCR and a bound on a UCR. A similar distinction should also be made with respect to other risk characteristics; for example, the distinction should be made between an estimate of the virtually safe dose (VSD) and a bound on the VSD.

Table 1

Effects of Different Choices of Data and
Procedures on Estimated Unit Risk

Multistage Model

<u>Response Of Concern</u>	<u>Model Characteristic</u>	<u>Assumed Basis for Species Equivalence</u>	<u>UCR ($\mu\text{g}/\text{m}^3$)⁻¹</u>
Brain Neoplasia in Male Rats	Upper Bound	Air Concentration	1.3×10^{-6}
		Exposure Days/Week	1.8×10^{-6}
		Body Weight	4.3×10^{-6}
		Surface Area	2.9×10^{-5}
	Fitted Model Value	Air Concentration	7.4×10^{-8}
		Exposure Days/Week	1.2×10^{-7}
		Body Weight	2.7×10^{-7}
		Surface Area	8.4×10^{-6}
Peritoneal Mesothelioma in Male Rats	Upper Bound	Air Concentration	2.0×10^{-6}
		Exposure Days/Week	2.8×10^{-6}
		Body Weight	6.8×10^{-6}
		Surface Areas	4.3×10^{-5}
	Fitted Model Value	Air Concentration	5.3×10^{-7}
		Exposure Days/Week	7.4×10^{-7}
		Body Weight	1.2×10^{-6}
		Surface Areas	1.4×10^{-5}
Brain Neoplasia in Female Rats	Upper Bound	Air Concentration	9.5×10^{-7}
		Exposure Days/Week	1.3×10^{-6}
		Body Weight	3.2×10^{-6}
		Surface Areas	2.6×10^{-5}
	Fitted Model Value	Air Concentration	2.1×10^{-7}
		Exposure Days/Week	3.2×10^{-7}
		Body Weight	4.2×10^{-7}
		Surface Areas	7.9×10^{-6}
Mononuclear Cell Leukemia in Female Rats	Upper Bound	Air Concentration	6.8×10^{-6}
		Exposure Days/Week	9.5×10^{-6}
		Body Weight	2.3×10^{-5}
		Surface Areas	1.5×10^{-4}
	Fitted Model Value	Air Concentration	4.7×10^{-6}
		Exposure Days/Week	6.3×10^{-6}
		Body Weight	1.3×10^{-5}
		Surface Areas	9.4×10^{-5}
Ratio: Largest Unit Risk/Smallest Unit Risk			2,000

Table 1 (continued)

Probit Model

<u>Response Of Concern</u>	<u>Model Characteristic</u>	<u>Assumed Basis for Species Equivalence</u>	<u>UCR ($\mu\text{g}/\text{m}^3$)⁻¹</u>
Brain Neoplasia in Male Rats	Upper Bound	Air Concentration	8.4×10^{-8}
		Exposure Days/Week	2.2×10^{-7}
		Body Weight	6.3×10^{-7}
		Surface Area	2.2×10^{-5}
	Fitted Model Value	Air Concentration	4.6×10^{-9}
		Exposure Days/Week	1.4×10^{-8}
		Body Weight	5.1×10^{-8}
		Surface Area	7.9×10^{-6}
Peritoneal Mesothelioma in Male Rats	Upper Bound	Air Concentration	1.1×10^{-6}
		Exposure Days/Week	2.0×10^{-6}
		Body Weight	4.0×10^{-6}
		Surface Areas	3.7×10^{-5}
	Fitted Model Value	Air Concentration	7.9×10^{-8}
		Exposure Days/Week	1.7×10^{-7}
		Body Weight	4.2×10^{-7}
		Surface Areas	1.4×10^{-5}
Brain Neoplasia in Female Rats	Upper Bound	Air Concentration	7.4×10^{-7}
		Exposure Days/Week	1.3×10^{-6}
		Body Weight	3.2×10^{-6}
		Surface Areas	2.0×10^{-5}
	Fitted Model Value	Air Concentration	4.5×10^{-8}
		Exposure Days/Week	8.9×10^{-8}
		Body Weight	2.0×10^{-7}
		Surface Areas	7.9×10^{-6}
Mononuclear Cell Leukemia in Female Rats	Upper Bound	Air Concentration	1.4×10^{-5}
		Exposure Days/Week	2.0×10^{-5}
		Body Weight	3.1×10^{-5}
		Surface Areas	1.3×10^{-4}
	Fitted Model Value	Air Concentration	2.2×10^{-6}
		Exposure Days/Week	3.7×10^{-6}
		Body Weight	6.8×10^{-6}
		Surface Areas	8.4×10^{-5}
Ratio:	Largest Unit Risk/Smallest Unit Risk		27,000
Ratio:	<u>Largest Unit Risk Using Both Models</u> Smallest Unit Risk Using Both Models		32,000

The variation in the UCR values (both estimates and bounds) is even greater if other choices are included. However, it may be more important to emphasize that the UCR as well as the other risk characteristics (such as the VSD) which do not reflect the time-to-response information are limited in their characterization of the risk of ethylene oxide vapor inhalation.

As an alternative to the procedures used by California Department of Health and EPA, we have used two procedures which are likely to give a more precise indication of the actual risk, though even these procedures contain some conservative assumptions which likely overstate the risk. Both of the procedures utilize animal carcinogenicity data since, as noted earlier, and as EPA has agreed, the available epidemiologic data are inadequate for quantitative risk assessment.

In our first approach, we have used the multistage model as EPA did, but we have made three adjustments to improve the precision of the estimates:

- We have developed maximum likelihood estimates based on two different data sets. The use of maximum likelihood estimates of risk, rather than upper confidence limits, is more scientifically justifiable, since that is the area where the dose-response curve is most likely to reside.
- We have selected body weight as the interspecies conversion factor, because we are convinced that this procedure provides, on average, a more precise estimate of the actual human risk (Crump et al.

1980) and, therefore, greater precision in the estimation of cancer risk from ethylene oxide than those used by the State or EPA.

- We have used the number of animals with significant tumors rather than the number of tumors, thus avoiding the error made by EPA of double-counting animals that have both leukemias and gliomas.

In our second approach, we have used the Hartley-Sielken time-to-response model (Hartley and Sielken 1977), a generalization of the multistage model to include time-to-tumor data. This provides estimates of potential loss of lifespan due to cancer.

Applying the multistage model to the incidence data on only mononuclear cell leukemia in female rats (the most sensitive tumor type and sex), the UCR is $8.5 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$ if all four dose levels are included and $1.3 \times 10^{-3} (\mu\text{g}/\text{m}^3)^{-1}$ if the highest dose level is deleted. The difference is due to the fact that the dose-response curve appears to flatten out at high-dose levels and does not fit the multistage model as closely if all four dose groups are included.

As noted earlier, the incidence data used by EPA for combined mononuclear cell leukemia and glioma in female rats were in error because four animals (two in the 100 ppm group and one each in the 33 and 10 ppm groups) had both leukemia and glioma. These animals were double-counted by EPA in Table 9-33 of its final Health Assessment Document for Ethylene Oxide (USEPA 1985b). We

have recalculated the UCR using the multistage model and the correct data set as listed below.

<u>Dose (ppm)</u>	<u>Incidence of leukemia or glioma or both</u>
0	23/186
10	14/71
33	26/72
100	30/73

Based on these data, the maximum likelihood estimate (MLE) of UCR using the multistage model is $9.5 \times 10^{-6} (\mu\text{g}/\text{m}^3)^{-1}$ if all four dose groups are included, and 1.0×10^{-5} if the highest dose level is omitted.

The 95% upper confidence limit (UCL) for each of these UCRs is 1.3×10^{-5} . We use the higher MLE value of $1.0 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ in the characterization of risks presented later, since this estimate is derived using all of the tumor types significantly associated with ethylene oxide exposure in female rats and is likely to give a better estimate of the risk than the use of an estimate based on mononuclear cell leukemia alone. The MLE value is selected rather than the UCL since the former is more consistent with the experimental data.

Using the Hartley-Sielken time-to-response model applied to female rat survival data, the estimates of loss of expected lifespan shown in Table 2 are obtained. Those estimates represent an added and valuable dimension to the characterization of risk. Assuming humans and female rats have equivalent time-to-response behavior on a dose-per-unit-body-weight (mg/kg/day) basis, these estimates can be used to estimate life shortening in humans exposed continuously to ethylene oxide (Table 2).

Table 2

Estimate of Decreases in the Average
Lifespan Based on Time-to-Response Modeling
of Survival Data From Snellings et al. (1981)¹

<u>Dose ($\mu\text{g}/\text{m}^3$) 24 hr/day, 7 days/week</u>	<u>Decrease in Female Rat's Estimated Mean Survival Time (months)</u>	<u>Percentage Decrease in the Rat's 25 Month Experimental Period</u>	<u>Corresponding Decrease in a Human 70 Year Period</u>
233	0.03	0.12	1.0 month
54	0.007	0.027	1.0 week
7.8	0.001	0.0039	1.0 day
0.32	0.00004	0.00016	1.0 hour
0.11	0.000014	0.00006	20.0 minutes

¹ Assumes that rats and humans have equivalent time-to-response behavior on a dose-per-unit-body-weight (mg/kg/day) basis.

For example, the air concentration of ethylene oxide that would reduce life expectancy by just one hour is $0.32 \mu\text{g}/\text{m}^3$; a one-day reduction would result from ethylene oxide concentrations of $7.8 \mu\text{g}/\text{m}^3$. A concentration of $1 \mu\text{g}/\text{m}^3$ would result in a decreased life expectancy of approximately 3 hours.

Conclusion

Two alternative analyses have been presented. Using the multistage model, which inherently does not make use of the time-to-response information, and using the increase in incidence of mononuclear cell leukemia and glioma in female rats exposed to ethylene oxide, the estimate of UCR (based on the best fit of the multistage model, with interspecies risk equivalence on a body weight basis) is $1.0 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$.

Alternatively, based on the more appropriate Hartley-Sielken model, the loss in average life expectancy from exposure to ethylene oxide at $1 \mu\text{g}/\text{m}^3$ would be estimated to be, at most, approximately 3 hours.

It is also possible that the risk of cancer or reduction in life expectancy is much less, even zero, if ethylene oxide is not a human carcinogen, or if it does not cause cancer at such low dose levels.

C. Exposure Assessment

An assessment of the magnitude and extent of exposure to ethylene oxide emissions from the Salinas plant was undertaken for McCormick and Company,

Inc. A detailed discussion of the methods used in this assessment have been presented in a separate document (ENVIRON 1986). The results of that analysis are summarized below.

Ethylene Oxide Concentrations

The assessment of ethylene oxide emissions was performed using the same general approach that the State had used for its exposure component of the risk assessment; i.e., the dispersion of ethylene oxide emissions from the plant was represented using a mathematical dispersion model developed for the EPA -- the Industrial Source Complex (ISC) Model.

Ethylene oxide concentrations were determined under three release scenarios:

- Case 1: Present operating conditions;
- Case 2: With the addition of a DEOXX scrubber;
- Case 3: With the addition of DEOXX scrubber and raising the height of the main stack to 48 feet.

From the model, it was possible to generate isopleths (lines on a map joining points of equal concentration of ethylene oxide) around the plant.

The highest ethylene oxide concentrations for all three release scenarios are found at the eastern boundary of the plant facility. They are: 89.1 $\mu\text{g}/\text{m}^3$ (case 1), 17.0 (case 2), and 2.8 $\mu\text{g}/\text{m}^3$ (case 3). However, the area to the east is virtually unpopulated. The most populated areas lie to the west-northwest (WNW) of the plant. Under current operating conditions

(case 1), the maximum annual average ethylene oxide concentrations to which the populated areas to the WNW of the plant are exposed are in the range of 1-2 $\mu\text{g}/\text{m}^3$. Installation of the DEOXX system (case 2), reduces ethylene oxide concentrations by approximately 5-fold (0.11-0.38 $\mu\text{g}/\text{m}^3$) and raising of the aeration stack after installation of the DEOXX system (case 3), effects an additional slight reduction (0.11 - 0.27 $\mu\text{g}/\text{m}^3$). The concentrations estimated for the WNW direction will be used in the development of risk estimates in the risk characterization step which follows.

Isopleths showing ethylene oxide concentrations out to 3.5 km from the plant were used to develop the WNW concentration ranges and are shown in Figures 1 through 3 for cases 1 through 3, respectively. The ranges themselves are listed in Table 3.

Population Exposures

The population residing within the 0.11 $\mu\text{g}/\text{m}^3$ isopleth under case 3 has been estimated. The 0.11 isopleth was chosen because, based on the unit risk value for ethylene oxide ($1.0 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$), exposures below 0.11 $\mu\text{g}/\text{m}^3$ (in areas outside the 0.11 isopleth) would result in lifetime risks of less than 1×10^{-6} and would, hence, be insignificant or de minimis. The population within the 0.11 isopleth is estimated to consist of approximately 100-200 residents and 2,100-2,200 workers in industrial plants. In addition, two inactive and five active migrant labor camps are located within the 0.11 isopleth. The migrant worker population has been estimated at 650-1,150. Thus, it is conservatively estimated that between 3,000 and 3,500 people may be exposed to concentrations of ethylene oxide in excess of 0.11

Table 3

Estimated Ethylene Oxide Concentrations

<u>Release Scenario</u> ¹	<u>Concentration ($\mu\text{g}/\text{m}^3$) at:</u>	
	<u>Eastern Boundary of Plant</u>	<u>Closest Population Area</u> ²
1	89.1	1-2
2	17.0	0.11-0.44
3	2.8	0.11-0.27

¹ See description in text.

² Located approximately 700-1400 meters to the west-northwest of the plant.

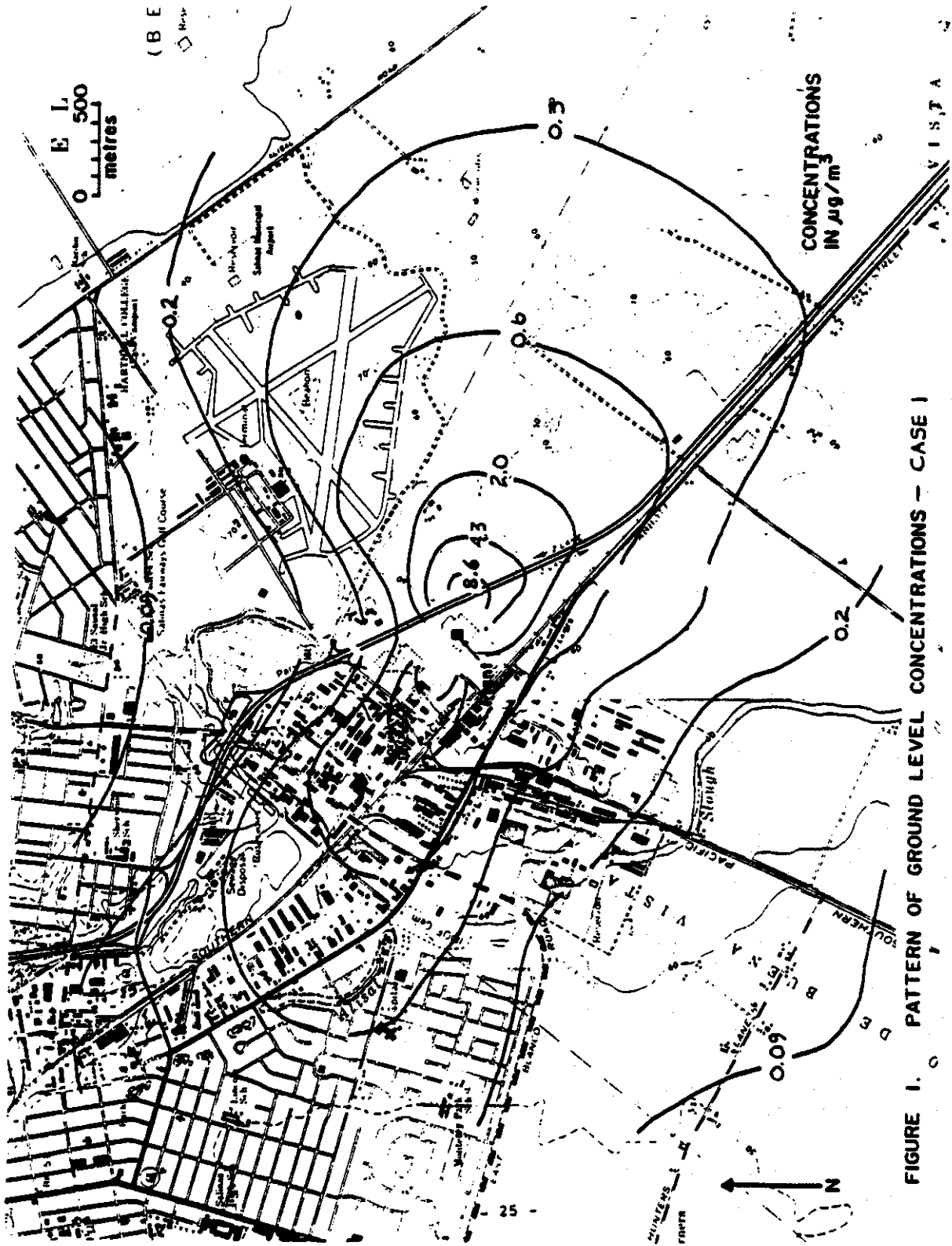


FIGURE 1. PATTERN OF GROUND LEVEL CONCENTRATIONS - CASE 1

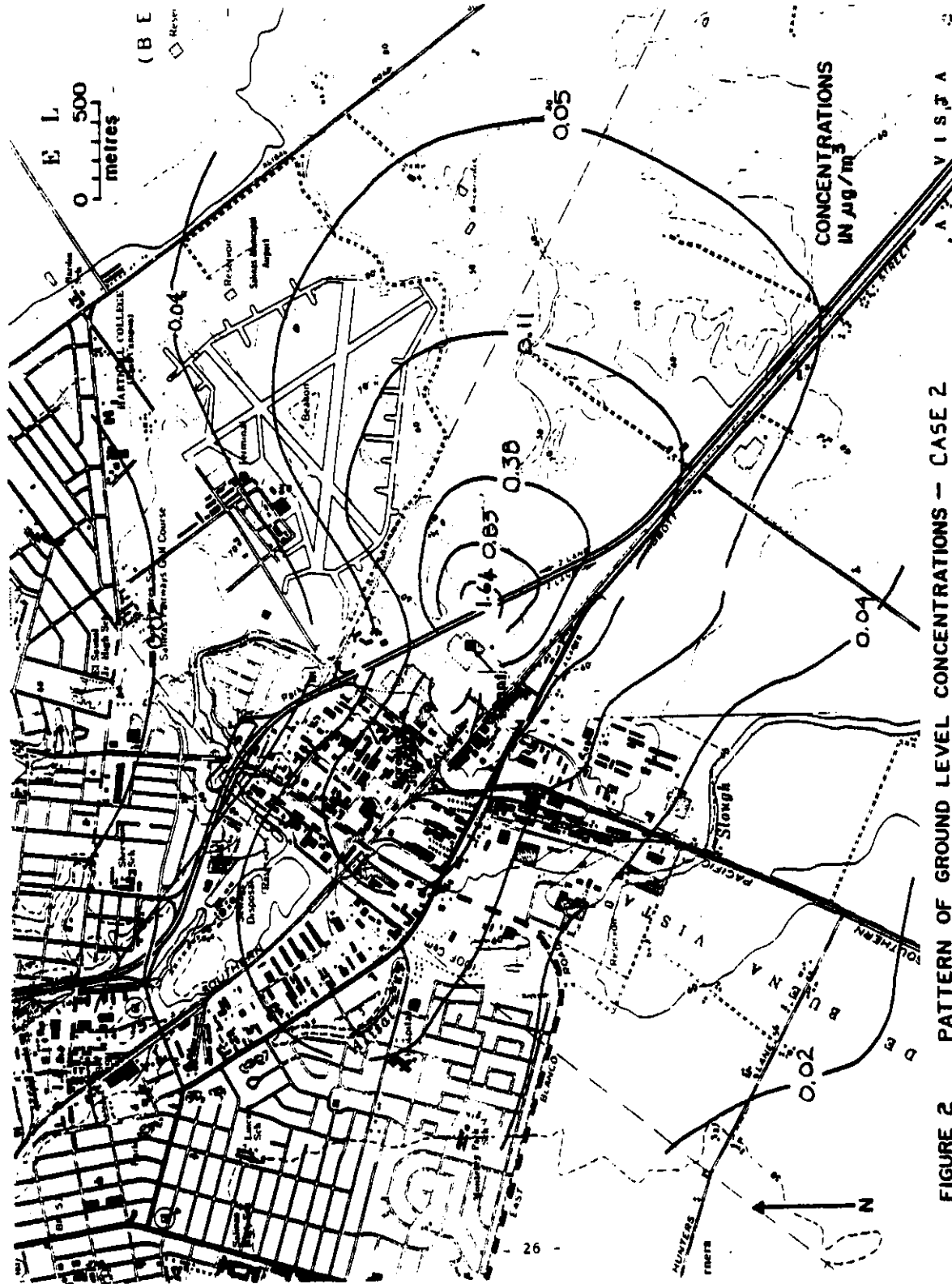


FIGURE 2. PATTERN OF GROUND LEVEL CONCENTRATIONS - CASE 2

A. V. I. S. J. A.

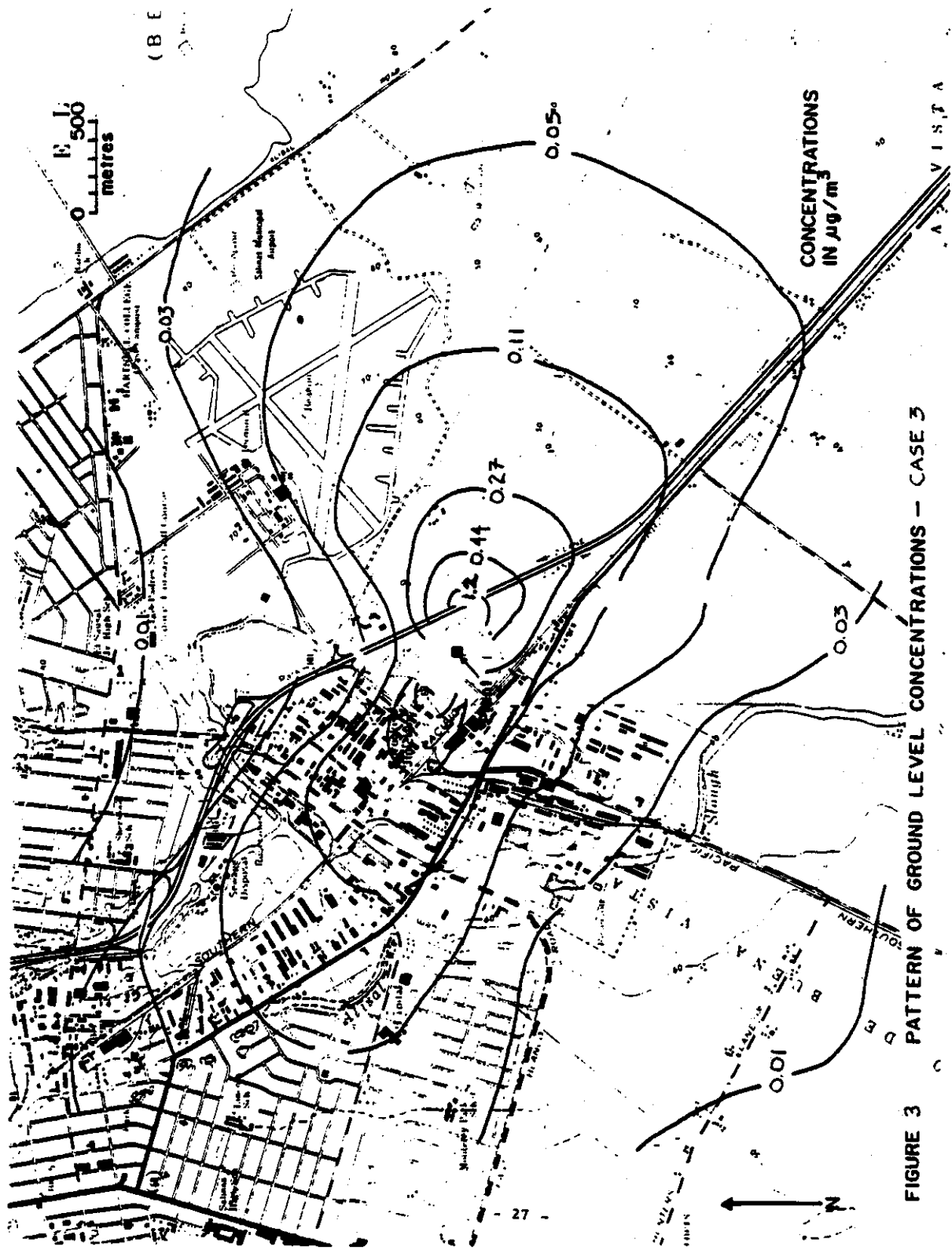


FIGURE 3 PATTERN OF GROUND LEVEL CONCENTRATIONS - CASE 3

$\mu\text{g}/\text{m}^3$ due to emissions from the McCormick facility. The industrial workers would be exposed for no more than 8 hours/day, 5 days/week. The migrant workers are likely to be exposed for only a fraction of the year and may not return in future years. Consequently, the number of individuals who might be exposed continuously for extended periods should be no greater than 100-200.

D. Risk Characterization

Based on the rationale provided in the dose-response assessment, we shall use a UCR value of $1.0 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ for ethylene oxide. Multiplying this value by the ethylene oxide concentrations estimated in the exposure assessment results in the predictions of excess cancer risks associated with estimated concentrations (Table 4). The lifetime risks predicted for the populated area located west-northwest (WNW) of the plant would be 2.0×10^{-5} if exposure were to continue unchanged (using the maximum concentration for the closest populated area), but would be reduced to about 3×10^{-6} after installation of the exhaust-treatment systems (under case 3). Since only about 3,500 people are estimated to live or work within the $0.11 \mu\text{g}/\text{m}^3$ isopleth (for case 3), and most of these are outside the $0.27 \mu\text{g}/\text{m}^3$ isopleth, the remediated emission of ethylene oxide from the Salinas plant is estimated to produce no more than 0.01 excess cases of cancer per lifetime in the surrounding population:

$$1 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1} \times 0.27 \mu\text{g}/\text{m}^3 \times 3,500 = 0.01$$

(UCR) x (concentration) x (population) = number of cases

Table 4

**Estimated Maximum Excess Cancer Risks
Associated with Ethylene Oxide Emissions from
McCormick Salinas Plant**

<u>Release Scenario</u>	<u>EtO Concentration¹</u>	<u>Estimated Lifetime Risk</u>	<u>Estimated Loss of Lifespan</u>
Case 1	2	2×10^{-5}	6.2 hours
Case 2	0.38	3.8×10^{-6}	1.2 hours
Case 3	0.27	2.7×10^{-6}	0.8 hours

¹ Values are the maximum concentrations for area between isopleths where residences are located to the west-northwest of the facility.

Because the UCR is based on continuous lifetime exposure, the number of excess cases of cancer in the population most likely to be exposed (the 100-200 residents) is estimated to be:

$$1 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1} \times 0.27 \mu\text{g}/\text{m}^3 \times 200 \approx 0.0005$$

All exposures beyond the 0.11 isopleth would result in risks of less than 1×10^{-6} and are, therefore, de minimis.

Further, the projected estimate of excess cancer cases per lifetime of 0.01 represents a conservative estimate and the actual risks are likely to be even lower, possibly zero, since:

- (1) data from the most sensitive species, strain, sex and tumor site were used to estimate low-dose risks;
- (2) a conservative low-dose extrapolation model (the multistage model) is used to generate low-dose risk estimates;
- (3) exposure is assumed to be continuous (24 hours/day, 365 days/year) for 70 years, a highly unlikely situation; and
- (4) the exposure estimate was based on a conservative estimate of the number of individuals living or working in the vicinity of the Salinas plant.

IV. CONCLUSIONS

There is conclusive evidence that ethylene oxide is an animal carcinogen. The evidence from epidemiologic studies is equivocal and is not adequate for use in quantitative risk assessment. In the interest of public health, and in the absence of substantial other evidence, it is frequently the practice for regulatory bodies to act as if ethylene oxide were a probable human carcinogen. However, before taking action, a regulatory authority has the responsibility of determining the magnitude of the risk and the likely health consequences to affected citizens. To be credible, such an assessment must avail itself of the state-of-the-art in scientific knowledge and understanding to establish whether the risks are significant or trivial.

Experts in the field of risk assessment differ in their choice or procedures for use in risk assessment. In our view, the procedures used by the California Department of Health and the Environmental Protection Agency are not the most appropriate for use in the present case. Based on what we conclude is the most appropriate procedure for risk assessment, installation of the exhaust treatment system and raising the stack height will reduce any potential risk to human health to a level of no more than approximately 0.3 in 100,000 (one in 370,000) even assuming lifetime exposure. This would be equivalent to a loss of lifespan of, at most, approximately 3 hours. Based on the estimate of population in the area, this corresponds to less than 0.01 cases of cancer per lifetime. For most of the surrounding population, the

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exposure, and hence the risk is even lower, and may even be zero. Such a risk level has been historically determined to be acceptable for the general population.

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JUNE 27, 1986, SUPPLEMENT TO

ASSESSMENT OF POSSIBLE HEALTH RISKS
ASSOCIATED WITH EXPOSURE TO ETHYLENE OXIDE
RELEASED TO THE ATMOSPHERE FROM THE
SALINAS PLANT OF MCCORMICK AND COMPANY, INC.
January 15, 1986

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Acknowledgement: McCormick and Company, Inc. gratefully acknowledges in the preparation of this report the technical and scientific contributions of Drs. Robert G. Tardiff and Robert L. Powell of ENVIRON Corporation and Dr. Colin Baynes of CJB Associates, Inc.

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I. INTRODUCTION

In 1985, the Monterey Bay United Air Pollution Control District became concerned that emissions of ethylene oxide (EtO) from stationary sources such as McCormick's Salinas (i.e. Shilling) plant might pose an unacceptable risk to the health of the population surrounding such sources. The District sought the assistance of California's Air Resources Board and the Department of Health Services, whose evaluations served to enlighten understanding of EtO exposures and toxic properties.

To assist the District in structuring the basis for recommendations to control emissions of EtO from the Salinas plant, McCormick undertook a risk assessment. That original assessment, completed on January 15th of 1986 (McCormick, 1986) and to which the present report is a supplement, concluded that raising the stack height and adding the DEOX process would yield (a) a unit cancer risk of no more than one estimated cancer case per 370,000 people exposed for a lifetime and (b), given the population size surrounding the plant, an estimated cancer incidence of no more than 0.01 case in 70 years. Those conclusions were based in part on average plant emission rates and meteorological data over a 24-hour cycle, even though the plant's actual operating cycle was only 17 hours in duration. To address any potential underestimates of exposure and hence risk, an uncertainty factor was introduced into the analysis.

The District, at the behest of California's Air Resources Board, requested a re-analysis of the meteorological data to enhance the precision of the exposure estimates. This Supplement describes the results of those recalculations and their impact on the estimated risks of developing cancer among the population surrounding the Salinas plant.

II. RISK ASSESSMENT FOR ETHYLENE OXIDE

The risks estimated from inhalation exposures to EtO are based in part on the hazard determination and dose-response assessment in the original report. The reader is encouraged to refer to those sections for some understanding of the toxic properties of EtO and of the studies critical to estimating human cancer risks.

A. Exposure Assessment

The original exposure analysis had been carried out by ENVIRON Corporation (ENVIRON, 1986) which provided estimates of exposures to air concentrations of EtO in the areas surrounding the Salinas plant. ENVIRON also performed this supplemental analysis.

In the present report, revised EtO concentration in air are estimated using an alternative dispersion model (i.e., ISCST as recommended by California's Air Resources Board) which, because it simulates emissions on an hourly time step, is capable of simulating the diurnal variation of EtO at the plant (there are no emissions between midnight and 7 a.m.). Previously, the modelling had not included this effect. Since a significant correlation exists between wind direction and time of day at Salinas, wind direction would be expected to impact exposures from plant emissions. Since there are no emissions at times when a disproportionate frequency of easterly winds was expected to occur, it was anticipated that the original (ISCLT) dispersion model would tend to overestimate concentrations to the west of the plant and underestimate concentrations to the east. Thus, it was suspected that the maximum levels, predicted to occur to the east, may be higher than estimated by the ISCLT model.

As in the original report, exposures are assessed for three scenarios: (1) under present operating conditions; (2) with the addition of a DEOXX scrubber; and (3) with the addition of a DEOXX scrubber and raising the height of the main stack to approximately 50 feet.

1. Dispersion Model

The dispersion of EtO emissions from the plant was represented using the Industrial Source Complex (ISC) model, a mathematical dispersion model recently developed for the Environmental Protection Agency (EPA). It was selected for its capability of simulating the emission sources of interest in this study (Bowers, et al., 1979). It consists of two separate computer codes: the first, ISCST, is a short-term or sequential model which uses hourly meteorological data for the site under study to simulate hourly ambient air concentrations downwind of emission points (these hourly values can also be aggregated to form averages over longer periods); the second, ISCLT, is a long-term or climatological model which uses joint frequency data of wind speed, wind direction, and atmospheric stability class to produce annual or seasonal ambient air concentrations around the emission points. The original exposure assessment, reported in January 1986, was based on the use of the ISCLT model. In the present study, ISCST was used to calculate the annual average concentrations which are of primary importance in the exposure assessment. Unlike ISCLT, the ISCST is capable of simulating the diurnal variations in EtO emissions at the plant.

The ISC model treats the dispersion of each emission source as a Gaussian plume, in which the concentration of pollutants within the plume follows a normal distribution, or "bell," curve in the vertical and horizontal, crosswind directions. Volume sources, of interest here, are represented as virtual point sources, i.e., as if they are point sources emitting at some distance upwind of the actual point of emission. This distance depends on the dimensions of the volume sources and atmospheric stability conditions. Concentrations are calculated at specified points downwind as a function of meteorological parameters, i.e., wind speed, atmospheric stability class, mixing height, and as a function of downwind distance. In the short-term version, ISC estimates concentrations at the required receptors for every hour over the period for which meteorological input data are provided. Average

concentration can then be computed for a period, e.g., one year; and a number of other statistical summaries of the hourly concentrations can also be generated.

2. Input Data

a. Meteorological/Topographic Data. The first set of input data required by the model are concerned with local meteorological and topographical conditions. The hourly meteorological data were obtained from the California Air Resources Board in the required pre-processed format suitable for direct input to the ISCST model. The data were derived from measurements taken at Salinas Airport over the five-year period 1960 to 1964, inclusive. The model was run using each of the five years of data separately. Topographic relief was not considered in the simulation. Since the emissions are released close to ground level and there are no major elevation changes in the vicinity of the plant, that was not considered a significant limitation of the analysis.

b. Emissions Data. The emission sources were treated conservatively as two separate volume sources, since the heights and locations of the various vents are such that emissions would likely be downwashed and mixed into the building wakes under some wind conditions. Exhaust from stacks 1 to 16 (Rice Mill, Mill Exhaust and Cinnamon Exhaust) was assumed to emanate from the first volume source of height 37 feet and an average cross-sectional dimension of 27 feet. The effective release height for this source was 18.5 feet. The exhaust from all other stacks was assumed to emanate from the second volume source of height 22 feet and an average cross-sectional dimension of 95 feet. The effective release height in that case was 11 feet. In the third scenario, emissions from stack 20 (aeration stack) were considered as being emitted from the stack raised to 48 feet. In that case, emissions from the stack were treated as a single point source, i.e., unaffected by building downwash effects. It

should be noted that, in all simulations, plume rise due to buoyancy or momentum of the exhausts has not been taken into account.

TABLE 1.

Emission rates (g/s) of EtO from the
McCormick's Salinas Plant

<u>Source Group</u>	<u>Scenario</u>		
	1	2	3
1 (Stacks 1 - 16)	0.0013	0.0013	0.0013
2 (Stacks 17 - 23)	0.348	0.0774	0.0091(2)
3 (Stack 20)	(1)	(1)	0.0683

Notes: (1) included in group 2
(2) excludes stack 20

The values in Table 1 are average hourly emission rates for the 17 hours of operation of the plant and were derived in the manner described in the January 1986 report.

The emission rates (g/s) used for the three source groups identified above under the three scenarios (existing conditions plus two emission control scenarios) are provided in Table 1.

c. Receptor Data. The final set of input data concerns the locations of the receptor points at which ambient concentrations are to be calculated by the model. In ISC, these must be specified by the user. To cover the potential impact area of plant emissions, a polar grid of receptors was specified between 300 m (the distance estimated to the closest residence) and 4.5 km from the plant. The distance increments used were 100 m between 300 m and 2 km, and 500 m between 2 km and 4.5 km.

Receptors along each radial arc were regularly spaced at 22.5 degree intervals, corresponding to directions N, NNE, NE, ENE, E, etc. from the plant.

3. Ethylene Oxide Concentrations

Figures 1, 2 and 3 show the predicted annual average patterns of concentrations at ground level for the three emission scenarios identified above, i.e., (1) under present conditions, (2) with the DEOXX scrubber, and (3) with the DEOXX scrubber and a raised main stack. The results are given for the year of meteorological data which gave the highest predicted concentrations (i.e., 1961). [A summary of the data for each of the five years is presented in the Appendix.] In all cases, the model predicted that the maximum concentration occurs 300 m from the plant, although the direction to the receptor having the highest potential exposure varies slightly (between E and ESE) according to the emission scenario. In addition, concentrations at a distance of 60 m from the plant, corresponding to the approximate position of the plant property line, have been crudely estimated by extrapolation of the model output. The model does not provide reliable results at such short distances from the emission source. The maximum concentrations are summarized in Table 2.

As in the earlier study, the highest concentrations are predicted to occur to the E and ESE of the plant, reflecting the predominance of W and WNW winds at Salinas, even when the diurnal effect is explicitly included in the modelling. Relatively high levels also occur to the WNW.

The highest ethylene oxide concentrations for all three release scenarios are found at the eastern boundary (60 meters) of the plant facility, and are virtually identical to the estimates generated in the original report. They are 90 $\mu\text{g}/\text{m}^3$ (scenario 1), 20 $\mu\text{g}/\text{m}^3$ (scenario 2), and 3 $\mu\text{g}/\text{m}^3$ (scenario 3). However, the area to the east is virtually unpopulated; and, therefore, no health risk is present at that location.

TABLE 2
 Ambient Air Concentrations of EtO Surrounding
 McCormick's Salinas Plant in 1961
 (The Year between 1960 and 1964
 that Yielded the Highest Estimated
 Concentrations) Estimated Using the ISCST Model.

Scenario	Maximum Concentration at 60 m ($\mu\text{g}/\text{m}^3$)	Maximum Concentration at 300 m ($\mu\text{g}/\text{m}^3$)	Direction to Critical Receptor
1	90	7.74	E
2	20	1.74	E
3	3	0.86	ESE

The populated areas lie to the west-northwest (WNW) of the plant. Using isopleths derived from the dispersion model, estimates were made of the concentrations of EtO to which individuals might be exposed. The population group of concern was that between the closest residences to the plant and the farthest point from the plant at which the concentrations of EtO would yield no greater risk than one per hundred 100,000 individuals per lifetime (the conventional threshold of risk acceptability governing regulatory decisions in this country). Under current operating conditions (scenario 1), the maximum annual average ethylene oxide concentrations to which populated areas to the WNW of the plant are exposed are in the range of 0.4-1.0 $\mu\text{g}/\text{m}^3$. Installation of the DEOXX system (scenario 2) reduces ethylene oxide concentrations by approximately 5-fold (0.05-0.20 $\mu\text{g}/\text{m}^3$); and raising of the aeration stack after installation of the DEOXX SYSTEM (scenario 3) effects no additional measured reduction (0.07-0.20 $\mu\text{g}/\text{m}^3$). The concentrations estimated for the WNW direction will be used in the development of risk estimates in the risk characterization step which follows.

Isopleths showing ethylene oxide concentrations out to 3.5 km from the plant were used to develop the WNW concentration ranges and are shown in Figures 1 through 3 for cases 1 through 3, respectively. The ranges themselves are listed in Table 2. A comparison of the present findings with the original exposure estimates indicates little or no significance differences at 60 meters between those derived with the first model incorporating a safety factor and the more precise estimates based on hourly meteorological data. By contract, greater reductions in EtO

Table 3
Comparison of EtO Concentration
at 300 Meters from McCormick's Salinas Plant
Using Two Dispersion Models
 $\mu\text{g}/\text{m}^3$

Scenario	Model 1*	Model 2*	% Reduction
1	12.2	7.7	37
2	2.3	1.7	26
3	1.0	0.9	10

* Model 1 uses meteorological data averaged over 24 hours; Model 2 uses hourly meteorological data for the 17 hours of operation each work day.

concentrations were estimated at 300 meters from the plant. Table 3 presents both sets of estimates at 300 meters.

4. Population Exposures

The population residing within the $0.1 \mu\text{g}/\text{m}^3$ isopleth under case 3 has been estimated. The $0.1 \mu\text{g}/\text{m}^3$ isopleth was chosen because, based on the unit risk value for ethylene oxide (1.0×10^{-5} , $(\mu\text{g}/\text{m}^3)^{-1}$), exposures below $0.1 \mu\text{g}/\text{m}^3$ (in areas outside the $0.1 \mu\text{g}/\text{m}^3$ isopleth) would result in lifetime risks of less than 1×10^{-6} and would, hence, be insignificant or de minimis. The population within the $0.1 \mu\text{g}/\text{m}^3$ isopleth is estimated to consist of approximately 100-200 residents and 2,100-2,200 workers in industrial plants. In addition, two inactive and five active migrant labor camps are located within

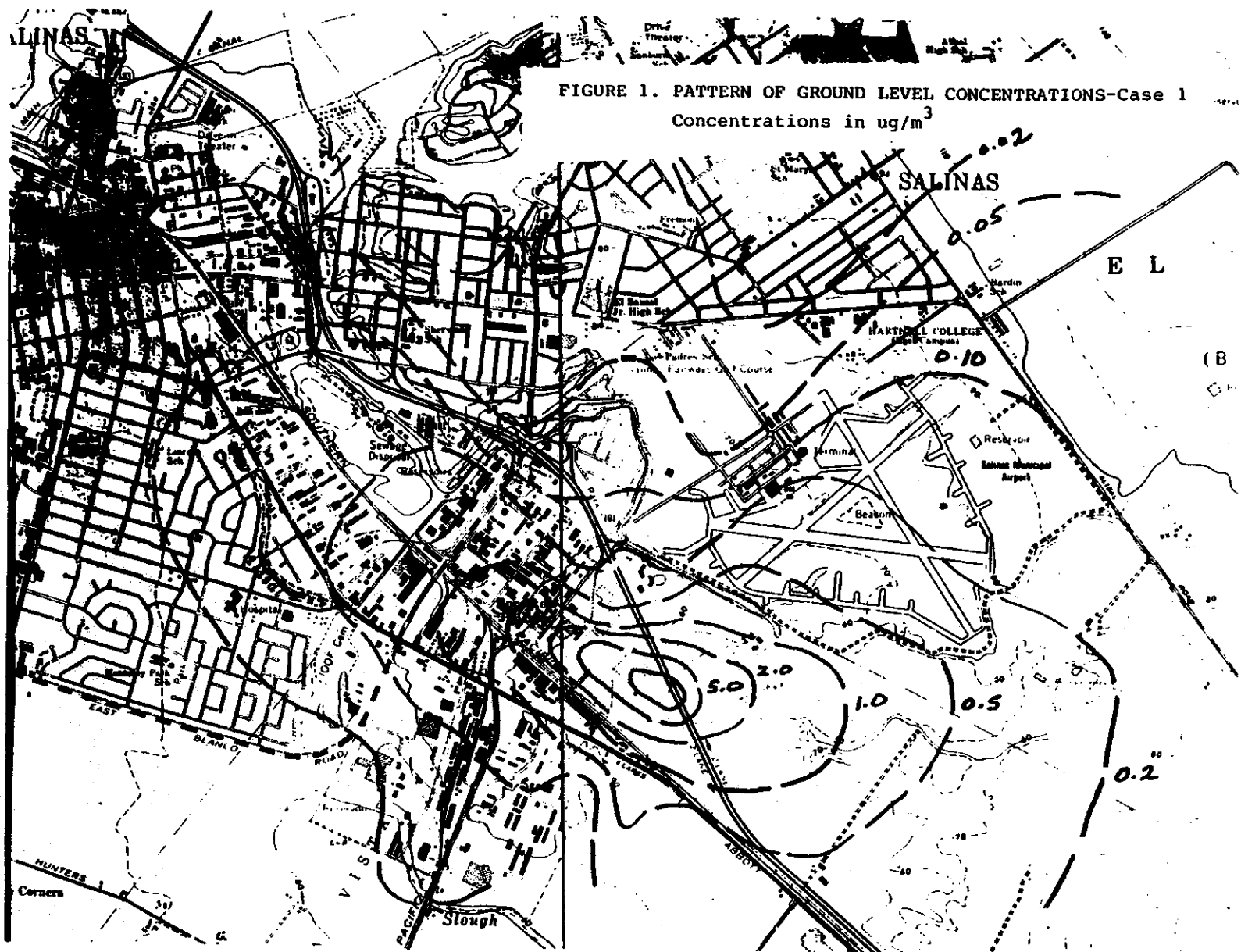
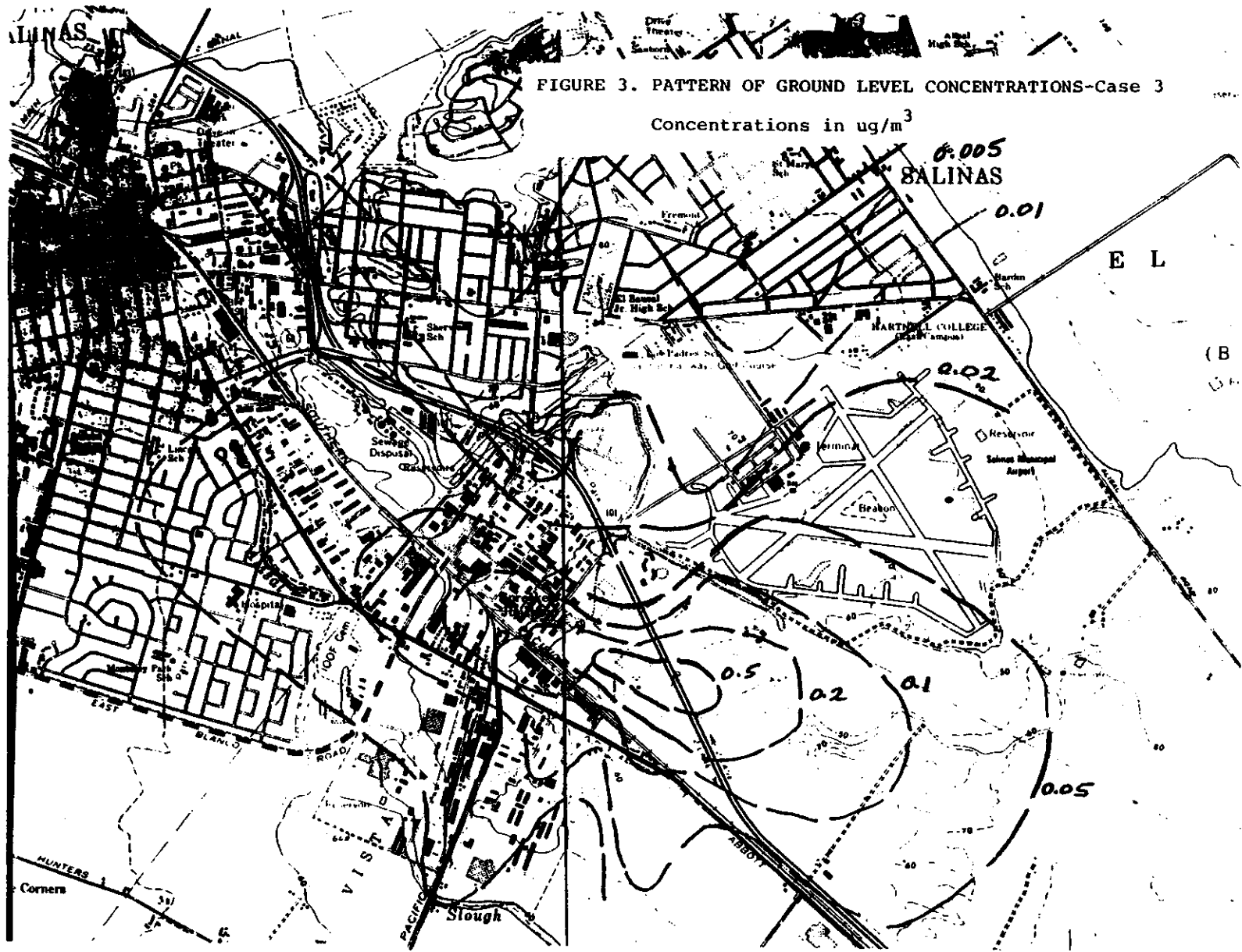


FIGURE 2. PATTERN OF GROUND LEVEL CONCENTRATIONS—Case 2

Concentrations in $\mu\text{g m}^{-3}$





the 0.1 isopleth. The migrant worker population has been estimated at 650-1,150. Thus, it is conservatively estimated that between 3,000 and 3,500 people may be exposed to concentrations of ethylene oxide in excess of $0.1 \mu\text{g}/\text{m}^3$ due to emissions from the McCormick facility. The industrial workers would be exposed for no more than 8 hours/day, 5 days/week. The migrant workers are likely to be exposed for only a fraction of the year and may not return in future years. Consequently, the number of individuals who might be exposed continuously for extended periods should be no greater than 100-200.

D. Risk Characterization

Based on the rationale provided in the dose-response assessment, we use a UCR value of $1.0 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1}$ for EtO. Multiplying this value by the EtO concentrations estimated in the exposure assessment results in the predictions of excess cancer risks associated with estimated concentrations (Table 4). The lifetime risks predicted for the populated area located west-northwest (WNW) of the plant would be 1.3×10^{-5} if exposure were to continue unchanged (using the maximum concentration for the closest populated area), but would be reduced to about 2.4×10^{-6} after installation of the exhaust-treatment systems (under case 3). Since only about 3,500 people are estimated to live or work within the $0.1 \mu\text{g}/\text{m}^3$ isopleth (for case 3), and most of these are outside the $0.2 \mu\text{g}/\text{m}^3$ isopleth, the remediated emission of ethylene oxide from the Salinas plant is estimated to produce no more than 0.007 excess cases of cancer per lifetime in the surrounding plantation:

$$1 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1} \times 0.2 \mu\text{g}/\text{m}^3 \times 3,500 = 0.007$$

$$\text{UCR) } \times (\text{concentration}) \times (\text{population}) = \text{number of cases}$$

Because the UCR is based on continuous lifetime exposure, the number of excess cases of cancer in the population most likely to be exposed (the 100-200 residents) is estimated to be:

$$1 \times 10^{-5} (\mu\text{g}/\text{m}^3)^{-1} \times 0.2 \mu\text{g}/\text{m}^3 \times 200 = 0.0004$$

All exposures beyond the 0.1 isopleth would result in risks of less than 1×10^{-6} and are, therefore, de minimis.

Table 4
Estimated Maximum Excess Cancer Risks
Associated with Ethylene Oxide Emissions from
McCormick Salinas Plant

Release Scenario	EtO Concentration ¹	Estimated Life-time Risk	Estimated Loss of Lifespan
Case 1	1.0	1.3×10^{-5}	4.0 hours
Case 2	0.2	2.8×10^{-6}	0.9 hours
Case 3	0.2	2.4×10^{-6}	0.7 hours

1 Values are the maximum concentrations for area between isopleths where residences are located to the west-northwest of the facility.

Further, the projected estimate of excess cancer cases per lifetime (i.e., 70 years) of 0.007 represents a conservative estimate and the actual risks are likely to be even lower, possibly zero, since:

1. data from the most sensitive species, strain, sex and tumor site were used to estimate low-dose risks;
2. a conservative low-dose extrapolation model (the multistage model) is used to generate low-dose risk estimates; whereas, equally plausible and apparently more rational models indicate far lower risks;
3. exposure is assumed to be continuous (24 hours/day), 365 days/year) for 70 years, a highly unlikely situation; and

4. the exposure estimate was based on a conservative estimate of the number of individuals living or working in the vicinity of the Salinas plant.

III. SUMMARY AND CONCLUSIONS

EtO has been identified by the State of California as a public health concern because of its known toxicity (including carcinogenicity) in laboratory animals and because of its widespread utilization. This report focuses on EtO dispersion to ambient air surrounding McCormick's Salinas plant that uses the substance to fumigate spices. An earlier report had estimated the cancer risk to the community of residents surrounding the plant, and found the risk to be de minimis. That assessment was based in part on an estimation of inhalation exposure from the dispersion of the compound into the atmosphere from the plant's exhaust stacks. The estimation was performed by mathematical model using meteorological data averaged over 24-hour days, and applying a safety factor to account for a daily discharge period of only 17 hours and a shift in wind direction from day to night.

The California Air Resources Board requested a more precise estimate of dispersion and ambient concentrations by using hourly meteorological data for only the 17 hours per day of operation. McCormick performed, by contractor, such an analysis using the three original operating scenarios: no change in plant operations; installing DEOXX to reduce emissions; and raising stack height to approximately 50 feet with the installation of DEOXX. This analysis found that, at the boundary of its plant property (60 meters), the original EtO concentrations, using the ISCLT model, are nearly the same as the estimates using the ISCST model. This result is likely due to the relative lack of sensitivity of the models at distances less than 100 meters from the source. By contrast, the EtO concentrations at 300 meters from the plant are estimated by the ISCST model to be lower by 37%, 26%, and 10% for scenarios 1, 2, and 3, respectively, when compared to the prior estimates. The estimations of cancer risk are correspondingly reduced by those changes in anticipated lifetime exposures. Consequently, continuing current emission practices would lead to an estimated cancer risk to residents living adjacent to the plant, of 1.3×10^{-5} and the addition of

DEOXX and increasing the height of the exhaust stack would lead to an estimated risk no greater than 2.4×10^{-6} . Those latter estimates are in the range of de minimis risks as defined by current regulatory policies. The actual risks are possibly much lower than the estimates would indicate. Given these risks, the projected hypothetical incidence is 0.007 cases of cancer in 70 years of exposures. For individuals residing beyond the 0.1 isopleth, the risk estimates are correspondingly lower.

VI. REFERENCES

Bowers, J.F., Bjorklund, J.R. and Cheney, C.S., Industrial Source Complex (ISC) Dispersion Model User's Guide, H.E. Cramer Inc., U.S. Envir. Prot. Agency Report No. EPA-450/4-79-30 (NTIS Acc. No. PB80 133044), December 1979.

APPENDIX

*** SALINAS -- CALIFORNIA STUDY -- CONCENTRATION -- ISCST MODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 12.08409 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)									
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0	
137.5 /	1.36034	0.65720	0.39109	0.26292	0.19171	0.14702	0.11715	0.09622	0.08173	
315.0 /	6.86270	3.66531	2.29801	1.59027	1.18154	0.91437	0.73166	0.60244	0.51290	
292.5 /	8.23147	4.37877	2.73353	1.88398	1.39395	1.07486	0.85726	0.70363	0.59811	
270.0 /	3.61070	1.84623	1.13081	0.77019	0.56808	0.43622	0.34694	0.28473	0.24068	
247.5 /	1.95613	1.07150	0.68607	0.48125	0.36424	0.28432	0.22898	0.19020	0.16191	
225.0 /	2.87658	1.56331	0.98793	0.68481	0.51355	0.39757	0.31799	0.26265	0.22232	
202.5 /	1.28308	0.70557	0.45640	0.32290	0.24785	0.19496	0.15803	0.13233	0.11266	
180.0 /	5.25298	3.00940	1.96958	1.40003	1.07380	0.84489	0.68480	0.57263	0.48868	
157.5 /	3.41321	1.80305	1.13775	0.79365	0.60138	0.46989	0.37911	0.31592	0.26895	
135.0 /	11.50390	6.25963	3.97102	2.76768	2.07781	1.61550	1.29737	1.07377	0.91484	
112.5 /	12.08409	6.46701	4.05658	2.80380	2.07774	1.60354	1.27954	1.05044	0.89374	
90.0 /	11.04985	5.80407	3.59967	2.47063	1.82313	1.40313	1.11770	0.91672	0.77887	
67.5 /	6.99318	3.72666	2.34210	1.62244	1.21141	0.93784	0.75025	0.61861	0.52565	
45.0 /	4.14036	2.19621	1.36911	0.94226	0.69584	0.53570	0.42662	0.34960	0.29754	
22.5 /	1.10092	0.56384	0.34748	0.23807	0.17626	0.13584	0.10836	0.08912	0.07566	
360.0 /	1.34096	0.72209	0.45564	0.31673	0.23659	0.18349	0.14719	0.12151	0.10357	

1960
Source GEP1

*** SALINAS - (CALIFORNIA STUDY - CONCENTRATION - ISCST MODE) ***

• 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) •

• FROM ALL SOURCES •
• FOR THE RECEPTOR GRID •

• MAXIMUM VALUE EQUALS 12.08409 AND OCCURRED AT (200.0, 112.5) •

DIRECTION / (DEGREES) /	RANGE (METERS)									
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0	
337.5 /	0.07026	0.06128	0.05409	0.04824	0.04339	0.03932	0.03587	0.03291	0.03035	
315.0 /	0.44051	0.38337	0.33737	0.29773	0.26848	0.24220	0.21988	0.20073	0.18416	
292.5 /	0.51268	0.44538	0.39130	0.34710	0.31045	0.27969	0.25357	0.23120	0.21186	
270.0 /	0.20573	0.17831	0.15635	0.13846	0.12367	0.11128	0.10079	0.09182	0.08408	
247.5 /	0.13923	0.12127	0.10676	0.09486	0.08495	0.07661	0.06952	0.06342	0.05815	
225.0 /	0.19035	0.16516	0.14492	0.12838	0.11468	0.10318	0.09343	0.08508	0.07786	
202.5 /	0.09714	0.08480	0.07481	0.06658	0.05972	0.05393	0.04999	0.04475	0.04107	
180.0 /	0.42157	0.36819	0.32494	0.28934	0.25964	0.23457	0.21320	0.19481	0.17885	
157.5 /	0.23164	0.20205	0.17814	0.15850	0.14214	0.12835	0.11660	0.10651	0.09775	
135.0 /	0.78661	0.68517	0.60337	0.53632	0.48057	0.43366	0.39376	0.35950	0.32984	
112.5 /	0.76630	0.66583	0.58504	0.51900	0.46424	0.41825	0.37922	0.34577	0.31686	
90.0 /	0.66752	0.57992	0.50959	0.45216	0.40458	0.36465	0.33078	0.30176	0.27669	
67.5 /	0.45083	0.39175	0.34419	0.30528	0.27297	0.24583	0.22278	0.20302	0.18593	
45.0 /	0.25500	0.22150	0.19458	0.17258	0.15434	0.13904	0.12605	0.11492	0.10531	
22.5 /	0.06487	0.05637	0.04955	0.04396	0.03934	0.03545	0.03215	0.02932	0.02688	
360.0 /	0.08905	0.07757	0.06831	0.06073	0.05442	0.04911	0.04460	0.04072	0.03737	

1960
Source
GIP1

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION - 1968 MODE ***

• 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) •

• FROM ALL SOURCES •
• FOR THE RECEPTOR GRID •

• MAXIMUM VALUE EQUALS 12.08407 AND OCCURRED AT (200.0, 112.5) •

DIRECTION /
(DEGREES) / 2000.0

RANGE (METERS)

337.5 /	0.02815
315.0 /	0.17039
292.5 /	0.19373
270.0 /	0.07779
247.5 /	0.03401
225.0 /	0.07219
202.5 /	0.03826
180.0 /	0.16656
157.5 /	0.09099
135.0 /	0.30604
112.5 /	0.29278
90.0 /	0.25376
67.5 /	0.17214
45.0 /	0.09726
22.5 /	0.02487
360.0 /	0.03460

1968
Sara GIP
1

1961

CASE 1

IN - DAY
365 DAY
SOURCE

*** SOURCE - CALIFORNIA STUDY - CONCENTRATION -- ISCST MODE ***

* 365 DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.61645 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	1.20883	0.83345	0.67570	0.57515	0.50179	0.45671	0.42503	0.40274	0.08714
315.0 /	6.01157	5.25870	4.65805	4.16028	3.76650	0.82660	0.66228	0.54591	0.46487
292.5 /	7.39431	6.98746	6.66605	6.41624	6.21105	0.99806	0.79754	0.65813	0.55777
270.0 /	4.02072	2.15774	1.63043	1.24967	0.96313	0.54942	0.44041	0.36424	0.30707
247.5 /	1.94981	1.13018	0.86854	0.68794	0.55560	0.29425	0.23788	0.19834	0.16922
225.0 /	2.41914	1.39760	1.05855	0.84601	0.68204	0.39776	0.32439	0.27316	0.23354
202.5 /	0.80285	0.59987	0.47177	0.39560	0.33705	0.09286	0.07366	0.06047	0.05145
180.0 /	4.26532	2.47166	1.87741	1.50004	1.21101	0.66099	0.55370	0.46442	0.39734
157.5 /	3.61451	1.91374	1.47671	1.16172	0.91170	0.48659	0.39011	0.32307	0.27356
135.0 /	10.62159	5.77071	4.57002	3.86651	3.39775	1.49992	1.20576	0.99949	0.85057
112.5 /	14.19853	7.59180	4.76326	3.19520	2.44906	1.89398	1.51419	1.24624	1.05969
90.0 /	14.61645	7.74306	4.82479	3.20073	2.46001	1.89706	1.51332	1.24358	1.05587
67.5 /	7.82566	4.10290	2.84953	1.95076	1.47078	1.00151	0.79895	0.65643	0.55814
45.0 /	5.25019	2.89402	1.91750	1.36295	0.95577	0.74456	0.59882	0.49617	0.42331
22.5 /	1.03269	0.51771	0.37865	0.31505	0.25766	0.12069	0.09567	0.07815	0.06611
360.0 /	1.35095	0.75101	0.54156	0.44802	0.37505	0.20919	0.16925	0.14126	0.12032

RT-104
 055 DATE
 SOURCE*

*** SOURCE AREA DATA *** CONCENTRATION ** TSCST MODE ***

* 355-DAY AVERAGE CONCENTRATION (MICROGRAMS-CUBIC METER) *

* FROM ALL SOURCES *
 * FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.51345 AND IS CORRECTED AT (200.0- 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.07455	0.06482	0.05885	0.05014	0.04474	0.04021	0.03637	0.03308	0.03024
315.0 /	0.09920	0.04753	0.03058	0.02137	0.02297	0.02190	0.01982	0.01843	0.01663
292.5 /	0.47524	0.41551	0.35500	0.32020	0.28555	0.26060	0.23839	0.21548	0.19739
270.0 /	0.28519	0.23097	0.20382	0.17979	0.16084	0.14491	0.13138	0.11978	0.10974
247.5 /	0.14565	0.12720	0.11280	0.09989	0.08959	0.08090	0.07350	0.06713	0.06181
225.0 /	0.20217	0.17710	0.15872	0.13989	0.12504	0.11389	0.10370	0.09491	0.08727
202.5 /	0.04410	0.03804	0.03366	0.02987	0.02707	0.02408	0.02183	0.01991	0.01825
180.0 /	0.04302	0.03811	0.03384	0.02999	0.02711	0.02395	0.02152	0.01987	0.01852
157.5 /	0.20445	0.20009	0.19375	0.18544	0.17419	0.12744	0.11543	0.10513	0.09523
135.0 /	0.70145	0.55717	0.41142	0.49907	0.44731	0.40383	0.36681	0.33504	0.30752
112.5 /	0.90925	0.79781	0.67000	0.61718	0.56044	0.49805	0.45187	0.41229	0.37805
90.0 /	0.90487	0.78502	0.65050	0.61285	0.54087	0.49390	0.44794	0.40858	0.37457
67.5 /	0.47048	0.41504	0.35870	0.32399	0.28581	0.25110	0.23573	0.21586	0.19782
45.0 /	0.16474	0.09744	0.07784	0.04983	0.02202	0.20108	0.18257	0.16668	0.15290
22.5 /	0.05817	0.05017	0.04074	0.03777	0.03087	0.03024	0.02733	0.02485	0.02270
0.0 /	0.01111	0.01111	0.01111	0.01111	0.01111	0.05723	0.05193	0.04738	0.04344

IN: 1A1
385 1A1
SER: 1A1

***** 15051 NODE ***

* USE THE FOLLOWING CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SURVEYS *
* FOR THE RECEIVER GRID *

* MAXIMUM VALUE FOUND: 14.61845 AND OCCURRED AT: 200.0 90.0 *

DIRECTION / (DEGREES) /	2000.0	RANGE (METERS)
337.5 /	0.02793	
315.0 /	0.15399	
292.5 /	0.19255	
270.0 /	0.10176	
247.5 /	0.05733	
225.0 /	0.08150	
202.5 /	0.01885	
180.0 /	0.13396	
157.5 /	0.08929	
135.0 /	0.28555	
112.5 /	0.34974	
90.0 /	0.34551	
67.5 /	0.18501	
45.0 /	0.14190	
22.5 /	0.02093	
0.0 /	0.04030	

DIRECTION 15.51 HDBE. ecc

* FROM THE RECEPTOR GRID *

* FROM THE SOURCES *

* MAXIMUM VALUE OCCURRED AT (2500.0, 112.5) *

DIRECTION (DEGREES)	RANGE (METERS)					
	2500.0	3000.0	3500.0	4000.0	4500.0	5000.0
337.5	0.01944	0.01440	0.01150	0.00917	0.00752	0.00545
315.0	0.10853	0.06180	0.04429	0.03267	0.02433	0.03789
292.5	0.12008	0.09521	0.07590	0.06180	0.05176	0.04415
270.0	0.07152	0.05395	0.04074	0.03494	0.02926	0.02501
247.5	0.04071	0.03039	0.02450	0.02019	0.01698	0.01455
225.0	0.05837	0.04462	0.03500	0.02750	0.02491	0.02141
202.5	0.01162	0.00356	0.00267	0.00187	0.00473	0.00402
180.0	0.09478	0.07648	0.06137	0.05076	0.04796	0.03702
157.5	0.05268	0.04713	0.03921	0.03334	0.02945	0.02160
135.0	0.20256	0.15265	0.12235	0.10294	0.08455	0.07251
112.5	0.24218	0.17562	0.14566	0.12009	0.10009	0.08606
90.0	0.24450	0.17676	0.14600	0.11910	0.10000	0.08550
67.5	0.12008	0.09521	0.07590	0.06180	0.05176	0.04415
45.0	0.10035	0.07152	0.05395	0.04074	0.03494	0.03528
22.5	0.01450	0.01078	0.00843	0.00651	0.00566	0.00479
0.0	0.00947	0.00710	0.00540	0.00410	0.00310	0.00494

*** SALINAS (CALIFORNIA STUDY) - CONCENTRATION - ISOST MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 12.42054 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	1.26653	0.60595	0.35343	0.23187	0.16466	0.12300	0.09552	0.07650	0.06380
315.0 /	5.46325	2.92566	1.83384	1.26615	0.93941	0.72484	0.57818	0.47483	0.40305
292.5 /	7.68972	4.12860	2.59618	1.79970	1.33847	1.03686	0.83040	0.68419	0.58322
270.0 /	5.14764	2.77237	1.75816	1.22760	0.92252	0.71878	0.57831	0.47915	0.40855
247.5 /	1.87439	0.95347	0.58272	0.39666	0.29302	0.22532	0.17930	0.14760	0.12501
225.0 /	2.47272	1.40276	0.91475	0.64923	0.49585	0.38765	0.31530	0.26327	0.22497
202.5 /	1.42575	0.72701	0.44554	0.30545	0.22676	0.17489	0.13963	0.11508	0.09772
180.0 /	3.54758	2.01900	1.32726	0.94979	0.73314	0.58047	0.47318	0.39773	0.34090
157.5 /	3.62969	1.93118	1.21466	0.84317	0.63014	0.48888	0.39192	0.32361	0.27593
135.0 /	10.83558	5.92173	3.77447	2.64077	1.99144	1.55268	1.24974	1.03689	0.88377
112.5 /	12.42054	6.55730	4.06849	2.78872	2.05260	1.57589	1.25210	1.02402	0.84857
90.0 /	11.77536	6.25760	3.91406	2.70208	2.00572	1.54963	1.23817	1.01851	0.86649
67.5 /	8.80413	4.63511	2.87550	1.97170	1.45391	1.11695	0.88782	0.72672	0.61651
45.0 /	5.00625	2.67358	1.67351	1.15406	0.85682	0.66072	0.52678	0.43279	0.36757
22.5 /	1.09364	0.56065	0.34305	0.23294	0.17023	0.12983	0.10253	0.08339	0.07046
360.0 /	0.83186	0.44131	0.27667	0.19173	0.14257	0.11042	0.08841	0.07281	0.06216

1962
Source Grid

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 12.42054 AND OCCURRED AT (200.0, 112.5) *

RECTION / DEGREES) /	RANGE (METERS)									
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0	
337.5 /	0.05376	0.04599	0.03985	0.03490	0.03085	0.02750	0.02468	0.02229	0.02025	
315.0 /	0.34514	0.29951	0.26284	0.23287	0.20803	0.18719	0.16950	0.15436	0.14127	
292.5 /	0.50135	0.43670	0.38462	0.34198	0.30655	0.27676	0.25143	0.22969	0.21087	
270.0 /	0.35162	0.30653	0.27012	0.24024	0.21537	0.19442	0.17659	0.16127	0.14799	
247.5 /	0.10705	0.09295	0.08165	0.07243	0.06481	0.05842	0.05300	0.04836	0.04435	
225.0 /	0.19414	0.16961	0.14973	0.13336	0.11970	0.10817	0.09833	0.08987	0.08252	
202.5 /	0.08380	0.07283	0.06401	0.05680	0.05082	0.04579	0.04153	0.03787	0.03470	
180.0 /	0.29536	0.25897	0.22937	0.20492	0.18445	0.16712	0.15230	0.13951	0.12809	
157.5 /	0.23718	0.20654	0.18103	0.16158	0.14474	0.13057	0.11852	0.10818	0.09923	
135.0 /	0.76057	0.66298	0.58417	0.51950	0.46568	0.42036	0.38178	0.34865	0.31994	
112.5 /	0.74283	0.64403	0.56482	0.50023	0.44678	0.40200	0.36404	0.33159	0.30358	
90.0 /	0.74366	0.64879	0.56886	0.50512	0.45224	0.40782	0.37009	0.33774	0.30976	
67.5 /	0.52724	0.45702	0.40068	0.35471	0.31666	0.28476	0.25772	0.23459	0.21463	
45.0 /	0.31478	0.27318	0.23976	0.21246	0.18983	0.17084	0.15472	0.14092	0.12900	
22.5 /	0.06002	0.05184	0.04530	0.03998	0.03559	0.03192	0.02881	0.02617	0.02388	
060.0 /	0.05347	0.04660	0.04106	0.03651	0.03273	0.02955	0.02684	0.02451	0.02250	

1962 Source Gp 1

*** SALINAS - CALIFORNIA STUDY CONCENTRATION -- ISCST NODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES +
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 12.42054 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.01851	0.01248	0.00907	0.00696	0.00554	0.00453
315.0 /	0.13049	0.09110	0.06812	0.05352	0.04346	0.03621
292.5 /	0.19519	0.13807	0.10444	0.08208	0.06794	0.05711
270.0 /	0.13725	0.09707	0.07337	0.05816	0.04760	0.03994
247.5 /	0.04111	0.02907	0.02201	0.01750	0.01437	0.01210
225.0 /	0.07675	0.05452	0.04136	0.03290	0.02699	0.02268
202.5 /	0.03217	0.02265	0.01707	0.01351	0.01103	0.00924
180.0 /	0.11982	0.08602	0.06586	0.05283	0.04365	0.03691
157.5 /	0.09196	0.06491	0.04898	0.03877	0.03169	0.02656
135.0 /	0.29709	0.21045	0.15937	0.12661	0.10380	0.08722
112.5 /	0.28011	0.19573	0.14656	0.11529	0.09377	0.07827
90.0 /	0.28638	0.20193	0.15226	0.12054	0.09856	0.08263
67.5 /	0.19809	0.13809	0.10314	0.08096	0.06570	0.05471
45.0 /	0.11932	0.08353	0.06261	0.04928	0.04009	0.03346
22.5 /	0.02197	0.01514	0.01120	0.00872	0.00703	0.00581
360.0 /	0.02001	0.01467	0.01106	0.00876	0.00716	0.00600

1962 Source Grid

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.21213 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	500.0	700.0	800.0	900.0	1000.0
337.5 /	0.91647	0.45093	0.27100	0.18255	0.13327	0.10176	0.08059	0.06585	0.05552
315.0 /	5.24748	2.79832	1.75432	1.21342	0.90400	0.69982	0.56009	0.46171	0.39219
292.5 /	8.78979	4.70960	2.94578	2.02944	1.50232	1.15727	0.92184	0.75601	0.64124
270.0 /	4.73940	2.49418	1.55736	1.07607	0.80383	0.62353	0.50025	0.41388	0.35204
247.5 /	2.03764	1.10417	0.70775	0.49836	0.38039	0.29877	0.24204	0.20244	0.17246
225.0 /	2.71666	1.48919	0.95526	0.67197	0.51397	0.40335	0.32647	0.27315	0.23238
202.5 /	2.46064	1.34736	0.85914	0.60003	0.45548	0.35523	0.28599	0.23810	0.20179
180.0 /	4.00037	2.21661	1.40346	1.01432	0.77570	0.60994	0.49438	0.41339	0.35322
157.5 /	6.45231	3.46900	2.18503	1.51357	1.13327	0.87750	0.70205	0.57960	0.49145
135.0 /	12.47626	6.82168	4.34621	3.03872	2.29085	1.78569	1.43717	1.19243	1.01572
112.5 /	11.59666	6.12146	3.82278	2.64050	1.96338	1.51987	1.21708	1.00376	0.85439
90.0 /	14.21213	7.61964	4.79245	3.32163	2.47750	1.91919	1.53669	1.26743	1.07900
67.5 /	8.49630	4.53531	2.84293	1.96377	1.45990	1.12739	0.90009	0.74034	0.62921
45.0 /	5.24360	2.85408	1.81651	1.27005	0.95531	0.74421	0.59858	0.49589	0.42324
22.5 /	0.92844	0.45863	0.27590	0.18596	0.13488	0.10271	0.08110	0.06586	0.05589
360.0 /	0.76101	0.39882	0.24848	0.17164	0.12716	0.09836	0.07868	0.06471	0.05527

1963
Source Grid

*** SALINAS - CALIFORNIA STUDY - OBJECTIVE - ION IS MODE

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.21213 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.04734	0.04093	0.03581	0.03164	0.02820	0.02533	0.02290	0.02082	0.01903
315.0 /	0.33641	0.29242	0.25704	0.22810	0.20409	0.18393	0.16680	0.15212	0.13942
292.5 /	0.34868	0.47584	0.41737	0.36965	0.33013	0.29698	0.26887	0.24482	0.22404
270.0 /	0.30270	0.26377	0.23244	0.20679	0.18549	0.16758	0.15235	0.13929	0.12797
247.5 /	0.14877	0.12993	0.11472	0.10218	0.09173	0.08291	0.07539	0.06892	0.06330
225.0 /	0.20024	0.17473	0.15409	0.13713	0.12299	0.11104	0.10090	0.09216	0.08458
202.5 /	0.17335	0.15086	0.13274	0.11789	0.10556	0.09518	0.08637	0.07880	0.07225
180.0 /	0.30490	0.26644	0.23527	0.20961	0.18819	0.17010	0.15466	0.14138	0.12985
157.5 /	0.42103	0.36531	0.32086	0.28437	0.25410	0.22870	0.20714	0.18867	0.17271
135.0 /	0.87416	0.76210	0.67165	0.59746	0.53575	0.48378	0.43935	0.40157	0.36866
112.5 /	0.73436	0.63969	0.56353	0.50122	0.44950	0.40604	0.36911	0.33743	0.31001
90.0 /	0.92669	0.80641	0.70956	0.63027	0.56443	0.50708	0.46204	0.42169	0.38677
67.5 /	0.53945	0.46867	0.41175	0.36522	0.32663	0.29422	0.26671	0.24315	0.22277
45.0 /	0.36429	0.31761	0.27993	0.24900	0.22327	0.20160	0.18316	0.16732	0.15359
22.5 /	0.04770	0.04128	0.03615	0.03197	0.02852	0.02563	0.02318	0.02109	0.01928
360.0 /	0.04755	0.04144	0.03652	0.03248	0.02913	0.02631	0.02390	0.02184	0.02005

1963
Source Gp 1

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTION GRID *

* MAXIMUM VALUE EQUALS 14.21213 AND OCCURRED AT 1 200.0 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.01756	0.01222	0.00913	0.00718	0.00584	0.00487
315.0 /	0.12909	0.09086	0.06846	0.05415	0.04427	0.03712
292.5 /	0.20688	0.14442	0.10000	0.08486	0.06893	0.05747
270.0 /	0.11885	0.08468	0.06453	0.05159	0.04258	0.03603
247.5 /	0.05898	0.04203	0.03202	0.02558	0.02107	0.01777
225.0 /	0.07885	0.05610	0.04266	0.03402	0.02798	0.02356
202.5 /	0.06724	0.04762	0.03611	0.02875	0.02361	0.01986
180.0 /	0.12098	0.08621	0.06559	0.05230	0.04300	0.03621
157.5 /	0.16008	0.11236	0.08444	0.06664	0.05433	0.04543
135.0 /	0.24235	0.24292	0.18427	0.14663	0.12041	0.10131
112.5 /	0.28736	0.20424	0.15524	0.12378	0.10189	0.08595
90.0 /	0.35832	0.25292	0.19096	0.15130	0.12380	0.10387
67.5 /	0.20607	0.14466	0.10872	0.08581	0.06996	0.05849
45.0 /	0.14256	0.10109	0.07659	0.06084	0.04989	0.04195
22.5 /	0.01775	0.01233	0.00917	0.00717	0.00580	0.00482
340.0 /	0.01854	0.01310	0.00989	0.00783	0.00641	0.00537

1963
Source GIP 1

*** SALINAS - CALIFORNIA STUDY - (CONCENTRATION -- ISCS) MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.12365 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	1.63383	0.82829	0.53018	0.36155	0.26463	0.20223	0.15995	0.13016	0.11024
315.0 /	4.49921	2.36743	1.47269	1.01449	0.75098	0.58022	0.46387	0.38179	0.32532
292.5 /	7.25095	3.91230	2.46658	1.71222	1.27707	0.98984	0.79292	0.65388	0.55689
270.0 /	4.12205	2.20871	1.38464	0.95613	0.70931	0.54740	0.43677	0.35873	0.30471
247.5 /	1.54940	0.82289	0.51688	0.35907	0.26832	0.20888	0.16823	0.13949	0.11952
225.0 /	1.84392	1.02538	0.64491	0.47160	0.36063	0.28395	0.23044	0.19276	0.16487
202.5 /	2.76990	1.52255	0.96859	0.67401	0.50999	0.39641	0.31820	0.26428	0.22344
180.0 /	3.33946	1.79409	1.08798	0.73453	0.54021	0.41266	0.32674	0.26761	0.22516
157.5 /	6.79930	3.76044	2.42257	1.70872	1.30403	1.02407	0.82955	0.69354	0.59194
135.0 /	10.88623	6.06744	3.91011	2.75434	2.08504	1.63106	1.31619	1.09373	0.93468
112.5 /	14.12365	7.71911	4.91524	3.43362	2.57958	2.00695	1.61225	1.33417	1.13665
90.0 /	12.08897	6.43164	4.02787	2.78447	2.06273	1.59348	1.27292	1.04565	0.89135
67.5 /	6.88316	3.71857	2.35501	1.64062	1.22667	0.95255	0.76409	0.63078	0.53849
45.0 /	2.62929	1.40236	0.88078	0.60994	0.45411	0.35136	0.28098	0.23139	0.19711
22.5 /	1.25695	0.68733	0.43558	0.30273	0.22490	0.17387	0.13885	0.11398	0.09727
360.0 /	1.13030	0.60754	0.38059	0.26197	0.19369	0.14888	0.11830	0.09678	0.08192

1964
Source Gpp 1

* 365-DAY AVERAGE CONCENTRATION (NITROGENS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.12355 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.09399	0.08125	0.07106	0.06275	0.05589	0.05015	0.04530	0.04115	0.03757
315.0 /	0.27965	0.24364	0.21487	0.19095	0.17126	0.15470	0.14062	0.12854	0.11808
292.5 /	0.47847	0.41652	0.36662	0.32575	0.29182	0.26328	0.23902	0.21820	0.20019
270.0 /	0.26098	0.22654	0.19886	0.17625	0.15751	0.14178	0.12843	0.11700	0.10712
247.5 /	0.10332	0.09051	0.08018	0.07170	0.06463	0.05868	0.05360	0.04923	0.04544
225.0 /	0.14248	0.12465	0.11018	0.09826	0.08830	0.07988	0.07269	0.06650	0.06112
202.5 /	0.19153	0.16636	0.14612	0.12957	0.11585	0.10433	0.09455	0.08618	0.07894
180.0 /	0.19180	0.16572	0.14490	0.12799	0.11405	0.10239	0.09254	0.08414	0.07690
157.5 /	0.31113	0.44693	0.39496	0.35220	0.31655	0.28645	0.26078	0.23869	0.21952
135.0 /	0.80572	0.70334	0.62053	0.55247	0.49576	0.44795	0.40720	0.37217	0.34179
112.5 /	0.97738	0.85133	0.74966	0.66630	0.59698	0.53865	0.48903	0.44644	0.40955
90.0 /	0.76546	0.66613	0.58619	0.52079	0.46650	0.42087	0.38211	0.34887	0.32010
67.5 /	0.46325	0.40373	0.35571	0.31634	0.28760	0.25603	0.23257	0.21243	0.19498
45.0 /	0.16920	0.14715	0.12939	0.11485	0.10278	0.09263	0.08400	0.07661	0.07020
22.5 /	0.08349	0.07260	0.06383	0.05664	0.05068	0.04566	0.04140	0.03774	0.03458
360.0 /	0.06995	0.06056	0.05302	0.04688	0.04180	0.03754	0.03393	0.03085	0.02819

1964
Source Grp 1

*** SALINAS - CALIFORNIA SPRAY INFILTRATION - ISOST MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SAMPLES *
 * FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 14.12365 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.03457	0.02387	0.01767	0.01375	0.01107	0.00916
315.0 /	0.10931	0.07751	0.05876	0.04674	0.03840	0.03234
292.5 /	0.10536	0.13085	0.09883	0.07835	0.05417	0.05388
270.0 /	0.09899	0.06927	0.05188	0.04080	0.03316	0.02767
247.5 /	0.04228	0.03067	0.02374	0.01924	0.01608	0.01377
225.0 /	0.05692	0.04061	0.03091	0.02466	0.02027	0.01787
202.5 /	0.07342	0.05185	0.03923	0.03118	0.02557	0.02149
180.0 /	0.07117	0.04958	0.03723	0.02933	0.02389	0.01996
157.5 /	0.20462	0.14659	0.11215	0.08992	0.07431	0.06287
135.0 /	0.31748	0.22554	0.17112	0.13610	0.11170	0.09374
112.5 /	0.37975	0.25833	0.20275	0.15077	0.13161	0.11044
90.0 /	0.29589	0.20857	0.15726	0.12445	0.10173	0.08528
67.5 /	0.18066	0.12775	0.09655	0.07655	0.06266	0.05259
45.0 /	0.06499	0.04568	0.03434	0.02710	0.02209	0.01847
22.5 /	0.03193	0.02235	0.01674	0.01315	0.01069	0.00890
0.0 /	0.02599	0.01800	0.01338	0.01045	0.00845	0.00701

1964
 Source G-P1

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION --- 16CST NODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTION GRID *

* MAXIMUM VALUE EQUALS 2.71611 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.30541	0.14768	0.08793	0.05914	0.04313	0.03308	0.02637	0.02166	0.01840
315.0 /	1.54286	0.82439	0.51703	0.35790	0.26594	0.20583	0.16473	0.13567	0.11550
292.5 /	1.85030	0.98472	0.61493	0.42395	0.31372	0.24194	0.19299	0.15845	0.13468
270.0 /	0.81057	0.41472	0.25412	0.17315	0.12773	0.09810	0.07804	0.06405	0.05415
247.5 /	0.43941	0.24083	0.15426	0.10826	0.08194	0.06397	0.05193	0.04281	0.03645
225.0 /	0.64592	0.35121	0.22204	0.15399	0.11549	0.08943	0.07195	0.05911	0.05003
202.5 /	0.28809	0.15834	0.10259	0.07263	0.05575	0.04386	0.03556	0.02978	0.02536
180.0 /	1.18009	0.67635	0.44281	0.31493	0.24156	0.19009	0.15411	0.12889	0.11000
157.5 /	0.76609	0.40506	0.25574	0.17850	0.13528	0.10572	0.08532	0.07111	0.06054
135.0 /	2.58434	1.40695	0.89291	0.62261	0.46747	0.36352	0.29200	0.24173	0.20596
112.5 /	2.71611	1.45421	0.91248	0.63088	0.46757	0.36090	0.28803	0.23692	0.20123
90.0 /	2.48289	1.30486	0.80959	0.55386	0.41024	0.31578	0.25158	0.20640	0.17536
67.5 /	1.57096	0.83766	0.52666	0.36498	0.27255	0.21103	0.16886	0.13926	0.11834
45.0 /	0.93028	0.49371	0.30790	0.21198	0.15657	0.12055	0.09602	0.07871	0.06699
22.5 /	0.24720	0.12670	0.07812	0.05355	0.03965	0.03056	0.02439	0.02006	0.01703
360.0 /	0.30140	0.16238	0.10250	0.07127	0.05320	0.04130	0.03314	0.02736	0.02332

1960
Source Grp 2

*** 240 DAYS *** 240 DAYS *** 240 DAYS *** CONCENTRATION *** ISCST MODE ***

* 240 DAY AVERAGE CONCENTRATION (MICROGRAMS CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 200.0 AND OCCURRED AT (200.0 90.0) *

DIRECTION / (DEGREES)	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.00629	0.00439	0.00322	0.00255	0.00207	0.00172
315.0 /	0.03468	0.02445	0.01943	0.01457	0.01191	0.00999
292.5 /	0.04112	0.02895	0.02187	0.01710	0.01374	0.01166
270.0 /	0.02292	0.01613	0.01218	0.00950	0.00767	0.00560
247.5 /	0.01291	0.00917	0.00692	0.00554	0.00451	0.00382
225.0 /	0.01835	0.01315	0.01005	0.00805	0.00655	0.00561
202.5 /	0.00360	0.00266	0.00200	0.00157	0.00127	0.00106
180.0 /	0.03130	0.02249	0.01722	0.01300	0.01144	0.00968
157.5 /	0.02010	0.01412	0.01081	0.00838	0.00680	0.00571
135.0 /	0.06429	0.04561	0.03480	0.02754	0.02260	0.01904
112.5 /	0.07674	0.05495	0.04139	0.03307	0.02704	0.02267
90.0 /	0.07602	0.05494	0.04143	0.03279	0.02686	0.02251
67.5 /	0.04122	0.02976	0.02180	0.01722	0.01400	0.01177
45.0 /	0.03195	0.02280	0.01700	0.01304	0.01110	0.00930
22.5 /	0.00471	0.00327	0.00240	0.00180	0.00144	0.00127
350.0 /	0.00904	0.00642	0.00473	0.00364	0.00290	0.00253

CONCENTRATION OF POLYCYCLODIC AROMATIC HYDROCARBONS IN AIR - 15CST MADE ***

785 1447
5580144

CONCENTRATION (MICROGRAMS PER CUBIC METER)

FROM ALL SOURCES
FOR THE RECEPTOR GRID *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.01678	0.01455	0.01275	0.01129	0.01007	0.00905	0.00819	0.00745	0.00681
315.0 /	0.08989	0.07822	0.06801	0.05911	0.05172	0.04535	0.04078	0.03748	0.0348
292.5 /	0.10769	0.09356	0.08226	0.07291	0.06521	0.05874	0.05324	0.04853	0.04446
270.0 /	0.05970	0.05190	0.04562	0.04048	0.03622	0.03263	0.02958	0.02698	0.02472
247.5 /	0.03284	0.02866	0.02527	0.02249	0.02017	0.01822	0.01655	0.01512	0.01388
225.0 /	0.04552	0.03988	0.03507	0.03150	0.02833	0.02555	0.02335	0.02138	0.01966
202.5 /	0.00993	0.00863	0.00753	0.00673	0.00602	0.00542	0.00492	0.00448	0.00411
180.0 /	0.07741	0.06781	0.0596	0.05259	0.04622	0.04068	0.03598	0.03198	0.02856
157.5 /	0.05277	0.04562	0.03964	0.03487	0.03187	0.02939	0.02759	0.02637	0.02557
135.0 /	0.15484	0.13544	0.11822	0.10335	0.09071	0.07991	0.07258	0.06744	0.06324
112.5 /	0.20468	0.17792	0.15527	0.13694	0.12239	0.11213	0.10173	0.09283	0.08512
90.0 /	0.20369	0.17694	0.15367	0.13492	0.12039	0.11120	0.10085	0.09200	0.08434
67.5 /	0.10772	0.09356	0.08129	0.07191	0.06521	0.05974	0.05524	0.05138	0.04798
45.0 /	0.09261	0.08140	0.07191	0.06521	0.06007	0.05580	0.05331	0.05138	0.04944
22.5 /	0.01270	0.01097	0.00957	0.00841	0.00758	0.00681	0.00616	0.00560	0.00511
350.0 /	0.02330	0.02055	0.01817	0.01594	0.01428	0.01289	0.01169	0.01067	0.00978

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- ISCST MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES +
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 2.79113 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.28429	0.13612	0.07944	0.05214	0.03703	0.02767	0.02149	0.01722	0.01436
315.0 /	1.22800	0.65788	0.41250	0.28490	0.21140	0.16314	0.13015	0.10691	0.09075
292.5 /	1.72871	0.92849	0.58402	0.40495	0.30120	0.23335	0.18690	0.15403	0.13129
270.0 /	1.15707	0.62349	0.39553	0.27627	0.20763	0.16179	0.13020	0.10789	0.09199
247.5 /	0.42074	0.21419	0.13097	0.08920	0.06590	0.05069	0.04039	0.03322	0.02814
225.0 /	0.55580	0.31542	0.20575	0.14609	0.11158	0.08769	0.07102	0.05927	0.05065
202.5 /	0.31998	0.16331	0.10037	0.06869	0.05101	0.03935	0.03142	0.02591	0.02200
180.0 /	0.79724	0.45397	0.29855	0.21375	0.16500	0.13066	0.10653	0.08936	0.07676
157.5 /	0.81539	0.43411	0.27317	0.18970	0.14179	0.11002	0.08822	0.07286	0.06213
135.0 /	2.43433	1.33109	0.84877	0.59410	0.44806	0.34940	0.28129	0.23343	0.19896
112.5 /	2.79113	1.47423	0.91502	0.62740	0.46188	0.35465	0.28183	0.23056	0.19556
90.0 /	2.64655	1.40710	0.88045	0.60821	0.45139	0.34880	0.27873	0.22934	0.19511
67.5 /	1.97801	1.04191	0.71663	0.44355	0.32712	0.25135	0.19782	0.16361	0.13880
45.0 /	1.12455	0.60088	0.37627	0.25958	0.19275	0.14844	0.11855	0.09743	0.08275
22.5 /	0.24566	0.12601	0.07714	0.05240	0.03830	0.02921	0.02307	0.01877	0.01586
360.0 /	0.18701	0.09927	0.06226	0.04116	0.03209	0.02486	0.01991	0.01640	0.01400

1962
Source Gp 2

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- ISCST MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 2.79113 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)									
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0	
337.5 /	0.01210	0.01035	0.00897	0.00786	0.00695	0.00619	0.00556	0.00502	0.00456	
315.0 /	0.07771	0.06744	0.05919	0.05244	0.04685	0.04216	0.03817	0.03477	0.03182	
292.5 /	0.11287	0.09831	0.08659	0.07699	0.06901	0.06231	0.05660	0.05171	0.04748	
270.0 /	0.07918	0.06903	0.06083	0.05410	0.04850	0.04379	0.03977	0.03632	0.03334	
247.5 /	0.02410	0.02092	0.01838	0.01631	0.01459	0.01315	0.01193	0.01089	0.00999	
225.0 /	0.04371	0.03819	0.03371	0.03003	0.02695	0.02436	0.02214	0.02024	0.01859	
202.5 /	0.01887	0.01640	0.01441	0.01279	0.01144	0.01031	0.00935	0.00853	0.00782	
180.0 /	0.06651	0.05832	0.05166	0.04615	0.04154	0.03764	0.03430	0.03143	0.02892	
157.5 /	0.05341	0.04651	0.04095	0.03639	0.03260	0.02941	0.02669	0.02437	0.02235	
135.0 /	0.17124	0.14927	0.13154	0.11698	0.10487	0.09466	0.08598	0.07853	0.07206	
112.5 /	0.16726	0.14502	0.12719	0.11265	0.10062	0.09053	0.08199	0.07468	0.06838	
90.0 /	0.16746	0.14565	0.12811	0.11376	0.10185	0.09185	0.08335	0.07608	0.06978	
67.5 /	0.11871	0.10290	0.09022	0.07987	0.07131	0.06413	0.05804	0.05284	0.04834	
45.0 /	0.07087	0.06151	0.05398	0.04784	0.04274	0.03847	0.03484	0.03174	0.02905	
22.5 /	0.01351	0.01167	0.01020	0.00900	0.00801	0.00719	0.00649	0.00589	0.00538	
0.0 /	0.01204	0.01050	0.00925	0.00822	0.00737	0.00666	0.00605	0.00552	0.00507	

1962
Source Crp 2

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- ISCST MODE ***

• 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) •

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

• MAXIMUM VALUE EQUALS 2.79113 AND OCCURRED AT (200.0, 112.5) •

DIRECTION /
(DEGREES) /

2000.0

RANGE (METERS)

337.5 /	0.00417
315.0 /	0.02939
292.5 /	0.04394
270.0 /	0.03092
247.5 /	0.00926
225.0 /	0.01729
202.5 /	0.00725
180.0 /	0.02699
157.5 /	0.02071
135.0 /	0.06691
112.5 /	0.06309
90.0 /	0.06455
67.5 /	0.04462
45.0 /	0.02687
22.5 /	0.00495
360.0 /	0.00469

1962
Source Exp 2

• 355-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) •

• FROM ALL SOURCES •
• FOR THE RECEPTOR GRID •

• MAXIMUM VALUE EQUALS 3.19319 AND OCCURRED AT (200.0, 90.0) •

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.20588	0.10138	0.06095	0.04107	0.02999	0.02290	0.01814	0.01483	0.01250
315.0 /	1.17937	0.62921	0.39460	0.27303	0.20343	0.15751	0.12607	0.10396	0.08830
292.5 /	1.97577	1.05900	0.66258	0.45661	0.33805	0.26045	0.20749	0.17021	0.14437
270.0 /	1.06469	0.56065	0.35021	0.24209	0.18086	0.14032	0.11260	0.09318	0.07926
247.5 /	0.45776	0.24822	0.15916	0.11213	0.08559	0.06724	0.05448	0.04557	0.03883
225.0 /	0.60978	0.33451	0.21469	0.15112	0.11560	0.09074	0.07347	0.06147	0.05230
202.5 /	0.55232	0.30261	0.19305	0.13491	0.10242	0.07990	0.06434	0.05358	0.04541
180.0 /	0.89840	0.49814	0.32229	0.22818	0.17451	0.13725	0.11127	0.09306	0.07952
157.5 /	1.44887	0.77941	0.49114	0.34038	0.25488	0.19740	0.15797	0.13044	0.11061
135.0 /	2.80298	1.53332	0.97726	0.68156	0.51537	0.40177	0.32344	0.26841	0.22864
112.5 /	2.60550	1.37608	0.85967	0.59400	0.44173	0.34200	0.27390	0.22595	0.19232
90.0 /	3.19319	1.71289	1.07777	0.74729	0.55746	0.43190	0.34589	0.28335	0.24293
67.5 /	1.90859	1.01932	0.63920	0.44169	0.32841	0.25365	0.20254	0.16664	0.14162
45.0 /	1.17810	0.64158	0.40850	0.28573	0.21495	0.16747	0.13473	0.11164	0.09529
22.5 /	0.20851	0.10309	0.06205	0.04184	0.03035	0.02312	0.01826	0.01483	0.01259
350.0 /	0.17110	0.08472	0.05592	0.03864	0.02863	0.02215	0.01772	0.01458	0.01245

1963
Source Grp 2

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION - ISCST MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 3.19319 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.01066	0.00922	0.00806	0.00713	0.00635	0.00570	0.00516	0.00469	0.00429
315.0 /	0.07575	0.06385	0.05788	0.05137	0.04596	0.04142	0.03757	0.03426	0.03140
292.5 /	0.12354	0.10714	0.09398	0.08324	0.07434	0.06688	0.06055	0.05514	0.05046
270.0 /	0.06815	0.05939	0.05234	0.04657	0.04177	0.03774	0.03431	0.03137	0.02883
247.5 /	0.03350	0.02926	0.02583	0.02301	0.02066	0.01867	0.01698	0.01552	0.01426
225.0 /	0.04507	0.03933	0.03469	0.03087	0.02769	0.02501	0.02272	0.02076	0.01905
202.5 /	0.03901	0.03396	0.02988	0.02654	0.02376	0.02143	0.01944	0.01775	0.01627
180.0 /	0.06864	0.05999	0.05297	0.04720	0.04238	0.03830	0.03483	0.03184	0.02925
157.5 /	0.09477	0.08228	0.07223	0.06402	0.05721	0.05149	0.04664	0.04249	0.03889
135.0 /	0.19679	0.17157	0.15121	0.13451	0.12062	0.10893	0.09897	0.09043	0.08302
112.5 /	0.16531	0.14400	0.12686	0.11284	0.10120	0.09141	0.08310	0.07597	0.06980
90.0 /	0.20865	0.18158	0.15978	0.14193	0.12711	0.11465	0.10405	0.09498	0.08712
67.5 /	0.12143	0.10550	0.09269	0.08222	0.07353	0.06624	0.06003	0.05473	0.05016
45.0 /	0.08202	0.07151	0.06303	0.05607	0.05028	0.04540	0.04123	0.03768	0.03459
22.5 /	0.01074	0.00930	0.00814	0.00720	0.00642	0.00577	0.00522	0.00473	0.00434
360.0 /	0.01071	0.00933	0.00823	0.00732	0.00656	0.00593	0.00538	0.00492	0.00452

1963
Source Grp 2

24-HOUR AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER)

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 3.19E-09 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.00395	0.00275	0.00206	0.00162	0.00131	0.00110
315.0 /	0.02908	0.02047	0.01542	0.01220	0.00997	0.00836
292.5 /	0.04659	0.03293	0.02433	0.01912	0.01553	0.01295
270.0 /	0.02677	0.01907	0.01454	0.01162	0.00959	0.00812
247.5 /	0.01328	0.00947	0.00721	0.00576	0.00475	0.00400
225.0 /	0.01776	0.01263	0.00961	0.00766	0.00630	0.00531
202.5 /	0.01514	0.01073	0.00813	0.00648	0.00532	0.00447
180.0 /	0.02725	0.01942	0.01478	0.01178	0.00969	0.00816
157.5 /	0.03605	0.02531	0.01902	0.01501	0.01224	0.01023
135.0 /	0.07709	0.05470	0.04130	0.03202	0.02712	0.02282
112.5 /	0.06470	0.04598	0.03495	0.02787	0.02294	0.01935
90.0 /	0.08070	0.05697	0.04302	0.03408	0.02789	0.02340
67.5 /	0.04640	0.03257	0.02448	0.01932	0.01575	0.01317
45.0 /	0.03211	0.02277	0.01725	0.01371	0.01124	0.00945
22.5 /	0.00400	0.00278	0.00207	0.00161	0.00131	0.00109
360.0 /	0.00418	0.00295	0.00223	0.00176	0.00144	0.00121

1963
Source Grp 2

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- ISUST MODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 3.17401 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (IN FEET)									
	200.0	300.0	400.0	500.0	500.0	700.0	800.0	900.0	1000.0	
337.5 /	0.36716	0.19296	0.11923	0.08133	0.05954	0.04551	0.03600	0.02930	0.02482	
315.0 /	1.01118	0.53233	0.33126	0.22826	0.15899	0.13058	0.10441	0.08591	0.07324	
292.5 /	1.62974	0.87970	0.55480	0.38525	0.26737	0.22277	0.17847	0.14721	0.12537	
270.0 /	0.92630	0.49655	0.31139	0.21510	0.15959	0.12318	0.09830	0.08076	0.06860	
247.5 /	0.34798	0.18489	0.11616	0.08071	0.06032	0.04696	0.03782	0.03136	0.02687	
225.0 /	0.41422	0.23048	0.14951	0.10609	0.08113	0.06389	0.05186	0.04339	0.03711	
202.5 /	0.62159	0.34185	0.21757	0.15150	0.11465	0.08914	0.07157	0.05945	0.05027	
180.0 /	0.79389	0.40273	0.24437	0.16508	0.12144	0.09279	0.07349	0.06021	0.05066	
157.5 /	1.52694	0.84501	0.54462	0.38435	0.29335	0.23042	0.18670	0.15611	0.13325	
135.0 /	2.44668	1.36423	0.87946	0.61979	0.45919	0.36708	0.29628	0.24625	0.21044	
112.5 /	3.17401	1.73549	1.10547	0.77254	0.58044	0.45166	0.36290	0.30037	0.25591	
90.0 /	2.71746	1.44648	0.90619	0.62663	0.46427	0.35870	0.28657	0.23348	0.20072	
67.5 /	1.54704	0.83620	0.52977	0.36919	0.27607	0.21441	0.17201	0.14204	0.12126	
45.0 /	0.59072	0.31525	0.19808	0.13723	0.10218	0.07907	0.06325	0.05210	0.04438	
22.5 /	0.28262	0.15460	0.09800	0.06813	0.05062	0.03914	0.03126	0.02567	0.02190	
360.0 /	0.25406	0.13661	0.08560	0.05894	0.04358	0.03350	0.02662	0.02179	0.01844	

1964
Source Gp 2

*** CALIFORNIA CALIFORNIA STUDY CORRELATION -- ISCST MODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTION GRID *

* MAXIMUM VALUE EQUALS 3.17101 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.02116	0.01829	0.01600	0.01413	0.01259	0.01129	0.01020	0.00927	0.00846
315.0 /	0.06296	0.05485	0.04833	0.04299	0.03856	0.03483	0.03166	0.02894	0.02659
292.5 /	0.10772	0.09378	0.08255	0.07335	0.06571	0.05928	0.05382	0.04914	0.04508
270.0 /	0.05876	0.05101	0.04478	0.03969	0.03547	0.03193	0.02892	0.02635	0.02413
247.5 /	0.02323	0.02035	0.01802	0.01611	0.01453	0.01319	0.01205	0.01106	0.01021
225.0 /	0.03207	0.02806	0.02480	0.02212	0.01988	0.01798	0.01637	0.01498	0.01376
202.5 /	0.04310	0.03744	0.03289	0.02915	0.02608	0.02349	0.02129	0.01940	0.01778
180.0 /	0.04316	0.03730	0.03261	0.02801	0.02567	0.02305	0.02083	0.01893	0.01732
157.5 /	0.11507	0.10062	0.08893	0.07930	0.07128	0.06450	0.05873	0.05376	0.04944
135.0 /	0.18142	0.15837	0.13973	0.12441	0.11165	0.10088	0.09171	0.08363	0.07699
112.5 /	0.22006	0.19169	0.16880	0.15004	0.13443	0.12130	0.11013	0.10055	0.09224
90.0 /	0.17238	0.15001	0.13202	0.11727	0.10506	0.09479	0.08606	0.07858	0.07210
67.5 /	0.10432	0.09092	0.08011	0.07124	0.06387	0.05766	0.05238	0.04785	0.04392
45.0 /	0.03810	0.03313	0.02914	0.02586	0.02315	0.02086	0.01892	0.01725	0.01581
22.5 /	0.01880	0.01635	0.01438	0.01276	0.01141	0.01028	0.00932	0.00850	0.00779
360.0 /	0.01575	0.01363	0.01194	0.01056	0.00941	0.00845	0.00764	0.00693	0.00635

1964
Source Grp 2

*** SALINAS - CALIFORNIA STUDY - CIVILIZATION -- TSC1 NODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTION GRID *

* MAXIMUM VALUE EQUALS 0.17401 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	200.0	250.0	300.0	350.0	400.0	450.0
337.5 /	0.00779	0.00538	0.00398	0.00310	0.00249	0.00206
315.0 /	0.02461	0.01745	0.01323	0.01052	0.00864	0.00728
292.5 /	0.04174	0.02947	0.02226	0.01765	0.01445	0.01213
270.0 /	0.02229	0.01560	0.01169	0.00919	0.00747	0.00623
247.5 /	0.00950	0.00689	0.00533	0.00432	0.00351	0.00309
225.0 /	0.01202	0.00914	0.00696	0.00555	0.00457	0.00384
202.5 /	0.01653	0.01168	0.00884	0.00702	0.00578	0.00484
180.0 /	0.01603	0.01119	0.00838	0.00661	0.00538	0.00450
157.5 /	0.04609	0.03302	0.02526	0.02026	0.01674	0.01418
135.0 /	0.07151	0.05080	0.03895	0.03066	0.02516	0.02116
112.5 /	0.08553	0.06044	0.04567	0.03622	0.02965	0.02488
90.0 /	0.06665	0.04698	0.03542	0.02803	0.02292	0.01921
67.5 /	0.04069	0.02878	0.02175	0.01724	0.01412	0.01185
45.0 /	0.01464	0.01029	0.00774	0.00611	0.00498	0.00416
22.5 /	0.00719	0.00503	0.00377	0.00296	0.00241	0.00201
360.0 /	0.00585	0.00405	0.00301	0.00235	0.00190	0.00158

1964 Source Grp 2

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- ISCST MODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 0.97782 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.12213	0.07620	0.05126	0.03668	0.02759	0.02154	0.01731	0.01424	0.01196
315.0 /	0.62297	0.44653	0.32500	0.24618	0.19314	0.15556	0.12795	0.10730	0.09155
292.5 /	0.71901	0.52332	0.38253	0.28988	0.22715	0.18265	0.14998	0.12556	0.10697
270.0 /	0.26379	0.18005	0.13079	0.10003	0.07936	0.06447	0.05335	0.04497	0.03851
247.5 /	0.11144	0.08452	0.06794	0.05432	0.04743	0.04020	0.03431	0.02963	0.02587
225.0 /	0.16495	0.12206	0.09611	0.07855	0.06552	0.05515	0.04681	0.04026	0.03502
202.5 /	0.05803	0.04259	0.03627	0.03200	0.02830	0.02481	0.02168	0.01908	0.01689
180.0 /	0.24105	0.19473	0.16826	0.14732	0.12890	0.11212	0.09740	0.08531	0.07526
157.5 /	0.17051	0.12390	0.10088	0.08545	0.07336	0.06308	0.05439	0.04739	0.04164
135.0 /	0.72198	0.55720	0.43632	0.35106	0.28842	0.24012	0.20227	0.17290	0.14975
112.5 /	0.97782	0.74108	0.55133	0.42213	0.33285	0.26868	0.22119	0.18551	0.15827
90.0 /	0.91134	0.66973	0.49059	0.37216	0.29171	0.23454	0.19256	0.16118	0.13732
67.5 /	0.47036	0.35559	0.27225	0.21529	0.17463	0.14406	0.12052	0.10245	0.08834
45.0 /	0.30362	0.23705	0.17849	0.13729	0.10842	0.08753	0.07204	0.06038	0.05149
22.5 /	0.07478	0.05482	0.04078	0.03151	0.02511	0.02046	0.01695	0.01430	0.01226
360.0 /	0.10490	0.07771	0.05800	0.04482	0.03570	0.02906	0.02409	0.02033	0.01743

1960
SALINA Grouping 3

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION --- ISCST MODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 0.97782 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.01026	0.00891	0.00783	0.00695	0.00622	0.00560	0.00508	0.00463	0.00424
315.0 /	0.07951	0.06984	0.06193	0.05537	0.04985	0.04517	0.04116	0.03770	0.03468
292.5 /	0.09283	0.08146	0.07218	0.06448	0.05802	0.05254	0.04784	0.04379	0.04026
270.0 /	0.03390	0.02945	0.02613	0.02337	0.02105	0.01907	0.01738	0.01591	0.01463
247.5 /	0.02284	0.02034	0.01824	0.01646	0.01495	0.01364	0.01250	0.01151	0.01064
225.0 /	0.03083	0.02739	0.02451	0.02208	0.02001	0.01823	0.01668	0.01534	0.01416
202.5 /	0.01507	0.01353	0.01221	0.01109	0.01012	0.00927	0.00853	0.00788	0.00731
180.0 /	0.06699	0.06004	0.05414	0.04910	0.04475	0.04098	0.03769	0.03480	0.03225
157.5 /	0.03696	0.03305	0.02975	0.02693	0.02452	0.02243	0.02061	0.01902	0.01761
135.0 /	0.17153	0.11660	0.10419	0.09376	0.08490	0.07730	0.07074	0.06503	0.06001
112.5 /	0.13752	0.12081	0.10713	0.09577	0.08622	0.07812	0.07117	0.06517	0.05994
90.0 /	0.11916	0.10459	0.09268	0.08280	0.07452	0.06749	0.06147	0.05628	0.05175
67.5 /	0.07734	0.06838	0.06096	0.05475	0.04948	0.04498	0.04110	0.03773	0.03477
45.0 /	0.04473	0.03929	0.03483	0.03113	0.02802	0.02537	0.02311	0.02115	0.01944
22.5 /	0.01069	0.00942	0.00838	0.00751	0.00677	0.00615	0.00561	0.00514	0.00473
360.0 /	0.01519	0.01339	0.01190	0.01066	0.00962	0.00873	0.00796	0.00730	0.00672

1960
Source Grouping 3

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- 1961 NODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTION GRID *

* MAXIMUM VALUE EQUALS 0.97782 AND OCCURRED AT (200.0, 112.5) *

DIRECTION /
(DEGREES) /

2000.0

RANGE (METERS)

337.5 /	0.00391
315.0 /	0.03205
292.5 /	0.03718
270.0 /	0.01352
247.5 /	0.00988
225.0 /	0.01314
202.5 /	0.00680
180.0 /	0.03002
157.5 /	0.01638
135.0 /	0.05565
112.5 /	0.05538
90.0 /	0.04781
67.5 /	0.03220
45.0 /	0.01796
22.5 /	0.00438
360.0 /	0.00627

1960
Saura Gp 3

1961
CASE 3

SUN-100

*** TEST MODE ***
 DIRECTION (DEGREES) / RANGE (METERS)
 * FROM ALL SITES *
 * FOR THE RECEIVER GRID *
 * MAXIMUM VALUE EQUALS 1.17516 AND OCCURRED AT (200.0, 112.5) *

DIRECTION /	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.08958	0.08409	0.04800	0.03731	0.02983	0.02435	0.02020	0.01705	0.01461
315.0 /	0.50221	0.38705	0.27300	0.21025	0.18702	0.15571	0.11233	0.09457	0.08105
292.5 /	0.60686	0.44543	0.33100	0.25495	0.20256	0.16453	0.13530	0.11490	0.09843
270.0 /	0.27772	0.19791	0.15000	0.11953	0.09783	0.08135	0.08851	0.05855	0.05075
247.5 /	0.10943	0.08212	0.06590	0.05435	0.04603	0.04108	0.03529	0.03055	0.02687
225.0 /	0.10957	0.08240	0.07190	0.05473	0.05000	0.05133	0.04514	0.03995	0.03520
202.5 /	0.05858	0.04058	0.03200	0.02473	0.01947	0.01570	0.01291	0.01052	0.00920
180.0 /	0.21840	0.13040	0.14140	0.12175	0.10550	0.09143	0.07923	0.06930	0.06110
157.5 /	0.19170	0.13059	0.10800	0.09958	0.07540	0.06399	0.05463	0.04722	0.04121
135.0 /	0.87404	0.50109	0.36800	0.31225	0.25743	0.21478	0.18123	0.15517	0.13454
112.5 /	1.17516	0.89708	0.63000	0.49370	0.40227	0.30940	0.25531	0.21482	0.18549
90.0 /	1.13957	0.80000	0.51300	0.37102	0.27509	0.20244	0.24985	0.21023	0.17980
67.5 /	0.58379	0.40000	0.31810	0.24599	0.19717	0.18072	0.13331	0.11252	0.09850
45.0 /	0.31012	0.20000	0.20340	0.18458	0.15574	0.11334	0.09570	0.08195	0.07109
22.5 /	0.06143	0.05000	0.04300	0.03241	0.02528	0.02025	0.01859	0.01580	0.01170
360.0 /	0.07383	0.05000	0.04500	0.03885	0.03327	0.02853	0.02454	0.02134	0.01811

CONCENTRATION -- ISOT NODE ***

JOB ID:
SCREUP#

8-DAY AVERAGE CONCENTRATION (MICROGRAMS CUBIC METER)

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.125 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)									
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0	2000.0
337.5 /	0.01273	0.01121	0.00995	0.00890	0.00802	0.00726	0.00662	0.00606	0.00557	0.00510
315.0 /	0.07061	0.05215	0.03520	0.02441	0.01454	0.00440	0.00364	0.00376	0.00376	0.00310
292.5 /	0.08575	0.07551	0.06709	0.06009	0.05418	0.04916	0.04484	0.04110	0.03784	0.03484
270.0 /	0.04457	0.03951	0.03500	0.03177	0.02877	0.02619	0.02397	0.02204	0.02034	0.01884
247.5 /	0.02381	0.02126	0.01911	0.01728	0.01570	0.01437	0.01319	0.01216	0.01126	0.01046
225.0 /	0.00179	0.02863	0.01590	0.01359	0.01157	0.01980	0.01826	0.01690	0.01566	0.01456
202.5 /	0.00802	0.03704	0.02800	0.02509	0.02200	0.02456	0.02415	0.02380	0.02350	0.02320
180.0 /	0.05437	0.04303	0.03400	0.02700	0.02100	0.01656	0.01332	0.01066	0.00832	0.00626
157.5 /	0.03637	0.03000	0.02400	0.01910	0.01470	0.01163	0.00981	0.00826	0.00686	0.00566
135.0 /	0.11823	0.10400	0.09000	0.07700	0.06542	0.05660	0.05370	0.05123	0.04890	0.04666
112.5 /	0.15953	0.14000	0.12100	0.10400	0.08900	0.07642	0.06960	0.06570	0.06400	0.06200
90.0 /	0.15847	0.13700	0.11700	0.10000	0.08500	0.07091	0.06266	0.05791	0.05464	0.05166
67.5 /	0.08416	0.07410	0.06500	0.05700	0.05000	0.04442	0.04144	0.03963	0.03763	0.03566
45.0 /	0.05252	0.04140	0.03200	0.02400	0.01711	0.01204	0.00842	0.00618	0.00452	0.00306
22.5 /	0.01020	0.00890	0.00790	0.00700	0.00600	0.00590	0.00572	0.00570	0.00510	0.00460
360.0	0.01255	0.01100	0.00950	0.00800	0.00694	0.00599	0.00517	0.00445	0.00381	0.00321

CONCENTRATION MICROTRANSLOGIC METER ***

* DAILY AVERAGE CONCENTRATION (MICROTRANSLOGIC METER) *

* FROM ALL DIRECTIONS *
* FOR THE RECEIVER GRID *

* MAXIMUM VALUE EQUALS 1.17516 AND OCCURRED AT 200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.00514	0.00354	0.00274	0.00215	0.00175	0.00145
315.0 /	0.02873	0.02044	0.01545	0.01225	0.01002	0.00840
292.5 /	0.03500	0.02493	0.01807	0.01498	0.01227	0.01030
270.0 /	0.01885	0.01357	0.01034	0.00827	0.00691	0.00574
247.5 /	0.01047	0.00751	0.00590	0.00470	0.00389	0.00329
225.0 /	0.01453	0.01077	0.00805	0.00677	0.00563	0.00479
202.5 /	0.00323	0.00229	0.00173	0.00132	0.00111	0.00093
180.0 /	0.02445	0.01792	0.01384	0.01115	0.00929	0.00785
157.5 /	0.01552	0.01125	0.00869	0.00685	0.00564	0.00474
135.0 /	0.01014	0.00709	0.00543	0.00448	0.00369	0.00312
112.5 /	0.03455	0.02433	0.01801	0.01443	0.01243	0.01080
90.0 /	0.05550	0.03913	0.02945	0.02304	0.02217	0.01850
67.5 /	0.03453	0.02433	0.01801	0.01443	0.01243	0.01080
45.0 /	0.02552	0.01819	0.01385	0.01171	0.00959	0.00812
22.5 /	0.00402	0.00280	0.00211	0.00165	0.00135	0.00113
350.0 /	0.00775	0.00555	0.00425	0.00332	0.00265	0.00224

SALINAS - CALIFORNIA STUDY (CONTINUATION) - 150ST MODE

365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER)
FROM ALL SOURCES +
FOR THE RECEPTOR ONLY +

MAXIMUM VALUE EQUALS 1.03274 AND OCCURRED AT (200.0, 112.5) +

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.11089	0.07421	0.05096	0.03672	0.02761	0.02148	0.01717	0.01404	0.01173
315.0 /	0.45948	0.33447	0.24632	0.18812	0.14876	0.12036	0.09929	0.08344	0.07129
292.5 /	0.68705	0.49815	0.36423	0.27645	0.21704	0.17486	0.14384	0.12063	0.10294
270.0 /	0.41259	0.29530	0.22089	0.17242	0.13584	0.11412	0.09531	0.08096	0.06979
247.5 /	0.12996	0.08856	0.06496	0.05017	0.04012	0.03280	0.02728	0.02309	0.01984
225.0 /	0.14729	0.11506	0.09356	0.07803	0.06599	0.05613	0.04802	0.04158	0.03637
202.5 /	0.08542	0.06281	0.04822	0.03842	0.03140	0.02607	0.02191	0.01871	0.01619
180.0 /	0.18330	0.14451	0.12255	0.10640	0.09282	0.08071	0.07016	0.06153	0.05435
157.5 /	0.24528	0.18867	0.14560	0.11542	0.09367	0.07730	0.06471	0.05504	0.04749
135.0 /	0.68045	0.51858	0.40791	0.33087	0.27393	0.22945	0.19418	0.16663	0.14476
112.5 /	1.03274	0.76425	0.56007	0.42400	0.33143	0.26975	0.21764	0.18174	0.15450
90.0 /	0.96863	0.71532	0.52764	0.40327	0.31826	0.25731	0.21217	0.17825	0.15232
67.5 /	0.66344	0.50132	0.37376	0.28697	0.22681	0.18337	0.15109	0.12680	0.10822
45.0 /	0.32904	0.25453	0.19571	0.15431	0.12457	0.10270	0.08538	0.07225	0.06214
22.5 /	0.08668	0.06391	0.04666	0.03517	0.02737	0.02186	0.01784	0.01484	0.01258
360.0 /	0.07289	0.05489	0.04054	0.03089	0.02430	0.01940	0.01613	0.01354	0.01156

1962
Sara Grp 3

'N'-DAY
365 DAYS
GROUP# 1

*** SALINAS CALIFORNIA STUDY - CONTINENTION -- 1962 NODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.00274 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.01001	0.00865	0.00756	0.00667	0.00594	0.00532	0.00480	0.00436	0.00397
315.0 /	0.06198	0.05448	0.04833	0.04321	0.03891	0.03526	0.03212	0.02941	0.02705
292.5 /	0.08944	0.07859	0.06971	0.06234	0.05615	0.05089	0.04639	0.04249	0.03910
270.0 /	0.06107	0.05398	0.04813	0.04322	0.03908	0.03553	0.03247	0.02982	0.02750
247.5 /	0.01731	0.01526	0.01358	0.01217	0.01098	0.00997	0.00910	0.00835	0.00769
225.0 /	0.03219	0.02872	0.02581	0.02333	0.02122	0.01939	0.01780	0.01641	0.01518
202.5 /	0.01421	0.01259	0.01125	0.01012	0.00917	0.00834	0.00764	0.00702	0.00648
180.0 /	0.04846	0.04351	0.03930	0.03570	0.03259	0.02989	0.02753	0.02546	0.02363
157.5 /	0.04162	0.03683	0.03286	0.02954	0.02672	0.02431	0.02223	0.02043	0.01885
135.0 /	0.12743	0.11317	0.10130	0.09128	0.08276	0.07543	0.06909	0.06357	0.05872
112.5 /	0.13383	0.11726	0.10375	0.09256	0.08318	0.07523	0.06844	0.06258	0.05748
90.0 /	0.13249	0.11652	0.10343	0.09254	0.08339	0.07562	0.06894	0.06318	0.05814
67.5 /	0.09403	0.08261	0.07324	0.06546	0.05892	0.05336	0.04860	0.04448	0.04089
45.0 /	0.05430	0.04793	0.04267	0.03828	0.03456	0.03138	0.02865	0.02628	0.02420
22.5 /	0.01087	0.00951	0.00840	0.00748	0.00671	0.00606	0.00550	0.00502	0.00460
360.0 /	0.01006	0.00886	0.00787	0.00705	0.00636	0.00577	0.00526	0.00483	0.00445

1962
Source Group 3

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- ISCST MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.0374 AND OCCURRED AT (200.0, 112.5) *

DIRECTION / RANGE (METERS)
(DEGREES) / 2000.0

337.5 /	0.00364
319.0 /	0.02499
292.5 /	0.03614
270.0 /	0.02547
247.5 /	0.00712
229.0 /	0.01412
202.5 /	0.00600
180.0 /	0.02202
157.5 /	0.01747
135.0 /	0.05449
112.5 /	0.05304
90.0 /	0.05376
67.5 /	0.03777
45.0 /	0.02240
22.5 /	0.00424
360.0 /	0.00411

1962
Source Grp 3

*** SALINAS CALIFORNIA STUDY - CONCENTRATION -- ISCST MODEL ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.02485 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.00338	0.00239	0.00180	0.00142	0.00116	0.00097
315.0 /	0.02406	0.01714	0.01298	0.01031	0.00845	0.00709
292.5 /	0.03934	0.02784	0.02096	0.01656	0.01351	0.01130
270.0 /	0.02124	0.01529	0.01168	0.00934	0.00771	0.00652
247.5 /	0.01074	0.00786	0.00606	0.00489	0.00406	0.00345
225.0 /	0.01399	0.01026	0.00793	0.00640	0.00531	0.00451
202.5 /	0.01172	0.00854	0.00656	0.00528	0.00437	0.00370
180.0 /	0.02191	0.01602	0.01236	0.00996	0.00825	0.00700
157.5 /	0.02917	0.02097	0.01597	0.01273	0.01045	0.00879
135.0 /	0.04106	0.04398	0.03356	0.02683	0.02208	0.01861
112.5 /	0.05027	0.03579	0.02710	0.02153	0.01764	0.01481
90.0 /	0.06739	0.04831	0.03676	0.02931	0.02408	0.02028
67.5 /	0.03803	0.02708	0.02049	0.01625	0.01329	0.01114
45.0 /	0.02597	0.01871	0.01428	0.01140	0.00938	0.00791
22.5 /	0.00352	0.00247	0.00185	0.00145	0.00118	0.00098
360.0 /	0.00372	0.00265	0.00200	0.00159	0.00131	0.00110

1963
Source Grp 3

*** SALINAS CALIFORNIA BENTONITE CONCENTRATION -- 1963 MODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.02490 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.08937	0.05623	0.03861	0.02810	0.02175	0.01729	0.01409	0.01174	0.00997
315.0 /	0.44289	0.30853	0.22607	0.17364	0.13809	0.11243	0.09324	0.07874	0.06754
292.5 /	0.75258	0.54221	0.39695	0.30205	0.23769	0.19175	0.15782	0.13238	0.11295
270.0 /	0.36876	0.25172	0.18510	0.14347	0.11524	0.09462	0.07901	0.06713	0.05789
247.5 /	0.12374	0.08911	0.06918	0.05771	0.04855	0.04153	0.03572	0.03109	0.02731
225.0 /	0.11775	0.08429	0.07230	0.06433	0.05725	0.05042	0.04417	0.03896	0.03455
202.5 /	0.11712	0.08361	0.06871	0.05907	0.05135	0.04451	0.03857	0.03373	0.02971
180.0 /	0.18301	0.14421	0.12381	0.10802	0.09431	0.08193	0.07113	0.06228	0.05494
157.5 /	0.37910	0.28110	0.22050	0.17400	0.14837	0.12431	0.10518	0.09022	0.07832
135.0 /	0.82512	0.61255	0.47384	0.38033	0.31282	0.26088	0.22010	0.18845	0.16341
112.5 /	0.92789	0.66656	0.48884	0.37354	0.29524	0.23909	0.19742	0.16608	0.14206
90.0 /	1.02485	0.77383	0.58776	0.46069	0.37089	0.30433	0.25374	0.21512	0.18516
67.5 /	0.58737	0.45089	0.34286	0.26805	0.21506	0.17586	0.14615	0.12354	0.10605
45.0 /	0.37885	0.28577	0.20144	0.16253	0.13371	0.11141	0.09392	0.08032	0.06960
22.5 /	0.07683	0.05564	0.04031	0.03011	0.02323	0.01844	0.01498	0.01242	0.01050
360.0 /	0.07149	0.05271	0.03841	0.02895	0.02258	0.01810	0.01483	0.01240	0.01056

1963
Source Gp 3

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION -- BEST MODE ***

• 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) •

• FROM ALL SOURCES •
• FOR THE RECEPTOR GRID •

• MAXIMUM VALUE EQUALS 1.07485 AND OCCURRED AT (200.0, 90.0) •

DIRECTION / (DEGREES) /	RANGE (METERS)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.00861	0.00753	0.00665	0.00593	0.00532	0.00481	0.00437	0.00399	0.00367
315.0 /	0.05886	0.05184	0.04607	0.04127	0.03722	0.03378	0.03081	0.02825	0.02601
292.5 /	0.09807	0.08611	0.07632	0.06820	0.06138	0.05559	0.05062	0.04633	0.04260
270.0 /	0.05066	0.04479	0.03995	0.03590	0.03247	0.02954	0.02702	0.02483	0.02291
247.5 /	0.02422	0.02165	0.01949	0.01765	0.01607	0.01471	0.01352	0.01248	0.01156
225.0 /	0.03084	0.02771	0.02504	0.02274	0.02076	0.01903	0.01752	0.01619	0.01502
202.5 /	0.02640	0.02363	0.02128	0.01927	0.01755	0.01605	0.01475	0.01361	0.01260
180.0 /	0.04889	0.04381	0.03950	0.03582	0.03265	0.02990	0.02750	0.02539	0.02353
157.5 /	0.06887	0.06109	0.05462	0.04916	0.04452	0.04054	0.03709	0.03409	0.03146
135.0 /	0.14365	0.12744	0.11395	0.10261	0.09296	0.08468	0.07752	0.07129	0.06582
112.5 /	0.12360	0.10873	0.09654	0.08640	0.07788	0.07063	0.06441	0.05904	0.05435
90.0 /	0.16192	0.14304	0.12745	0.11443	0.10342	0.09401	0.08592	0.07889	0.07275
67.5 /	0.09257	0.08164	0.07263	0.06511	0.05875	0.05333	0.04867	0.04463	0.04110
45.0 /	0.06115	0.05424	0.04849	0.04365	0.03954	0.03602	0.03277	0.03032	0.02799
22.5 /	0.00906	0.00791	0.00698	0.00621	0.00557	0.00503	0.00457	0.00417	0.00382
360.0 /	0.00917	0.00806	0.00715	0.00639	0.00576	0.00522	0.00476	0.00437	0.00402

1963
Source Grp 3

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.03613 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)								
	200.0	300.0	400.0	500.0	600.0	700.0	800.0	900.0	1000.0
337.5 /	0.13119	0.09883	0.07284	0.05514	0.04298	0.03435	0.02805	0.02335	0.01980
315.0 /	0.40428	0.29085	0.21138	0.15936	0.12471	0.10016	0.08224	0.06887	0.05874
292.5 /	0.58955	0.43278	0.32181	0.24807	0.19727	0.16044	0.13289	0.11207	0.09605
270.0 /	0.32683	0.23975	0.17842	0.13738	0.10898	0.08841	0.07307	0.06148	0.05259
247.5 /	0.12205	0.08793	0.06493	0.04975	0.03936	0.03189	0.02635	0.02219	0.01901
225.0 /	0.10023	0.07710	0.06321	0.05333	0.04553	0.03900	0.03354	0.02915	0.02558
202.5 /	0.11288	0.08164	0.06906	0.05062	0.05340	0.04665	0.04061	0.03563	0.03145
180.0 /	0.19750	0.13653	0.10315	0.08192	0.06699	0.05560	0.04670	0.03984	0.03443
157.5 /	0.33910	0.25523	0.21075	0.17972	0.15484	0.13341	0.11518	0.10044	0.08833
135.0 /	0.69694	0.54806	0.43526	0.35384	0.29291	0.24526	0.20752	0.17803	0.15464
112.5 /	0.99677	0.75998	0.58096	0.46087	0.37481	0.30989	0.25978	0.22123	0.19105
90.0 /	1.03613	0.78323	0.57806	0.43909	0.34388	0.27620	0.22656	0.18946	0.16130
67.5 /	0.51118	0.37592	0.30225	0.23673	0.19013	0.15567	0.12956	0.10967	0.09428
45.0 /	0.17934	0.13971	0.10754	0.08476	0.06838	0.05615	0.04682	0.03968	0.03414
22.5 /	0.09824	0.07967	0.06065	0.04689	0.03712	0.03003	0.02474	0.02076	0.01772
360.0 /	0.09612	0.07047	0.05172	0.03931	0.03086	0.02484	0.02039	0.01706	0.01452

1964
Source Grp 3

*** SALINAS - CALIFORNIA STUDY - CONCENTRATION - TEST MODE ***

* 366-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
* FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.00613 AND OCCURRED AT 1 200.0. 90.01 *

DIRECTION / (DEGREES) /	RANGE (IN FEET)								
	1100.0	1200.0	1300.0	1400.0	1500.0	1600.0	1700.0	1800.0	1900.0
337.5 /	0.01712	0.01497	0.01322	0.01177	0.01056	0.00954	0.00866	0.00791	0.00725
315.0 /	0.05103	0.04485	0.03980	0.03562	0.03211	0.02913	0.02657	0.02436	0.02244
292.5 /	0.08372	0.07376	0.06557	0.05875	0.05300	0.04810	0.04389	0.04024	0.03706
270.0 /	0.04574	0.04021	0.03568	0.03191	0.02874	0.02604	0.02373	0.02173	0.01998
247.5 /	0.01656	0.01459	0.01297	0.01162	0.01049	0.00953	0.00870	0.00798	0.00735
225.0 /	0.02268	0.02027	0.01823	0.01650	0.01502	0.01374	0.01262	0.01164	0.01078
202.5 /	0.02798	0.02506	0.02257	0.02045	0.01863	0.01704	0.01566	0.01444	0.01337
180.0 /	0.03015	0.02665	0.02376	0.02133	0.01927	0.01751	0.01597	0.01467	0.01352
157.5 /	0.07843	0.07016	0.06317	0.05722	0.05211	0.04768	0.04382	0.04044	0.03745
135.0 /	0.13614	0.12093	0.10825	0.09757	0.08847	0.08066	0.07389	0.06801	0.06283
112.5 /	0.16747	0.14822	0.13227	0.11890	0.10757	0.09787	0.08949	0.08222	0.07585
90.0 /	0.13977	0.12285	0.10886	0.09779	0.08755	0.07931	0.07225	0.06615	0.06089
67.5 /	0.08243	0.07280	0.06486	0.05823	0.05263	0.04784	0.04372	0.04015	0.03702
45.0 /	0.02985	0.02637	0.02349	0.02108	0.01904	0.01730	0.01580	0.01451	0.01337
22.5 /	0.01541	0.01355	0.01203	0.01075	0.00969	0.00878	0.00801	0.00733	0.00674
360.0 /	0.01259	0.01104	0.00977	0.00872	0.00784	0.00709	0.00645	0.00590	0.00542

1964
Source GP3

*** SALINAG - CALIFORNIA STUDY - CONCENTRATION -- 15651 NODE ***

* 365-DAY AVERAGE CONCENTRATION (MICROGRAMS/CUBIC METER) *

* FROM ALL SOURCES *
 * FOR THE RECEPTOR GRID *

* MAXIMUM VALUE EQUALS 1.03611 AND OCCURRED AT (200.0, 90.0) *

DIRECTION / (DEGREES) /	RANGE (METERS)					
	2000.0	2500.0	3000.0	3500.0	4000.0	4500.0
337.5 /	0.00668	0.00468	0.00349	0.00273	0.00221	0.00183
315.0 /	0.02076	0.01481	0.01125	0.00896	0.00736	0.00620
292.5 /	0.03429	0.02443	0.01851	0.01470	0.01205	0.01012
270.0 /	0.01847	0.01309	0.00987	0.00780	0.00636	0.00532
247.5 /	0.00681	0.00487	0.00371	0.00296	0.00243	0.00205
225.0 /	0.01002	0.00730	0.00562	0.00452	0.00374	0.00316
202.5 /	0.01244	0.00906	0.00697	0.00560	0.00464	0.00392
180.0 /	0.01252	0.00895	0.00678	0.00539	0.00442	0.00371
157.5 /	0.03485	0.02543	0.01959	0.01570	0.01307	0.01108
135.0 /	0.05832	0.04213	0.03222	0.02579	0.02125	0.01793
112.5 /	0.07030	0.05045	0.03840	0.03062	0.02517	0.02118
90.0 /	0.05622	0.03985	0.03007	0.02380	0.01945	0.01629
67.5 /	0.03429	0.02457	0.01868	0.01488	0.01222	0.01028
45.0 /	0.01258	0.00885	0.00671	0.00533	0.00437	0.00366
22.5 /	0.00623	0.00442	0.00333	0.00263	0.00214	0.00179
360.0 /	0.00500	0.00351	0.00263	0.00207	0.00168	0.00140

1964
 Source Gp 3

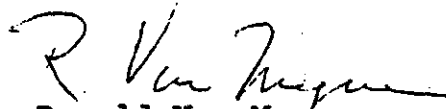
J. Ethylene Oxide Industry Council

The EOIC comments are attached, along with documents referred to in the comments. We would be happy to discuss any of these issues further if you wish.

Very truly yours,



Geraldine V. Cox, Ph.D.
Vice President-Technical
Director
Chemical Manufacturers
Association



Ronald Van Mynen_B
Chairman
Ethylene Oxide Industry
Council

Attachments

Ethylene Oxide Industry Council

2501 M Street, N.W. • Suite 200 • Washington, D.C. 20037 • (202) 887-1100

January 14, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
1102 Q Street
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff:

The Ethylene Oxide Industry Council (EOIC) wishes to express appreciation for the opportunity to comment on the California Air Resources Board Draft Report on Ethylene Oxide.

The EOIC was organized in July 1981, following completion of an industry-funded rat inhalation study on EO conducted at the Bushy Run Research Center. The primary objectives of the EOIC are to develop and to communicate information regarding responsible industry programs to control exposure to EO, to generate scientific and other information regarding EO, and to work with governmental bodies considering regulatory controls pertaining to EO to assure that any such regulations are reasonable, scientifically sound, health protective and economically effective.

The EOIC operates as a special program of the Chemical Manufacturers Association. The members of the EOIC account for over 90 percent of domestic production of EO and cover a broad spectrum of EO users, including companies that convert EO to other products as well as companies that use EO in the manufacture of food, pharmaceutical, cosmetic, medical and health products. Industry trade associations, such as the Health Industry Manufacturers Association, the Pharmaceutical Manufacturers Association, the American Spice Trade Association and INDA Association of Nonwoven Fabrics Industry, also belong to the EOIC. A current list of members is attached.

The EOIC's brief comments will focus on Part B of the draft report, which addresses the health effects of ethylene oxide. We understand that others are addressing the accuracy of the emissions estimates used in Part A.

Ethylene Oxide Industry Council

Membership

Abbott Laboratories
North Chicago, IL

American Spice Trade Assn.
Englewood Cliff, NJ

Andersen Products Inc.
Oyster Bay, NY

Balchem, Inc.
Slate Hill, NY

BASF Corporation
Parsippany, NJ

Becton Dickinson & Co.
Franklin Lakes, NJ

Canadian Res. Mfgs.
Med. Devices
Weston, Ontario, Canada

Celanese Chemical Co.
Dallas, TX

Dow Chemical U.S.A.
Midland, MI

Enron Chemical Company
Omaha, NE

Ethox Corporation
Buffalo, NY

Griffith Micro-Science, Inc.
Willowbrook, IL

Health Industry Mfg. Assn.
Washington, D.C.

ICI Americas, Inc.
Wilmington, DE

Keller & Heckman
Washington, D.C.

McCormick & Co. Inc.
Hunt Valley, MD

Nalco Chemical Company
Naperville, IL.

Olin Chemical Group
Stamford, CT

Pharmaceutical Manufacturers
Washington, D.C.

PPG Industries Inc.
Pittsburgh, PA

Shell Oil Company
Houston, TX

SunOlin Chemical Company
Claymont, DE

3M Industrial Hygiene Service
St. Paul, MN

Texaco Chemical Company
Bellaire, TX

Travenol Laboratories
Deerfield, IL

Union Carbide Corporation
Danbury, CT

U. S. Chemicals Company
Rolling Meadows, IL

Vista Chemical Company
Houston, TX

Warren Chemicals Co., Inc.
Seabrook, MD

Zimmer, Inc.
Warsaw, IN

ETHYLENE OXIDE INDUSTRY COUNCIL COMMENTS
ON THE CALIFORNIA AIR RESOURCES BOARD
PRELIMINARY DRAFT REPORT ON ETHYLENE OXIDE

I INTRODUCTION

In general, the Ethylene Oxide Industry Council ("EOIC") believes that the qualitative discussion of health effects contained in the Preliminary Draft Report on Ethylene Oxide is basically thorough and in many respects sound. The EOIC does have reservations regarding the analyses of certain studies. In the area of quantitative risk assessment, however, the EOIC believes that the Air Resources Board (ARB) should integrate all of the data, including the modeling results, into a comprehensive, scientific assessment of risk. The EOIC also believes that the results from the epidemiologic reports that the ARB report has compared with numerical extrapolations from animal data are not suitable for that purpose.

II EOIC COMMENTS ON THE QUANTITATIVE RISK ASSESSMENT

A. ARB Should Perform a Comprehensive Scientific Risk Assessment for EO

The ARB report's method to quantify the potential carcinogenic risk associated with exposure to EO consists solely of two types of extrapolation -- one from a rat inhalation study and one used as a comparison from the epidemiologic case reports. Both of these extrapolations are

based on limited data and fail to consider all of the available scientific information.

As the ARB report acknowledges, extrapolation from animal studies incorporates several sources of uncertainty. Mathematical models for risk assessment have not been biologically validated and are merely statistical procedures or tools to assist the scientist in assessing risk. Mathematical models use only a limited portion of the available data and do not incorporate relevant information such as biochemical and biological mechanisms, metabolism and pharmacokinetics, and tumor types and relevance to man. Recent developments, including judicial decisions, illustrate the dangers of over-reliance on mathematical extrapolation and the need to perform a complete, scientific evaluation.

Although extrapolations from human data do not present all of the uncertainties associated with animal studies, there are still many difficulties in using epidemiologic studies. Studies must be carefully evaluated before they are used for extrapolation to the general population. In this case, the ARB report uses two studies in an effort to obtain a comparison of the results of human and animal results for leukemia. One study, by Hogstedt, et al, (JAMA (1986) 255:1575-1578) is fraught with uncertainties, and is not credibly appropriate for regulatory decision making. Attached is a copy of a letter submitted on behalf of the EOIC to the editors of the Journal of the American Medical Association regarding the Hogstedt

report. The second study by Morgan, et al (1981), found zero leukemias, yet is used to demonstrate that "statistically" the animal and human results are compatible.

Moreover, with regard to the Hogstedt report, the estimation procedure for plant 1 (4.8 predicted deaths) appears to be in error. Applying the lifetime ambient exposure of .63 ppm and using the model slope of .11 yields a lifetime probability of leukemia of .07, $[P = 1 - e^{(-.11 \times .63)}]$, which when multiplied by the cohort size of 230 yields 15 excess deaths. When this is compared with the expected number of .09, it is much greater than the 2 actual deaths reported by Hogstedt and the 4.8 prediction in the draft report. The model values used in the draft are not consistent with the Hogstedt report.

Further, as ARB itself has acknowledged, the conservative assumptions that are made in performing the modeling, including the use of a linearized multistage model and of upper limits of risk, render the results of only limited use in assessing actual risk. A paper by Dr. E. Anderson, then Director, Office of Health and Environmental Assessment, EPA, presented at Harvard in 1984 included a chart showing that six (6) of the assumptions can affect the results by a factor of as much as 10,000. Indeed, a sensitivity analysis performed by Dr. Robert Sielken, Jr., then of the Department of Statistics, Texas A&M University, demonstrated that variations range up to a factor of 32,000. A copy of Dr. Sielken's paper is attached.

In order to assist the regulators in making their decisions, it is necessary to present the best available scientific characterization of the risk. The report issued by OSTP "Chemical Carcinogens; A review of the Science and its Associated Principles, February 1985" (50 Fed. Reg. 10372, March 14, 1985) states (Principle 27) that the modeling data that are used should be "expressed as an envelope of risk estimates from a variety of plausible models." The "best estimate" of risk and both the "upper" and "lower" bounds should be presented and considered, along with any uncertainties, assumptions and comments on the underlying data.

Further, the precarious nature of the use of the mathematical extrapolations included in the ARB report is highlighted by the fact that the animal data must be extrapolated four (4) orders of magnitude, using a biologically unvalidated model, to reach the estimated and unmeasured ambient air concentration projected for the cancer risk analysis.

The EOIC recognized the need for a valid, scientific assessment of the potential hazards posed by EO and requested Dr. Leon Golberg to supervise the preparation of a comprehensive hazard assessment. The resulting EOIC Hazard Assessment considers and discusses all of the relevant data and presents Dr. Golberg's expert opinion on the hazards presented by EO. Numerical extrapolations are presented, but are used as only one piece of data in the entire evaluation. The EOIC

approach has been supported by peer reviews of the Hazard Assessment. A copy of Dr. Golberg's book is provided for the ARB's use. We are also enclosing copies of letters from Dr. Robert A. Squire, D.V.M., Ph.D. and Dr. J. W. Grisham, M.D. commenting on the Golberg evaluation.



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June 24, 1983

Mr. Robert C. Barnard
Counsel
Ethylene Oxide Industry Council
2501 M Street, Suite 200
Washington, DC 20037

Dear Mr. Barnard:

Pursuant to the request, made in your letter of June 14, I have read and critically evaluated the draft copy of the "Hazard Assessment of Ethylene Oxide" (dated May 31, 1983), which was prepared under the auspices of the Ethylene Oxide Energy Council by a working group led by Dr. Leon Golberg. In evaluating this document I have also examined the Federal Register, Vol. 48, No. 78, of Thursday, April 21, 1983, pages 17284-17319, which pertains to the proposed rulemaking by the Occupational Safety and Health Administration (OSHA) regarding occupational exposure to ethylene oxide. I have also read the OSHA document "Preliminary Quantitative Risk Assessment for Ethylene Oxide" (exhibit 6-18). I am pleased to have the opportunity to comment on the "Hazard Assessment of Ethylene Oxide" by Golberg and associates.

The Golberg report reviews and critically discusses the literature on the chemical properties of ethylene oxide and on the metabolism of this chemical in several animal species. The Golberg report also reviews and critically discusses the experimentally determined acute and chronic toxic effects of ethylene oxide in laboratory animals, the industrial hygienic aspects of ethylene oxide exposures, and reports of epidemiologic studies on workers exposed to ethylene oxide. Based on the reviews of all of the cited reports, the Golberg document concludes by attempting to make a hazards assessment of ethylene oxide for man.

I find the Golberg report to be a scholarly, well documented survey of the available literature pertaining to aspects of the chemical characteristics and biological actions of ethylene oxide. The Golberg report critically discusses these data and interprets them thoughtfully and authoritatively. The hazards assessment included in the Golberg report is a brief, but comprehensive, discussion of the complexity and ambiguity of risk assessment from studies in laboratory animals. It honestly presents and discusses various approaches to risk assessment, including mathematical modeling based narrowly on tumor production in rats, as is done in the OSHA risk assessment document (document 6-18). I fully agree with the conclusion of the Golberg report that precise hazard assessment for man of low levels (less than 10 ppm) of ethylene oxide is largely judgemental. In my opinion, this is a realistic conclusion

that should not be obscured by the apparent, but deceptive, precision of a mathematical extrapolation to man of data from studies in genetically uniform laboratory animals, data that have only limited direct biological relevance to man. Unlike the OSHA hazard assessment, the Golberg hazard assessment attempts to base judgements globally on all published information available, rather than on only a limited number of studies. I fully agree that no data are available that indicate that exposure to 1 ppm ethylene oxide presents any apparent acute or chronic hazard for man.

Mathematical formulations of risk for man from data on tumorigenicity in a species as biologically remote from man as the rat must be interpreted cautiously, in my opinion. In developing risk assessments for man for a chemical, such as ethylene oxide, one must attempt to determine the active dose that comes in contact with the tissues at risk (target tissues), as well as the relative sensitivities of the target tissues in the two species compared to the toxic actions of the active chemical. This means that not only the toxic outcome must be quantitated (in the case of the studies used by OSHA, the toxic outcome was mononuclear cell leukemia and peritoneal mesothelioma), but also the metabolism, transport to the target tissues, and excretion of the chemical and the repair rates of the initial cellular lesions must be quantitated in the two species compared and must be utilized in risk assessment. Unfortunately, we do not know enough about the metabolism and cellular action of ethylene oxide in the rat and man to accomplish that goal. Hence, the results of mathematical modeling from disease outcomes (tumors) in the rat cannot be used to quantitatively assess risk for man with known precision. The studies utilized in the OSHA report do demonstrate the toxicity of ethylene oxide for rats, and they can be interpreted to indicate a qualitative risk for man, but they cannot be used, in my opinion, to precisely quantitate the risk for man.

There is no doubt that ethylene oxide is toxic for man, as for animals of other species. Certainly, workers should be protected from exposure to levels of ethylene oxide that produce toxicity in man. In my opinion, there is no conclusive evidence that exposure to ethylene oxide in concentrations less than 10 ppm causes toxicity in man. However, more data are needed for exposure ranges of 5 to 10 ppm ethylene oxide to be confident in this assessment. The proposed level of 1 ppm or less seems to me to be conservatively safe.

I wish to comment further on the OSHA proposal to screen for chromosomal damage as a medical surveillance procedure for workers exposed to ethylene oxide (Appendix C-Medical Surveillance Guidelines for Ethylene Oxide, Federal Register, Vol. 48, No. 78, Thursday, April 21, 1978, page 17315). In my opinion, this proposal has no merit. The technology for assessing chromosomal damage is far from standardized, and the procedures are laborious and cumbersome. The prevalence of chromosomal aberrations in the general population, not known to be exposed to chemicals, is unknown. Some studies suggest that this background rate may vary considerably and may be episodically increased by certain viral infections, unrelated to chemical exposure. Most chemicals, including ethylene oxide, produce chromatid-type aberrations, whose scoring is subjective and difficult. Furthermore, chromatid aberrations are transitory, and most are lost at the first division of the affected cell following exposure. Of most importance, there are no studies of which I am aware that have evaluated the potential relationship of random, acquired chromosomal aberrations in somatic cells and the subsequent occurrence of any chronic disease, including cancer. Thus, the information from chromosomal analyses on a population of workers exposed to ethylene oxide could not be used to predict future risk of chronic disease, and the technique does not provide a sensitive or necessarily precise dosimeter of chemical exposure. Therefore, I conclude that analysis of chromosomal aberrations is

not now a scientifically valid or cost-effective means to screen populations of workers for extent of exposure to ethylene oxide in the work place or for assessment of risk to future development of chronic disease.

The evaluation of sister chromatid exchange (SCE) is technically less demanding and cheaper to perform than is the analysis of chromosomal aberrations. However, as with chromosomal aberrations, SCE has not been correlated with any disease outcome and, indeed, there is evidence suggesting that SCE may not represent a pathological (toxic) cellular reaction. Reported evidence suggests that SCE evaluation might serve as a sort of biological dosimeter for ethylene oxide exposure, but other analytical methods to quantitate exposure would appear to be more sensitive and reproducible.

I hope these comments are useful. I regret that previous commitments prevent me from participating personally as a witness at the OSHA hearing. Please call me at (919) 966-4678 if you have any questions.

Sincerely,



J. W. Grisham, M.D.
Professor and Chair

ROBERT A. SQUIRE ASSOCIATES, INC.

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TELEPHONE 301-821-0054

June 29, 1983

Robert C. Barnard
Ethylene Oxide Industry Council
Suite 200
2501 M Street, N.W.
Washington, D.C. 20037

Dear Mr. Barnard:

I have reviewed the draft document entitled "Hazard Assessment of Ethylene Oxide" dated May 31, 1983 and find it to be a comprehensive and objective statement on the issues. Time permits me to respond only very briefly and my comments are limited to the issue of extrapolation of animal data to human risk.

I agree with the position taken on page 153 of the document that mathematical models ignore much of the biological information necessary for interspecies extrapolations. They reduce the risk assessment process to merely a consideration of dose-response relationships, on the unwarranted assumptions that man and the test animals will be equally susceptible, and that biological effects will be the same at high and low exposure levels. Most available biological and toxicological evidence contradicts both assumptions. Risk assessment which takes into account the nature and extent of all of the biological evidence, not merely dose-response data in the observable range, is more likely to lead to an accurate hazard assessment.

The nature of the tumors identified to be treatment related in the test animals in the ethylene oxide study is particularly important. Fischer rat mononuclear cell leukemia, and peritoneal mesotheliomas are relatively unique tumors in this species and strain and they have a high background incidence which contrasts with the incidence in humans. The reported spontaneous incidences for leukemia in this strain are approximately 10% in females and 12% in males.(1) For mesotheliomas in males, the incidence is approximately 2.3%. As compared to human tumor incidences at any site, these are extremely high and one must acknowledge an unusual susceptibility to these tumors in the test animals.

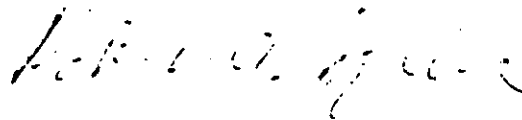
Spontaneous incidences as high as these at any tissue site in test animals indicates a population of "initiated" or latent neoplastic cells which would be highly susceptible to enhancing

(1) Goodman, D.G. et. al. Toxicol. Appl. Pharm. 48:237, 1979.

or promoting stimuli associated with chronic tissue damage and cellular replication. Among the known human and animal carcinogens there is a high (80%+) correlation of sites affected, so the background tumor rates at specific sites are important considerations in interspecies extrapolation. Induction of tumors that have a high natural occurrence in the test animals is less relevant to human risk than is the induction of tumors that are normally rare - unless, of course, there is also a high background incidence in humans at the site in question. In this instance, there is no biological basis to assume that humans would be as susceptible as the test rats at comparable exposure levels, yet this is the assumption which is inherent in the applications of mathematical models. The statement in the report on page 136 "...the relevance to man of the tumorigenic effects observed in F344 rats is uncertain," is, therefore, clearly justified.

In summary, I agree with the theme of the report that it is more appropriate to rely upon the weight of biological evidence rather than the application of mathematical models in hazard assessment when extrapolating the results of the ethylene oxide animal study to humans. The use of mathematical models alone would almost certainly provide a misleading estimate of human risk, in my view.

Sincerely,



Robert A. Squire, D.V.M., Ph.D.

A Sensitivity Analysis
of the Quantitative Risk Assessment
for Ethylene Oxide

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June, 1985

EXECUTIVE SUMMARY

In keeping with the EPA Science Advisory Board's encouragement, this paper explores some of the uncertainty and sensitivity of a quantitative risk assessment for ethylene oxide. The emphasis is on the quantitative impact of several of the choices made in the risk assessment.

The quantitative effects of the choices are considered separately initially and then cumulatively later. The choices are not necessarily in order of importance. While many of the important choices and areas of uncertainty for an ethylene oxide risk assessment are investigated, there are other choices and areas.

Choice 1. The Definition of the Response of Concern

In the Bushy Run Research Center (BRRC) study and the NIOSH study of ethylene oxide inhalation the carcinogenic events which have been most frequently modeled are mononuclear cell leukemia, peritoneal mesothelioma, and brain neoplasia. (The relevance of these experimental events to humans is a very important biological issue; however, this issue is not addressed herein, nor are any value judgements intended.) Dose-response and time-to-response models were fit to the BRRC experimental data for each of the following six definitions of a response:

- 1) brain neoplasia in a male rat,
- 2) peritoneal mesothelioma in a male rat,
- 3) brain neoplasia in a female rat,
- 4) mononuclear cell leukemia in a female rat,
- 5) death of a male rat, and
- 6) death of a female rat.

The last two responses represent the occurrence of a particular health effect as opposed to carcinogenic events which might encompass highly variable health effects. In addition these two responses combine ethylene oxide's effects on all potential causes of death.

In general the estimated risks are smallest when the response of concern is defined to be brain neoplasia in male rats and are greatest when the response of concern is defined to be either mononuclear cell leukemia in a female rat or the death of a female rat. The other three responses (peritoneal mesothelioma in a male rat, death of a male rat, and brain neoplasia in a female rat) have estimated risks relatively far away from the extremes. The ranking of the estimated risks among these latter three responses varies.

All of the numerical results are based on the BRRRC experimental data as opposed to the NIOSH data since the NIOSH data appears to be generally consistent with the BRRRC data and the BRRRC data set contains more direct experimental evidence on the low-dose behavior. The BRRRC experiment included both 10 ppm and 33 ppm whereas the lowest non-zero experimental dose level was 50 ppm in the NIOSH study.

Choice 2. The Risk Characteristic

The risk associated with a particular exposure can be expressed in terms of either (1) the probability of the specified response by a specified time or (2) the expected amount of time (the mean free period) without the response having occurred. The latter reflects when the response might occur during a period instead of just the cumulative probability at the end of the period. Using these two risk expressions, the risk at a particular dose level can be described as either (1) the

increased probability of the specified response by a specified time at the particular dose level relative to that at the zero dose level (actually the control level) or (2) the percentage decrease in the mean free period at the particular dose level relative to the mean free period at the zero dose level.

Table ES.1 contains estimated increases in probability and percentage decreases in the mean free period for BRRC rats exposed to 10.0 ppm, 1.0 ppm, and 0.1 ppm. (These estimates correspond to the fitted Hartley-Sielken model which is a multistage model extended to include each animal's individual observation time.) These estimates indicate that there is at least a ten fold reduction in the estimated risk as the dose level decreases from 10.0 ppm to 1.0 ppm and at least another ten-fold decrease from 1.0 ppm to 0.1 ppm. The magnitude of the differences between the risk characteristics for different definitions of the response of concern is also apparent in Table ES.1. There each risk characteristic varies at least 8-fold and at most 450-fold over the six definitions of the response.

The virtually safe dose (VSD) and mean free dose (MFD) are two different definitions of a maximum acceptable dose. The VSD corresponds to a maximum increase in the probability of the specified response. The MFD corresponds to a maximum decrease in the mean free period. The estimated virtually safe dose for an increase in probability of 0.000001 (one in a million) varies 450-fold over the six definitions of the response and usually is 100-fold smaller than the VSD for an increase in probability of 0.0001 (one in a thousand). The estimated mean free dose for a decrease in the rat's mean free period equivalent to one day in 70 years varies 43-fold over the six definitions of the response and is between 5 and 30-fold smaller than the MFD for a decrease equivalent to one month in 70 years.

Choice 3. The Time in the Risk Characteristic

For late occurring responses, such as those associated with ethylene oxide inhalation, the time or length of time period used in the definition of the risk characteristic has a substantial impact. If the VSD is defined in terms of the increase in probability by the end of 18 months (approximately 3/4 of an average rat lifetime) instead of the increase in probability by the end of 25 months (approximately one average rat lifetime), then the estimated VSD is 2-4 times larger. Similar increases occur for the MFD.

Choice 4. The Mathematical Model

The current dose-response models are simplistic representations of an unknown, highly complex biological phenomenon. The existing biological information is not sufficient to indicate which of the existing models, if any, are appropriate. Nor are the statistical goodness-of-fit tests sufficient to differentiate between existing models. Nevertheless, the mathematical form of the model makes a many-fold difference in the estimated risk. For instance, the estimated VSD for an increase of 0.000001 in the probability of a brain neoplasia in a male rat varies 54-fold over five quantal-response models (probit, logit, Weibull, multihit, and multistage models). For brain neoplasia in a female rat, peritoneal mesothelioma in a male rat, and mononuclear cell leukemia in a female rat the variations are 57-fold, 146-fold, and 48,000-fold respectively.

Choice 5. The Inclusion or Exclusion of the Experimental Data at 100 ppm

The current quantal-response model families (multistage, Weibull, etc.) do not contain curves capable of reflecting both the similarity between the response rates at 0 ppm and 10 ppm and the observed behaviors at 33 ppm and 100 ppm in the BRRC study. The limitations on the shapes in the model families prevent the fitted models from passing close to the observed response proportions at both 33 ppm and 100 ppm and, instead, force the fitted models to try to "compromise" by passing below the response rate at 33 ppm and above the response rate at 100 ppm. Furthermore, such fitted models are very non-responsive to the experimental data at 10 ppm. The "compromising" at high doses and non-responsiveness at low doses can both be considerably lessened by fitting the models to only the data at 0 ppm, 10 ppm, and 33 ppm. This was done in most calculations.

Excluding the 100 ppm data causes the VSDs and MFDs to decrease roughly 2-fold when the response is defined to be mononuclear cell leukemia in a female rat. On-the-other-hand, they increase by roughly 2-fold for brain neoplasia in a female rat and peritoneal mesothelioma in a male rat and increase 8-fold for brain neoplasia in a male rat.

Choice 6. The Fitted Model Value and Bounds

The fitted model value is the estimate most consistent with the presumed family of models.

Upper bounds on a risk can be computed. In fact, there is more than one way to compute an upper bound. The purpose of an upper bound is not to

estimate a risk but to be large enough to exceed the risk. Not all values less than an upper bound are equally likely to be the true risk. The values nearer to the fitted model value are more likely to be the true risk when the true dose-response relationship is in the model family.

The same procedures used to generate upper bounds (upper confidence limits) can also be used to generate lower bounds (lower confidence limits). The difference between the upper and lower bound provides an indication of how precisely the true location of the risk is being identified. The farther apart the upper and lower bounds are, the less likely the true risk is to being near either bound.

Using the multistage model and its usual bounding procedure, the upper bounds on the increase in the probability of a response at 1.0 ppm, for example, are approximately 17, 4, 3.5, and 1.5 times the fitted model values when the response of concern is defined to be brain neoplasia in a male rat, peritoneal mesothelioma in a male rat, brain neoplasia in a female rat, and mononuclear cell leukemia in a female rat respectively. Furthermore, the distance to the lower bounds from the fitted model value is even greater than the distance from the fitted model value to the upper bounds. In fact, all of the corresponding lower bounds are negative which implies that a decrease in the probability of a response is as statistically consistent with the experimental data as the upper bounds are using the particular bounding criterion. Thus, an exceedingly wide variety of dose-response relationships are not sufficiently inconsistent with the experimental data to be recognized as bad fits using the statistical criterion which serves as the basis for the computation of the bounds.

The bounds currently attainable for the other quantal-response models and time-to-response models are not uniformly better. Part of the problem

is the bounding procedures themselves, but a larger part of the problem is the ambiguity in the model family which often prevents the observed dose-response behavior in the range of the non-zero experimental doses from being strongly reflected in the low-dose behavior of the model.

The fitted multistage model's estimates of several risk characteristics were re-evaluated for several variations in the response proportions at 0 ppm and 10 ppm in order to demonstrate the amount of variability in the risk characteristic estimates that was due to the statistical variability (randomness) in the experimental data. The observed variability in the risk estimates was substantially less than that suggested by the difference between the bounds and the fitted model values. In particular, the upper bounds (computed from the original BRRC data) on the increased probabilities of a response tended to be roughly two times farther away from the fitted model values (computed from the original BRRC data) than were the largest estimates observed among the fitted model values corresponding to the variations of the original data. Analogously, the lower bounds (computed from the original BRRC data) on the VSD were approximately twice as far from the fitted model values (computed from the original BRRC data) for the VSD as were the smallest estimated VSDs observed among the fitted model values obtained from the variations of the original data.

Choice 7. The Human Dose Levels Assumed to have the Same Response Frequencies as the Rat Experimental Dose Levels

The relevance of experimental animal results depends on many factors such as the similarities in exposure patterns, pharmacokinetics, carcinogenic mechanisms, immune systems, repair systems, etc. Several

different assumptions could be made about which dose levels for "continuously" exposed humans would be equivalent (in terms of response frequencies) to the experimental dose levels administered to the Fischer 344 rats for 6 hours/day, 5 days/week, for almost an entire lifetime. The quantitative impact of four different assumptions are explored. The four assumptions presume that the frequency of response will be the same for humans as it is for experimental rats if the exposures are equal on the basis of

- i) air concentration (ppm),
- ii) exposure days per week (ppm times the number of exposure days per week divided by seven),
- iii) body weight (mg/kg/day), or
- iv) surface area (mg/kg^{2/3}/day).

Theoretically, if the dose-response relationships were linear, then the estimated risks for a human continuously exposed (all day, every day) at a given ppm level compared to the risks for an experimental rat at the same ppm level would be approximately

- i) equal under the air concentration equivalence assumption,
- ii) 1.4 times greater under the exposure days per week equivalence assumption,
- iii) $3.8 = (1.4)(2.7)$ times greater under the body weight equivalence assumption, and
- iv) $20.8 = (1.4)(2.7)(5.5)$ times greater using male rats or $25.7 = (1.4)(2.7)(6.8)$ times greater using female rats under the surface area equivalence assumption.

The dose-response models were fit to the observed frequencies of response at 0 ppm, 10 ppm, and 33 ppm but with these dose levels converted

to their assumed equivalent human dosages. For each definition of the response of concern four fitted models were obtained (one for each equivalence assumption). The risks estimated under the exposure days per week equivalence assumption were approximately 1.4 times greater than the estimated risks under the air concentration equivalence assumption. The estimated risks for a 1.0 ppm human exposure were 2-4 times greater under the body weight equivalence assumption than they were under the air concentration equivalence assumption -- the differences were greater for human exposure levels larger than 1.0 ppm and less for levels smaller than 1.0 ppm. The estimated risks for a 1.0 ppm human exposure were 15-200 times greater under the surface area equivalence assumption than under the air concentration equivalence assumption and 7-50 times greater under the surface area equivalence assumption than under the body weight equivalence assumption. Using the multistage model, the estimated virtually safe doses corresponding to an increase of 0.000001 in the probability of a response by the end of a lifetime were 1.2, 8.6, 11.4, and 19.5 times smaller under the surface area equivalence assumption than under the air concentration equivalence assumption when the response of concern was brain neoplasia in a male rat, peritoneal mesothelioma in a male rat, brain neoplasia in a female rat, and mononuclear cell leukemia in a female rat respectively. These same estimated VSDs were 6.0, 5.4, 6.7, and 6.7 times greater under the surface area equivalence assumption than under the body weight equivalence assumption.

Although the body weight and surface area equivalence assumptions may, at first glance, appear reasonable, the amount of a carcinogen which reaches its target site is not necessarily a simple function of either body weight or body surface area due to the different pharmacokinetic processes

involved. It is important to note that the equivalent human dose is intended to be equivalent in the sense of causing the same frequency of response as observed in the rats and is not necessarily intended to be equivalent on any other physical or biological scales.

The Cumulative Quantitative Impact of the Choices Made in a Quantitative Risk Assessment

The cumulative impact of several of the choices made in the quantitative risk assessment for ethylene oxide inhalation can be schematically represented in the form of "choice trees" such as those shown in Figures 33-62. (Choice trees are similar to decision trees.) Each choice tree shows how the values of a particular pair of risk characteristics such as a MFD and VSD (one characteristic emphasizing the *time to response and one not*) change progressively with each choice made in the risk assessment. There is one choice tree for each combination of one of six responses and one of five pairs of risk characteristics.

Table ES.2 attempts to summarize much of the paper's discussion of most choices by listing the options explicitly examined for each choice along with the range of their quantitative effects on the estimated risks at 1.0 ppm (the estimated increase in the probability of a response at 1.0 ppm and the estimated decrease in the mean free period at 1.0 ppm) and the estimated VSDs for an increase of 0.000001 in the probability of a response. Table ES.2 does not, however, bring out the importance of using time-to-response data and time-to-response models not only to improve the estimation of probabilities but, more importantly, to allow the risk to be characterized in terms which reflect the time the response might occur.

The Variation in the Unit Risk Values: An Example of the Cumulative Impact of Even a Few of the Choices in a Quantitative Risk Assessment

A single number can not realistically characterize the risk of a chemical exposure. Nevertheless, a "unit risk" and its associated "potency index" are often considered. The unit risk is the increased probability of a specified response at an exposure of one unit relative to that at an exposure of zero units. The unit of exposure is usually ppm or $\mu\text{g}/\text{m}^3$ or $\text{mg}/\text{kg}/\text{day}$. For humans and ethylene oxide vapor inhalation,

$$\text{Unit Risk per } \mu\text{g}/\text{m}^3 = \frac{\text{Unit Risk per ppm}}{1.9 \times 10^3}$$

Unit Risk per $\text{mg}/\text{kg}/\text{day}$

$$= \frac{\text{Unit Risk per } \mu\text{g}/\text{m}^3}{2.86 \times 10^{-4}}$$

$$= \frac{\text{Unit Risk per ppm}}{(1.9 \times 10^3)(2.86 \times 10^{-4})} \approx 1.84 \text{ Unit Risk per ppm ;}$$

so that, a unit risk on one unit scale only differs by a known constant from the unit risk on another unit scale. The "potency index" is taken to be the unit risk on the $\text{mg}/\text{kg}/\text{day}$ scale times the molecular weight of ethylene oxide (44.1).

Table ES.3 indicates the range of unit risk values that are obtained just by varying the following four choices:

1. The Response of Concern:

1.1) Brain Neoplasia in a Male Rat

1.2) Peritoneal Mesothelioma in a Male Rat

- 1.3) Brain Neoplasia in a Female Rat
- 1.4) Mononuclear Cell Leukemia in a Female Rat
2. The Mathematical Model:
 - 2.1) Multistage Model
 - 2.2) Probit Model
3. The Value Representing the Mathematical Model:
 - 3.1) Fitted Model Value
 - 3.2) Upper Bound
4. Assumed Basis for Species Equivalence:
 - 4.1) Air Concentration
 - 4.2) Exposure Days per Week
 - 4.3) Body Weight
 - 4.4) Surface Area.

The unit risk value for each of the corresponding 64 combinations of choices is shown. The ratio of the largest unit risk to the smallest unit risk is approximately 32,000. Thus the unit risk value obtained for ethylene oxide vapor inhalation varies over three orders of magnitude depending on these four choices alone. Even if the mathematical model is limited to the multistage model, the unit risk value varies 1,300-fold over the three remaining choices. Furthermore, these variations do not include the fact that the lower bounds on the unit risk are negative.

Unfortunately, the discussion of unit risks in the EPA Health Assessment Document for Ethylene Oxide only reports the unit risk values associated with the upper bounds on the multistage model. The Health Assessment Document does not report the unit risk values associated with the fitted multistage model values or those associated with the lower

bounds on the multistage model. (Nor does it report unit risk values for other models.) Furthermore, the Health Assessment Document refers to the unit risk values based on the upper bounds as unit risk estimates instead of bounds on the unit risk. This misleading terminology should not be used and a careful distinction should be made between an estimate of a unit risk and a bound on a unit risk. (A similar distinction should also be made with respect to other risk characteristics; for example, the distinction should be made between an estimate of the virtually safe dose (VSD) and a bound on the VSD.)

The variation in the unit risk values (both estimates and bounds) is even greater if other choices are included. However, it may be more important to emphasize that the unit risk as well as the other risk characteristics (such as the virtually safe dose) which do not reflect the time to response information are inadequately characterizing the actual risk of ethylene oxide vapor inhalation.

The numbers emerging from any quantitative risk assessment of ethylene oxide inhalation are not mathematical certainties but rather the results of numerous choices which may be influenced by policy decisions, value judgements, and assumptions. The consequences of several of these choices have been quantified in the overall sensitivity analysis presented herein.

Unfortunately, in light of the particular risk characteristics emphasized in the EPA Health Assessment Document for Ethylene Oxide and the numerical sensitivities existing in the quantitative risk assessment, it is easy to see how the important similarity in the observed experimental behavior of the BRRC rats at 10 ppm and the rats in the two BRRC control groups does not emerge more strongly than it does.

Table ES.1 Estimated risk characteristics for six different definitions of the response of concern

RESPONSE OF CONCERN	ESTIMATED RISKS					
	Decrease in Mean Free Period at Dose Level			Increase in Probability at Dose Level		
	10.0 ppm	1.0 ppm	0.1 ppm	10.0 ppm	1.0 ppm	0.1 ppm
Brain Neoplasia in a Male Rat	0.13%	0.001%	0.0%	0.006	0.00007	0.000001
Brain Neoplasia in a Female Rat	0.15%	0.012%	0.002%	0.008	0.0006	0.00006
Death in a Male Rat	0.33%	0.002%	0.0%	0.012	0.0001	0.000001
Peritoneal Mesothelioma in a Male Rat	0.29%	0.02%	0.002%	0.014	0.0010	0.00010
Mononuclear Cell Leukemia in a Female Rat	1.06%	0.10%	0.01%	0.048	0.0043	0.00043
Death in a Female Rat	1.03%	0.10%	0.01%	0.041	0.0041	0.00041
Ratio: Largest/Smallest	8	100	-	8	61	430

ESTIMATED MAXIMUM ACCEPTABLE DOSES (PPM)

	Mean Free Dose		Virtually Safe Dose	
	Fractional Decrease in Mean Free Period		Increase in Probability	
	<u>1 Month</u> 70 Years	<u>1 Day</u> 70 Years	0.0001	0.000001
Brain Neoplasia in a Male Rat	9.7	1.71	3.93	0.08
Brain Neoplasia in a Female Rat	8.2	0.34	0.18	0.002
Death in a Male Rat	6.0	1.07	0.92	0.09
Peritoneal Mesothelioma in a Male Rat	4.9	0.20	0.10	0.01
Mononuclear Cell Leukemia in a Female Rat	1.2	0.04	0.023	0.0002
Death in a Female Rat	1.2	0.04	0.025	0.0002
Ratio: Largest/Smallest	8	43	171	450

Table ES.2 Several of the choices involved in the quantitative risk assessment for ethylene oxide inhalation as well as some of the available options and the range of their quantitative impact on two of the estimated risk characteristics

CHOICE: Options	QUANTITATIVE IMPACT	
	<u>Largest Estimated Risk</u> <u>Smallest Estimated Risk</u>	<u>Largest Estimated Risk</u> <u>Smallest Estimated Risk</u>
	Risk at 1.0 ppm	VSD for an Increase in Probability of 0.000001
Response of Concern:	71	362
Brain Neoplasia in a Male Rat		
Peritoneal Mesothelioma in a Male Rat		
Death of a Male Rat		
Brain Neoplasia in a Female Rat		
Mononuclear Cell Leukemia in a Female Rat		
Death of a Female Rat		
Risk Characteristic:		
Examples Emphasizing Probability:	Examples Emphasizing the Time of the Response:	
Increased Probability at 10.0 ppm	Decrease in Mean Free Period at 10.0 ppm	
Increased Probability at 1.0 ppm	Decrease in Mean Free Period at 1.0 ppm	
Increased Probability at 0.1 ppm	Decrease in Mean Free Period at 0.1 ppm	
Virtually Safe Dose for an Increased Probability of 0.0001	Mean Free Dose for a Fractional Decrease in the Mean Free Period Equivalent to 1 Month in 70 Years or 1 Day in 70 Years	
Virtually Safe Dose for an Increased Probability of 0.000001		
	Range over Responses of <u>Largest Estimated Risk</u> / <u>Smallest Estimated Risk</u>	
	Risk at 1.0 ppm	VSD for an Increase in Probability of 0.000001
Time Specified in Risk Characteristic:	2.5-4	1.6-4
Full Lifetime		
3/4 Lifetime		
Mathematical Form of Quantal-Response Model:	4.4-16	54-48,000
Probit		
Logit		
Weibull		
Multihit		
Multistage		
Quantal-Response Model versus Time-to-Response Model:	1.0-2.1	1.5-9.6
Multistage vs Hartley-Sielken		
Inclusion or Exclusion of Experimental Data at 100 ppm:	1.1-5.9 (Ranges for Multistage Model)	1.1-8.2
Value Representing the Mathematical Model:	1.4-17*	1.5-25**
Fitted Model Value	Lower Bounds are All Less than Zero	Upper Bounds are All Greater than 10 ppm
Upper and Lower Bounds	*Range is for [Upper Bound] / [Fitted Model Value] for Multistage Model. **Range is for [Fitted Model Value] / [Lower Bound] for Multistage Model.	
Dose Levels at Which Humans and Rats are Assumed to Have Equal Response Frequencies:	21-112 (Ranges for Multistage Model)	6.2-20
Air Concentration		
Exposure Days Per Week		
Body Weight		
Surface Air		

Table 15.3 The Variation in the Unit Risk Values

AN EXAMPLE OF THE CUMULATIVE IMPACT OF EVEN A FEW OF THE CHOICES IN A QUANTITATIVE RISK ASSESSMENT

Response of Concern	Model Characteristics	Assumed Basis for Species Equivalence	Multistage Model			Potency Index	log ₁₀ Potency Index
			ppm	mg/m ³	mg/kg/day		
Brain Neoplasia in Male Rats	Upper Bound	Air Concentration	2.4x10 ⁻³	1.3x10 ⁻⁶	4.4x10 ⁻¹	2x10 ⁻¹	-0.7
		Exposure Days / Week	3.4x10 ⁻³	1.8x10 ⁻⁶	6.3x10 ⁻³	3x10 ⁻¹	-0.6
		Body Weight	8.1x10 ⁻³	4.3x10 ⁻⁶	1.5x10 ⁻²	7x10 ⁻¹	-0.2
		Surface Area	5.6x10 ⁻²	2.9x10 ⁻⁵	1.0x10 ⁻¹	5x10 ⁰	0.7
	Fitted Model Value	Air Concentration	1.4x10 ⁻⁴	7.4x10 ⁻⁷	2.6x10 ⁻⁴	1x10 ⁻²	-1.9
		Exposure Days / Week	2.2x10 ⁻⁴	1.2x10 ⁻⁷	4.0x10 ⁻⁴	2x10 ⁻²	-1.8
		Body Weight	5.2x10 ⁻⁴	2.7x10 ⁻⁷	9.7x10 ⁻⁴	4x10 ⁻²	-1.4
		Surface Area	1.6x10 ⁻²	8.4x10 ⁻⁶	2.9x10 ⁻²	1x10 ⁰	0.1
Peritoneal Mesothelioma in Male Rats	Upper Bound	Air Concentration	3.8x10 ⁻³	2.0x10 ⁻⁶	7.0x10 ⁻³	3x10 ⁻¹	-0.5
		Exposure Days / Week	5.3x10 ⁻³	2.8x10 ⁻⁶	9.8x10 ⁻³	4x10 ⁻¹	-0.4
		Body Weight	1.3x10 ⁻²	6.8x10 ⁻⁶	2.4x10 ⁻²	1x10 ⁰	0.02
		Surface Area	8.2x10 ⁻²	4.3x10 ⁻⁵	1.5x10 ⁻¹	7x10 ⁰	0.8
	Fitted Model Value	Air Concentration	1.0x10 ⁻³	5.3x10 ⁻⁷	1.8x10 ⁻³	8x10 ⁻²	-1.1
		Exposure Days / Week	1.4x10 ⁻³	7.4x10 ⁻⁷	2.6x10 ⁻³	1x10 ⁻¹	-0.9
		Body Weight	2.2x10 ⁻³	1.2x10 ⁻⁶	4.0x10 ⁻³	2x10 ⁻¹	-0.7
		Surface Area	2.6x10 ⁻²	1.4x10 ⁻⁵	4.8x10 ⁻²	2x10 ⁰	0.3
Brain Neoplasia in Female Rats	Upper Bound	Air Concentration	1.8x10 ⁻³	9.5x10 ⁻⁷	3.3x10 ⁻³	1x10 ⁻¹	-0.8
		Exposure Days / Week	2.5x10 ⁻³	1.3x10 ⁻⁶	4.6x10 ⁻³	2x10 ⁻¹	-0.7
		Body Weight	6.0x10 ⁻³	3.2x10 ⁻⁶	1.1x10 ⁻²	5x10 ⁻¹	-0.3
		Surface Area	4.9x10 ⁻²	2.6x10 ⁻⁵	9.0x10 ⁻²	4x10 ⁰	0.6
	Fitted Model Value	Air Concentration	4.0x10 ⁻⁴	2.1x10 ⁻⁷	7.4x10 ⁻⁴	3x10 ⁻²	-1.5
		Exposure Days / Week	6.0x10 ⁻⁴	3.2x10 ⁻⁷	1.1x10 ⁻³	5x10 ⁻²	-1.3
		Body Weight	9.0x10 ⁻⁴	4.7x10 ⁻⁷	1.7x10 ⁻³	7x10 ⁻²	-1.1
		Surface Area	1.5x10 ⁻²	7.9x10 ⁻⁶	2.8x10 ⁻²	1x10 ⁰	0.09
Mononuclear Cell Leukemia in Female Rats	Upper Bound	Air Concentration	1.3x10 ⁻²	6.8x10 ⁻⁶	2.4x10 ⁻²	1x10 ⁰	0.02
		Exposure Days / Week	1.8x10 ⁻²	9.5x10 ⁻⁶	3.3x10 ⁻²	1x10 ⁰	0.2
		Body Weight	4.4x10 ⁻²	2.3x10 ⁻⁵	8.1x10 ⁻²	4x10 ⁰	0.6
		Surface Area	2.8x10 ⁻¹	1.5x10 ⁻⁴	5.2x10 ⁻¹	2x10 ¹	1.4
	Fitted Model Value	Air Concentration	9.0x10 ⁻³	4.7x10 ⁻⁶	1.7x10 ⁻²	7x10 ⁻¹	-0.1
		Exposure Days / Week	1.2x10 ⁻²	6.3x10 ⁻⁶	2.2x10 ⁻²	3x10 ⁰	-0.02
		Body Weight	2.5x10 ⁻²	1.3x10 ⁻⁵	4.6x10 ⁻²	2x10 ⁰	0.3
		Surface Area	1.8x10 ⁻¹	9.4x10 ⁻⁵	3.3x10 ⁻¹	1x10 ¹	1.2
Ratio: Largest Unit Risk / Smallest Unit Risk			1,300	1,300	1,300		

Table B.3 (Continued)

Response of Concern	Model Characteristic	Assumed Basis for Species Equivalence	Probit Model			Potency Index	Log ₁₀ Potency Index
			ppm	ug/m ³	mg/kg/day		
Brain Neoplasia in Male Rats	Upper Bound	Air Concentration	1.6x10 ⁻⁴	8.4x10 ⁻⁶	2.9x10 ⁻⁴	1x10 ⁻²	-1.9
		Exposure Days / Week	4.1x10 ⁻⁴	2.2x10 ⁻⁷	7.5x10 ⁻⁴	3x10 ⁻²	-1.5
		Body Weight	1.2x10 ⁻³	6.3x10 ⁻⁷	2.2x10 ⁻³	1x10 ⁻¹	-1.0
		Surface Area	4.2x10 ⁻²	2.2x10 ⁻⁵	7.7x10 ⁻²	3x10 ⁰	0.5
	Fitted Model Value	Air Concentration	8.6x10 ⁻⁶	4.6x10 ⁻⁹	1.6x10 ⁻⁵	7x10 ⁻⁴	-3.1
		Exposure Days / Week	7.7x10 ⁻⁵	1.4x10 ⁻⁵	5.0x10 ⁻⁵	2x10 ⁻³	-2.7
		Body Weight	9.6x10 ⁻⁵	5.1x10 ⁻⁵	1.8x10 ⁻⁴	6x10 ⁻³	-2.1
		Surface Area	1.5x10 ⁻²	7.9x10 ⁻⁶	2.8x10 ⁻²	1x10 ⁰	0.09
Peritoneal Mesothelioma in Male Rats	Upper Bound	Air Concentration	2.0x10 ⁻³	1.1x10 ⁻⁶	3.7x10 ⁻³	2x10 ⁻¹	-0.8
		Exposure Days / Week	3.8x10 ⁻³	2.0x10 ⁻⁶	7.0x10 ⁻³	3x10 ⁻¹	-0.5
		Body Weight	7.6x10 ⁻³	4.0x10 ⁻⁶	1.4x10 ⁻²	6x10 ⁻¹	-0.2
		Surface Area	7.0x10 ⁻²	3.7x10 ⁻⁵	1.3x10 ⁻¹	6x10 ⁰	0.8
	Fitted Model Value	Air Concentration	1.5x10 ⁻⁴	7.9x10 ⁻⁸	2.8x10 ⁻⁴	1x10 ⁻²	-1.9
		Exposure Days / Week	3.2x10 ⁻⁴	1.7x10 ⁻⁷	5.9x10 ⁻⁴	3x10 ⁻²	-1.6
		Body Weight	7.9x10 ⁻⁴	4.2x10 ⁻⁷	1.5x10 ⁻³	6x10 ⁻²	-1.2
		Surface Area	2.7x10 ⁻²	1.4x10 ⁻⁵	5.0x10 ⁻²	2x10 ⁰	0.3
Brain Neoplasia in Female Rats	Upper Bound	Air Concentration	1.4x10 ⁻³	7.4x10 ⁻⁷	2.6x10 ⁻⁵	1x10 ⁻¹	-0.9
		Exposure Days / Week	2.4x10 ⁻³	1.3x10 ⁻⁶	4.4x10 ⁻³	2x10 ⁻¹	-0.7
		Body Weight	4.4x10 ⁻³	2.3x10 ⁻⁶	8.1x10 ⁻³	4x10 ⁻¹	-0.4
		Surface Area	3.6x10 ⁻²	2.0x10 ⁻⁵	7.0x10 ⁻²	3x10 ⁰	0.5
	Fitted Model Value	Air Concentration	8.5x10 ⁻⁵	4.5x10 ⁻⁹	1.6x10 ⁻⁴	7x10 ⁻³	-2.2
		Exposure Days / Week	1.7x10 ⁻⁴	8.9x10 ⁻⁸	3.1x10 ⁻⁴	1x10 ⁻²	-1.9
		Body Weight	3.6x10 ⁻⁴	2.0x10 ⁻⁷	7.0x10 ⁻⁴	3x10 ⁻²	-1.5
		Surface Area	1.5x10 ⁻²	7.9x10 ⁻⁶	2.8x10 ⁻²	1x10 ⁰	0.09
Munonuclear Cell Leukemia in Female Rats	Upper Bound	Air Concentration	2.6x10 ⁻²	1.4x10 ⁻⁵	4.8x10 ⁻²	2x10 ⁰	0.3
		Exposure Days / Week	3.8x10 ⁻²	2.0x10 ⁻⁵	7.0x10 ⁻²	3x10 ⁰	0.5
		Body Weight	5.6x10 ⁻²	3.1x10 ⁻⁵	1.1x10 ⁻¹	5x10 ⁰	0.7
		Surface Area	2.4x10 ⁻¹	1.3x10 ⁻⁴	4.4x10 ⁻¹	2x10 ¹	1.3
	Fitted Model Value	Air Concentration	4.1x10 ⁻³	2.2x10 ⁻⁶	7.5x10 ⁻³	3x10 ⁻¹	-0.5
		Exposure Days / Week	7.0x10 ⁻³	3.7x10 ⁻⁶	1.3x10 ⁻²	6x10 ⁻¹	-0.2
		Body Weight	1.3x10 ⁻²	6.8x10 ⁻⁶	2.4x10 ⁻²	1x10 ⁰	0.02
		Surface Area	1.6x10 ⁻¹	8.4x10 ⁻⁵	2.9x10 ⁻¹	1x10 ¹	1.1
Ratio:	Largest Unit Risk / Smallest Unit Risk		27,000	27,000	27,000		
Ratio:	Largest Unit Risk Using Both Models / Smallest Unit Risk Using Both Models		32,000	32,000	32,000		

USAN G. AUSTIN, SC.D.

700 BREAKWATER DRIVE
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July 1, 1986

Editor
Journal of the American Medical Association
535 North Dearborn Street
Chicago, Illinois 60610

Dear Sir:

The Ethylene Oxide Industry Council recently engaged the service of myself and two of my colleagues in reviewing an article which appeared in the March 28, 1986 issue of your Journal. They subsequently asked if we would be willing to submit it as a Letter to the Editor of JAMA, which we now do.

The attached critique of the article by Hogstedt, "Epidemiologic Support for Ethylene Oxide as a Cancer-Causing Agent" which appeared in the March 28, 1986 issue of JAMA by myself, Dr. Leon Golberg and Dr. Robert Morgan, is being submitted in its entirety. We hope that its length will not hinder its publication; if a shorter critique is required, we are prepared to accommodate the Journal. However, we do feel that the length of this letter is justified due to the fact that Professor Hogstedt reviews and updates two previously published studies and has also included a third new study.

Sincerely,



Susan G. Austin, Sc.D.
Environmental Epidemiologist
Austin Health Consultants, Inc.

The article "Epidemiologic Support for Ethylene Oxide as a Cancer-Causing Agent" by Hogstedt et al, (1) which appeared in the March 28, 1986 issue of JAMA draws renewed attention to the potential carcinogenicity of Ethylene Oxide (EtO). In this article, the authors review and update the experience of workers at three Swedish plants where EtO was used or produced, and conclude that available evidence from these occupational groups provides support for an increased risk of malignancy (leukemia and stomach cancer) in individuals with extended and intermittent exposure to low concentrations of EtO. However, careful reading of this article and the authors' previous two reports, (2,3) raises serious questions regarding the interpretation that the authors have placed on this body of data.

The first major concern regards the appropriateness of combining the cases of leukemia identified at Plant 1 with the results of the cohort studies conducted at Plants 2 and 3. Plant 1 was not studied epidemiologically, as the authors themselves acknowledge by their statement: "Our initial report of cases in 1979 was not an epidemiologic study; . . .". Since Plant 1 was not a valid epidemiologic study, it is inappropriate to statistically combine it with the results of the other two plants.

Second, the completeness of the cohort studied at Plant 2 (3) must be questioned as this group of workers consisted of those who had been included (perhaps voluntarily) in a 1960 hematologic screening study (4). To the extent that this cohort may be incomplete, bias may have been introduced. The appropriateness of combining maintenance workers with EtO operators in reporting five total leukemia cases at Plants 2 and 3 in Tables 5 and 6 must also be questioned. One of the four cases at Plant 2 occurred in the maintenance group and the single case at Plant 3 occurred in the maintenance group. Maintenance workers commonly have had exposures to a wide variety of potentially hazardous materials (including benzene-containing solvents); thus additional cancer cases in this group do nothing to strengthen the evidence that EtO is the responsible agent. The allegation of a causal association between leukemia and EtO exposure is based on three cases at a single location (Plant 2).

Third, there is no evidence of a dose-response relationship in the Swedish data for EtO exposure and leukemia or stomach cancer. With respect to stomach cancer specifically, three of the six cases at Plant 2 occurred in years 1 - 4, resulting in a lower ratio of observed to expected for longer periods of employment. Since length of employment is traditionally employed as a surrogate for dose, the Hogstedt data indicate a reverse dose-response relationship, a finding inconsistent with a postulated causal association. (It is curious that the authors consider the six stomach cancers in Plant 2 to be "highly significant", but do not mention any incidence or mortality from this cause in the other plants.)

A fourth concern regards the manner in which the author has evaluated other published EtO cohort studies. Despite the limitations of the independent studies conducted by Thiess (5) and Morgan (6) of EtO exposed production workers, these represent the only existing independent investigations by other authors and their results do not provide support for any association between EtO and leukemia or stomach cancer.

In view of the above described differences in methodology, one can argue that the three leukemia cases from Plant 1 offer little in the way of valid epidemiologic evidence and that the small excess of leukemia found among the potentially biased group of 89 EtO operators at Plant 2 (based on three cases) is somewhat offset by the lack of any leukemia cases among 128 operators at Plant 3. (We appreciate that the power of these studies was insufficient for the detection of moderately elevated risks.) Therefore, this report does not appear to offer any new evidence to strengthen the hypothesis of an association between occupational exposure to EtO and leukemia or stomach cancer risk.

Because of the many questions regarding the Swedish studies, it would be most helpful if the authors could provide some additional information regarding these investigations. For example, what proportion of all eligible EtO operators were included in the original hematologic study and subsequent cohort mortality study conducted at Plant 2, and could bias have been introduced in the selection process (particularly if this was a volunteer study)? What is the total number of expected leukemia and stomach cancer cases at Plant 2 when no latent-induction period is required in the analysis? What is the number of observed and expected stomach cancer cases at Plant 3?

It is unfortunate that the title of this article and the conclusions within are so poorly substantiated from the data, most of which have been previously published.

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January 13, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff,

Would you please substitute the enclosed letter dated January 12, 1987 (corrected version) for the one dated January 12, 1987 which was transmitted to you earlier this week.

The original submission had several typographical errors including an important one on the first page.

My apologies for this inconvenience.

Sincerely,



Malcolm G. Ridgway, Ph.D., CCE
Vice President
HRI Engineering Services

MGR/jhc



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January 12, 1987 (corrected version)

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
P. O. Box 2815
Sacramento, CA 95812

Dear Mr. Loscutoff,

Health Resources Institute (HRI) is a wholly-owned subsidiary of the Hospital Council of Southern California, which is a not-for profit hospital association with 232 member hospitals in six southern California counties. This subsidiary which until very recently did business under the name Council Shared Services (CSS) provides a number of services to the Council's member hospitals on a fee for service basis. One of the services that we have provided for a number of years is ethylene oxide safety surveys and it is an area where we have become well acquainted with the recent concern about the chemical's potential adverse health effects. We started doing ethylene oxide safety surveys in 1978 and have, to date, completed more than 600 site surveys at well over 200 sites in about 160 hospitals.

We have followed the progress of the work described in the draft report, which was distributed for comment on December 4, 1986, with considerable interest and would like to offer the following comments and observations for consideration by both the Board and the Scientific Review Panel.

1. We had been concerned about the accuracy of the method used to estimate the amount of ethylene oxide discharged from the hospitals surveyed in the inventory area because we believed that very few hospitals would really know how many pounds of gas their sterilizers use per load. However it appears that the staff has done a good job of cross checking for consistency with cylinder usage, and the emission data presented in Table C-1 (page C-7) is reasonably consistent with one or two spot checks that we made. For example, we know that Kaiser Hospital-Sunset averages about two 8.8 cu. ft. loads per day. This average workload would utilize about 0.55 lbs of ethylene oxide per day.

2. Although, as the report states, hospitals tend to be the major source of ethylene oxide emissions for most urban areas, the report's estimate of the resulting ambient levels shows that the amount to which the general public may be exposed is extremely small. The estimated ambient exposure level from hospital-released ethylene oxide (8 parts per trillion) is about 125,000 times lower than the 1 part per million concentration which is the occupational exposure level currently permitted by both State and federal regulations. The contribution of hospital-released ethylene oxide to the public's overall exposure from ethylene oxide is estimated to be 32 times lower than the amount normally ingested from food and 443 times lower than the amount inhaled from smoking one pack of cigarettes per day.

3. The estimated risk of additional cancer deaths attributable to hospital-released ethylene oxide is correspondingly small. Using the report's relatively conservative modelling technique the added risk is about 5 ten-thousandths of 1%. Suppressing or eliminating these emissions will therefore have only a very small effect on the health of the citizens.

4. On the other hand there is another factor, which is also difficult to quantitate, which could have an adverse effect on the public health. That factor is the growing concern on the part of hospitals and other health care providers about the risk of litigation alleging negligence on their part if they continue to use ethylene oxide sterilizers. Even though they may not be found negligent in such cases, the diversion of resources required by such suits is being taken very seriously. More and more hospitals are asking about alternatives to gas sterilization. The adverse impact of such a trend is that many of the alternative techniques using less potent disinfectants are much less effective in reducing microbiological burdens. At a time when we are facing continued problems with hospital infections and increasing complications from at least one major infectious disease (AIDS) we need to encourage not discourage use of the most effective sterilization techniques. The legislation defines a Toxic Air Contaminant as an air pollutant...."which may cause or contribute to an increase in mortality or an increase in serious illness, or which may pose a present or potential hazard to human health". We need to be mindful that the end result of this process is intended to be an overall net benefit to the public health.

5. Although it has apparently not yet become a part of the study process, it is our understanding that effective and reliable technology which will make meaningful reductions in the amount of ethylene oxide released from the sizes of sterilizer usually found in hospitals is not yet available, and not likely to become available in the near future. The methods that have been developed for the larger industrial-size sterilizers are awkward, expensive and not very effective. Even so we do encounter hospital architects already recommending to hospitals that they start making provisions for roof top-mounted emissions control devices of one kind or another. We are concerned that such recommendations will become another "nail in the coffin" of hospital-based ethylene oxide sterilizers.

In summary, we believe that the draft report represents a thorough and necessarily conservative analysis of the potential adverse effect of ambient ethylene oxide on the public health. The perspective provided by the findings should be a very valuable guideline to an appropriate response. We do not believe that the severity of the hazard, as it is documented in the report, can reasonably be used to justify placing additional onerous obligations on current healthcare users of ethylene oxide sterilizers. Indeed we would urge the Board and the Scientific Review Panel to go one step further than this; we would like to request that the Board and/or the Panel issue a finding, at this point in the process, that the estimated risk is so small that healthcare providers using sterilizers with chambers of less than, say, 100 cu. ft. will be exempted from any obligation to install an emissions control device until such time as the total cost of installing such a device can be reduced to a reasonable cost, say, 40% of the current replacement value of the sterilizer.

We believe that this positive reassurance would go a long way towards stopping speculation that this process will eventually culminate in requiring expensive control devices and thus eliminate one of the factors which is causing hospitals to turn away from ethylene oxide sterilization.

Thank you for this opportunity to offer these comments on the draft report.

Sincerely,

Malcolm G. Ridgway.

Malcolm G. Ridgway, Ph.D., CCE
Vice President
HRI Engineering Services

MGR/jhc

L. Kaiser Permanente
(Kaiser Foundation Hospitals)



KAISER PERMANENTE
Kaiser Foundation
Hospitals

January 13, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
P.O. Box 2815
Sacramento, California 95812

Dear Mr. Loscutoff:

Re: Preliminary Draft Report
on Ethylene Oxide

I have reviewed the report on ethylene oxide emissions and commend the care with which these emissions were characterized for hospital operations. I would like to add a caution, however, in the use of the aggregate number. Hospitals are, as a result of this study, being approached with the suggestion that equipment can be purchased to control these emissions. Unfortunately, although the aggregate may look like something to be controlled, equipment of the type being suggested cannot be effective for the individual hospital releasing undetectable levels of ethylene oxide to the atmosphere.

On a second topic, I would like to suggest the Air Resources Board consider an exemption level for small quantity generators. This state has promulgated many environmental laws and regulations that are open-ended resulting in internal chaos due to the unmanageable nature of the regulations. For example, MSDS's are being sought and training being given regarding the hazards of typewriter correction fluid. Since the risk factor is so small, (.0005% in this case) it seems prudent to evaluate such an exemption.

Thank you for your attention to these items. I would appreciate being kept informed on further activity on this matter.

Sincerely,

W. Thomas Schipper, CCE, FASHE
Regional Director
Plant, Technology, and Safety Management

WTS/dh

**II. Air Resources Board Responses to
Part A - Related Comments**

Comment: Chemrox, Inc. agrees that the use of water-sealed once-through vacuum pumps on sterilizers results in fugitive ethylene oxide emissions. However, it should be noted that a number of companies in California have already installed closed-loop systems and many others are in the process of doing so. Such a closed-loop system would completely eliminate ethylene oxide discharges to the sewer system and associated fugitive emissions of ethylene oxide.

Response: Statements have been inserted into the report to the effect that some companies recently installed closed-loop vacuum pump systems which can eliminate ethylene oxide discharges to wastewater, with this Chemrox, Inc. letter cited as the reference for this information.

Comment: Chemrox, Inc. states that their experimental data indicates that the hydration of ethylene oxide to ethylene glycol is a first-order process with respect to ethylene oxide in the presence of excess water, and that the rate constant is strongly dependent upon pH.

Response: The Chemrox experimental data is consistent with the information provided in the report. The hydration of ethylene oxide to ethylene glycol reported on Figure II-3 of Part A of the report provides a rate constant that is second-order. However, the rate shows a first-order dependence on the ethylene oxide concentration if the hydrogen ion concentration is fixed. Page II-16 of Part A of the report includes a tabulation of half-lives calculated for ethylene oxide at pH values ranging from 2 to 11, and these times vary greatly relative to pH (which is the negative logarithm of the hydrogen ion concentration). Because the statements in this comment are consistent with the information provided in the report, no change was made in the report.

AIR RESOURCES BOARD STAFF RESPONSES TO PUBLIC COMMENTS
ON THE DRAFT PART A REPORT ON ETHYLENE OXIDE

Comment: Sterile Design, Inc. states that their Sacramento facility closed in December, 1985.

Response: As 1985 was the latest inventory year for which emissions information could be collected for this report, Sterile Design was included. ARB staff has footnoted Table III-1 (Emission Estimates) to indicate the closure.

Comment: Sterilization Services of California states that the SCAQMD permits them to emit 40 lb/day of ethylene oxide which would be, at most, 7.3 tons/year, not 18 tons/year as reported in the preliminary draft report.

Response: ARB staff has revised the emission estimate in Table III-1 from 18 tons/year to 7.3 tons/year.

Comment: Botanicals International reports changes in their process which, since June 2, 1986, have reduced the emissions of ethylene oxide from their facility by 60%. He states this will have a significant impact on ethylene oxide concentrations in the Exposure Area from all sources in the Inventory Area.

Response: Table III-1 has been footnoted to reflect the information given regarding reduced emissions in the future. However, because Botanicals

International's facility in Long Beach is not within the inventory area used for the modeling study (see page I-3, Figure I-1, Map of Ethylene Oxide Modeling Area), no impact on the ethylene oxide concentrations in the exposure area would result.

Comment: Griffith Micro-Science (formerly Micro-Biotrol, Inc.) notes the company's intent to install an emission control system and similar action or intent on the part of other companies.

Response: Because the stated emissions are for 1985, no change was made in the report. Actual reductions in emissions since 1985 by other companies have been footnoted in Table III-1.

Comment: Liquid Carbonic Corp. states the estimate of less than 1/2% to 2% fugitive losses is in error. The company also notes APB staff's estimate that approximately 18% of the sterilant gas mixture is exhausted from cylinders at repackaging plants, and believes the figure to be more in the area of 10% or less.

Response: The fugitive loss estimate was developed by the Engineering Division of the South Coast Air Quality Management District. This estimate was based on inventory balancing by industry sources contacted. Ethylene oxide quantities were measured before and after processes such as transport, storage, transfer, blending and drumming.

As stated on pages F-2 and F-3 of the report, the figure 18% for sterilant gas mixture returned as residual is based on actual measurements of sterilant gas obtained from a recovery/recycle system by Union Carbide. ARB staff telephoned Liquid Carbonic on January 16, 1987 for any documentation regarding estimates of fugitive loss percentages or sterilant gas returned, but the company was unable to provide this. Shortly before this Final Draft Report was completed, ARB staff was informed that documentation was now available. This new data will be analyzed by ARB staff, and any changes that may be appropriate will be made before submission of the Final Report.

Comment: Liquid Carbonic Corp. states that the time period used as input to the ISCST model for Liquid Carbonic Corp. (emissions between 6:30 A.M. and 3:00 P.M. daily) is in error and cites a letter dated June 9, 1986 stating that the scrubbing equipment at the Los Angeles facility was used a maximum of four (4) hours per day.

Response: The letter from Liquid Carbonic Corp. dated June 9, 1986 was not received in time to be used as input for the modeling study. ARB staff had telephoned the lab manager at Liquid Carbonic on April 18, 1986, who indicated facility operating hours were 6:30 A.M. to 3:00 P.M. Although emissions can only occur for four hours, emissions can occur at any time during this period. Therefore, the emissions were averaged for the whole period.

Because the modeling output was annual concentrations and exposures, little change would be anticipated from re-running the model assuming that the same

emissions occurred over a period of four (unspecified) hours per day rather than between 6:00 A.M. and 3:00 P.M. daily. Therefore staff made no change.

Comments: Liquid Carbonic Corp. comments that the ARB staff statement that "the two Liquid Carbonic plants bubble the residual ethylene oxide gas through water at neutral or near neutral pH" is incorrect and cites the letter dated June 18, 1986, which states that the Los Angeles scrubber solution uses 5% sulfuric acid by weight.

Response: When ARB staff first contacted the lab manager at Union Carbide's Torrance plant on April 4, 1986, he reported the plant was using a scrubber that bubbled the gas through a basic solution. He said the solution was composed of one liter of a 1M solution of sodium hydroxide in 50 gallons of water, and was monitored for glycol buildup. After receiving the letter dated June 18, 1986, staff called on July 10 to reconcile the discrepancies between the content of the letter and the information previously provided. In that conversation, the lab manager stated that they had changed the scrubber solution from slightly basic to 5% acid, in May 1986.

The modeling output is stated as 1985 concentrations and exposures. Therefore, it was appropriate for ARB staff to use 1985 emissions data. However, Table III-1 (Emission Estimates) has been footnoted to indicate the changes made in 1986.

Comment: Union Carbide's Linde Division in Torrance states that the 18% return factor is true for cylinders of sterilant gas composed of 12% ethylene oxide/88% inert gas but not for all ethylene oxide sold.

Response: Staff understood this to be the case, and that is how the return factor was used in the calculations demonstrated on page F-4. The statement attributed to Mr. Bolen of Union Carbide on page F-3 has been corrected to more accurately express staff's understanding and use of the return factor.

Comment: Union Carbide states that Oxyfume 12 sold in bulk trailer quantities, and pure ethylene oxide sold, both result in much smaller residual amounts.

Response: This is consistent with the statement on page F-1 that residual amounts are generally small for cylinders of pure ethylene oxide. For this reason, ARB staff's calculations of emissions were based only on ethylene oxide sterilant gas mixture sold in cylinders.

Comment: Union Carbide states "the 18% return figure is inflated by the fact that often times full unused cylinders are returned for credit when they pass their expiration date."

Response: Full, unused cylinders are processed through a recovery or disposal system along with used cylinders. Any ethylene oxide which escaped the control equipment would be emitted. Therefore, no change was made to the report.

Comment: Union Carbide states that reference was made to their scrubber with an efficiency rate of 90% which was retired in 1986, and indicates that the new scrubber has a design efficiency of 99.999%.

Response: The emission inventory on distributors was for inventory year 1985 at which time the 90% efficient scrubber would have been in operation. APP staff has footnoted the report of Table III-1 to indicate the 1986 introduction of a more efficient scrubber. Staff noted on Page F-2 that the Union Carbide plant in Torrance had applied to the SCAQMD for permission to build a new scrubber. Staff is not aware of any source tests which would establish the efficiency of Union Carbide Torrance's new scrubber under actual operating conditions. If ethylene oxide is identified as a toxic air contaminant, then new information would be reviewed in the development of a subsequent report ("regulatory needs report").

Comment: Union Carbide Torrance states that no mention was made of the recovery/recycling system at Torrance, and estimates that emissions from the Torrance facility are less than 100#/yr, with both the recovery unit and scrubber in operation.

Response: As a result of this comment bringing the recovery/recycling system at Torrance to staff's attention, emissions for the Torrance facility were recalculated. 1985 process emissions were obtained from a company submission* to EPA in compliance with the Clean Air Act. Fugitive emissions for 1985 were also recalculated.

* "Requested Information for Bulk Distributors, Repackagers, and Blenders of Ethylene Oxide" submitted to EPA in its Clean Air Act, Section 114 Information Request, by Union Carbide Corporation, Linde Division, Package Gas Operations.

The new emission estimate totals 740 lb/yr (0.37 tons/year). If ethylene oxide is identified as a toxic air contaminant, ARB may subsequently investigate the level of emissions from sources subject to its jurisdiction, as part of the risk management process. At that time, emissions estimates will be further refined, and the efficiency of control equipment will be verified.

Comment: Health Industry Manufacturers Association (HIMA) recommends that CARB coordinate with EPA and local California Air Quality Management Districts in the analysis of emissions data for California facilities. CARB was also asked to review HIMA's position paper submitted to EPA, which emphasizes the reduction in number of ethylene oxide emission sources, and the use (and projected increased use) of ethylene oxide emission control devices.

Response: ARB staff has been in contact with EPA, and obtained on January 31, 1987, a comparison of EPA's and CARB's ethylene oxide data bases. The emissions estimates in the Final Draft Report have been revised to reflect this information as well as information obtained recently from the South Coast Air Quality Management District.

ARB staff notes that emission reductions have occurred at various California facilities, and that others have closed down. However, since the release of the November, 1986 report, staff has also identified other companies that emit ethylene oxide. Overall, staff has revised downward the estimate of

statewide emissions by about seven percent. Some closures and emission reductions through improved controls have been noted.

Comment: ARC Chemical Division, Balchem Corporation suggest that APB staff's original data on emissions offered in the Draft Report may be in error, both for reasons of assumptions made to arrive at them, and because facilities in the State of California will shortly introduce further emission controls to reduce present emission levels.

Response: In the Final Draft Report, ARB staff clarified that emission estimates are for 1985, and has included footnotes to indicate all more recent changes of which staff is aware.

Comment: Based upon ARC's blending experiences outside California, and "conversations with several California blenders," APC "question the fugitive emissions value of 1/2 - 2% as stated by Zwiacher (1983), and suggest that the value (for blenders, at least) must be somewhat lower." APC further states that conversations with one unspecified California blending facility lead them to state that differences in return rates and scrubbing efficiency "should alter your calculation of emissions by a factor of 3-6 times."

Response: ARB staff has had discussions with the two of the three known distributors of ethylene oxide with blending facilities in California, and responses to their written comments are in this Part C of the Final Draft Report. In particular, ARB staff suggested to one distributor the nature of

additional documentation that would be appropriate to support their assertion of lower emissions, and that information was provided to ARB just as this report was being finalized. ARB staff will analyze this new information to determine if further changes should be made to this report.

Comments: ARC attached articles on the health benefits of ethylene oxide sterilization and on ethylene oxide emission control devices.

Response: ARC's attachments on health risk benefits of ethylene oxide sterilization and ethylene oxide emission control devices are interesting, but are more appropriate submissions during a possible subsequent risk management phase, rather than during the present risk assessment phase.

Comment: Environ Corporation states that annual emissions from McCormick's Schilling plant are 6.1 tons/year, not 20 tons/year as ARB presents in the Draft Report. He derives this from McCormick's "measured average total emissions of ethylene oxide from all stacks and vents of 0.349 g/second."

It is also stated that "exposure concentrations represent maximum rather average concentrations," and that cancer risk is related to lifetime average dose, not maximum concentration that represents only occasional excursions.

Response: ARB staff agrees that exposure concentrations should represent average concentrations. The Draft Report provides maximum annual concentrations, not maximum excursions. Furthermore, public exposures were obtained from the use of annual average isopleths in conjunction with census tract data.

Response: Because none of the reports provided by Environ Corp provides a discussion on how the emissions were determined, ARB contacted Environ by telephone regarding the derivation of the above stated emission rate. Apparently, for a sterilizer chamber charged with 56 pounds of ethylene oxide, McCormick accounted for 11.48 pounds of emissions via the primary exhaust vent, auxiliary air vent, and secondary air vent. McCormick also determined that 24.79 pounds was accounted for in water, leaving 19.73 pounds in the spice products, drums, pallets, and unaccounted for.

ARB staff agrees that if the 11.48 pounds of direct air emissions were the only emissions to air, then the Schilling plant would emit 6.1 tons/year. However, in the absence of documentation showing that the 19.73 pounds is not subsequently emitted to the atmosphere, ARB staff believes it should be included in total emissions. Also, ARB staff reports cited in the report provide a somewhat lower figure for ethylene oxide in water. Furthermore, much of the ethylene oxide initially accounted for in the water could be re-emitted to the atmosphere near the facility. Therefore, ARB staff has not changed the 20 ton/year emission estimate.

III. Department of Health Services Responses to
Part B - Related Comments

Department of Health Services
Staff Responses to Public Comments

(November 1986 Draft)

Three sets of public comments were submitted in response to part B of the Draft Report to the Air Resources Board on Ethylene Oxide, November, 1986 (hereafter referred to as part B), one each by ARC Chemical Division - Balchem Corporation, Ethylene Oxide Industry Council (EOIC), and Environ Corporation, a consulting firm.

1.) Comments from ARC, dated 1/8/87.

a.) Comment. A copy of an unpublished epidemiologic study of a group of male and female sterilizer workers from Johnson and Johnson was submitted. An increase in breast cancer incidence in women workers exposed to ethylene oxide was demonstrated. Only one case of leukemia, which also occurred in a woman but was not a statistically significant excess, was observed.

Response. As stated by the authors of the Johnson and Johnson study, the report is preliminary and has not been peer-reviewed. The paper is interesting, however, since the association between breast cancer and ethylene oxide exposure was not an a priori hypothesis. Case ascertainment is still incomplete, thus the one case of leukemia (vs. 0.28 expected) may or may not represent a chance finding. DHS staff also notes that the analyses presented in this paper had no required minimum length of employment for inclusion in the cohort, and, in fact, the manuscript

contained no information on exposure. The preliminary results of this investigation neither confirm nor refute previous studies.

b.) Comment. In the Snellings et al. (1984) animal carcinogenesis report, only female rats exposed to 100 ppm ethylene oxide had a significant increase in mononuclear cell leukemia relative to the controls.

Response. Experimental results summarized in Table 9-25 (EPA 1985) and in Table 4.2 (part B) indicate that the increase at 33 ppm is also significant. Furthermore, the more relevant analysis in which only the animals that survived to the time of first tumor (Table 7.1, part B) are considered, shows that the incidence at 10 ppm is significantly different from the controls (p = .0425 by the Fisher exact test).

c.) Comment. The NIOSH study of carcinogenesis (Lynch et al. 1984) in rats at 50 and 100 ppm does not show a NOEL (No Observed Effect Level). The data of Snellings et al. indicate the existence of a NOEL between 0 and 10 ppm.

Response. As noted above, an effect is demonstrable even at 10 ppm. More importantly, DHS considers carcinogenesis to be a nonthreshold process unless there is compelling evidence to the contrary (CDHS 1985).

d.) Comment. DHS and EPA use an overly cautious interspecies extrapolation by neglecting to consider rats' higher breathing rates relative to humans resulting in increased uptake of ethylene oxide at a given exposure concentration.

Response. Tyler and McKelvey (1983) studied uptake of labelled ethylene oxide to determine the doses actually delivered to the rats. The latter numbers were used to calculate equivalent human dose.

e.) Comment. The animal carcinogenesis experiments were conducted at ethylene oxide concentrations 20 to 200 times the OSHA "action level" of 0.5 ppm. The lowest dose of 10 ppm in the Snellings study is 20,000 times higher than the estimated ambient level of 50 ppt.

Response. These observations are true. However, ethylene oxide reacts directly with DNA. Because of the nonthreshold nature of carcinogenesis, even very low exposures carry some risk, albeit small. Even a negative study of several hundred rats of a single strain would not exclude mutagenic/carcinogenic effects in a large, heterogeneous human population. In fact there are several positive animal carcinogenesis studies. The DHS risk assessment indicates that OSHA's "action level" of 0.5 ppm may not adequately protect workers against ethylene oxide's carcinogenic effects.

f.) Comment. The studies by Hogstedt et al. (1986) do not provide "convincing evidence that low exposures to ethylene oxide" are associated with an increased risk of leukemia. Divine and Amanollahi (1986) have rebutted the association between ethylene oxide and leukemia reported by Hogstedt et al. (1986).

Response. DHS staff notes that Divine and Amanollahi pointed out the absence of cases of leukemia in exposure groups A and B at plant 3. The expected number of cases in these groups is so small that even a risk ratio of 6 (as was observed overall at plant 3) is not inconsistent with the zero leukemia deaths observed. That is, the statistical power was extremely low

in the subcohort to which Divine and Amanollahi refer. In reply to the letter of Divine and Amanollahi, Hogstedt (1986) notes that "cases could only have been expected if ethylene oxide had outstanding carcinogenic properties at very low levels".

g.) Comment. Where no other carcinogens were found, no leukemias were observed.

Response. This comment refers to groups A and B at plant 3, where not only were the numbers small, but the exposures to ethylene oxide were also very low.

h.) Comment. The plants studied by Hogstedt et al. involved different processes and working conditions and therefore should not be combined in the analysis.

Response. DHS staff notes that the excesses of leukemia were observed even without combining the studies. The fact that an excess of leukemia was observed in workers exposed to ethylene oxide under different conditions strengthens, rather than weakens, the argument for causality. If conditions were identical, it would be more plausible that an alternative exposure could be responsible for the increase, i.e., that the association between ethylene oxide and leukemia was spurious due to a common confounder in the three plants. Even so, the confounding exposure would have to be a strong carcinogen, carrying a risk ratio of around six at the levels to which workers in all three plants were exposed. While the existence of such an unidentified carcinogenic exposure cannot be ruled out, this explanation is not likely because of the variety of different chemicals in different

plants. ARC also invokes the data of Morgan et al. (1981), showing no excess leukemias among ethylene oxide-exposed workers. As discussed in Part B of the document, the exposures of these workers were much lower than those in the studies of Hogstedt et al. The production areas were, in fact, out-of-doors.

i.) Comment. The report of Hemminki et al. (1982) on the association between ethylene oxide exposure and spontaneous abortion was found by OSHA to be qualitative, not quantitative. Additional data are needed.

Response. We agree that additional data on this important endpoint are needed; however, this is no reason to exclude discussion of the original report.

j.) Comment. The federal Occupational Safety and Health Administration (OSHA) stated that there was "no direct (epidemiological) evidence of an excess risk of cancer at chronic exposure levels below approximately 14 ppm." Subsequently, OSHA presumed "that a threshold value for exposure does not exist." This was improper because OSHA has the burden of proof regarding the nonexistence of a threshold (citing Industrial Union Department, AFL-CIO v. American Petroleum Institute et al., 448 U.S. 607, 653-54, 1980 ["benzene case"]). Thus, OSHA's earlier statement is still valid.

Response: The weight of the evidence regarding ethylene oxide's direct action on genetic material and its carcinogenicity supports the notion that its genotoxic and carcinogenic effects occur with no identifiable threshold (summarized in Chapters 4 and 5 of part B). OSHA's initial statement on

this issue, while of interest, is irrelevant, because no epidemiologic studies involving ethylene oxide exposure contain enough subjects to demonstrate the existence of a threshold. Judgement about the nonthreshold nature of ethylene oxide's carcinogenicity is based on laboratory evidence, not epidemiology. Furthermore, OSHA's initial statement was contained in a brief supporting its denial of a petition to issue an emergency standard regulating occupational exposure to ethylene oxide. In this case the court held that OSHA's refusal to issue an emergency standard was arbitrary and capricious and constituted an abuse of discretion (Public Citizen Health Research Group et al. v. Aucter et al., 554 F. Supp. 242 (D.D.C. 1983)). While the court did not rule specifically on the threshold issue, OSHA's subsequent issuance of an emergency standard of 1 ppm clearly vitiates its earlier assertion about the lack of evidence of a human carcinogenic effect at exposure levels below 14 ppm. ARC's claim about OSHA's burden of proof with regard to the issue of a carcinogenic threshold is not only irrelevant but misleading. If ARC's claim were indeed valid, the revised occupational exposure standard would have been successfully challenged by now. Justice Stevens' dictum in the benzene case refers to OSHA's failure to document the magnitude of the health risk of benzene exposure and has nothing to do with disproving the existence of a threshold.

k.) Comment. "Ethylene oxide has been used as a sterilant for over 40 years now, often at exposures exceeding 50 ppm." OSHA's risk assessment would predict an increase in cancer among these workers.

Response. DHS staff is unaware of any large cohorts of sterilizing personnel whose exposures to ethylene oxide have been well-quantified, and

for which cancer mortality has been assessed in a methodologically sound analysis which accounts for latency and confounding. We would be pleased to consider any such studies.

2.) Comments from EOIC, dated 1/14/87.

a.) Comment. The DHS staff's extrapolation consists solely of two types - one from a rat inhalation study and one from human "case reports".

Response. The EOIC appears to have misunderstood the methods used for the quantitative risk assessment by DHS staff. No extrapolation was made from human data. Extrapolation was from animal data only. The calculations involving the epidemiologic data were to determine if the extrapolation models provided predictions consistent with the available human data. The conclusion was that the predicted risks based on the animal data were consistent with the data from occupational epidemiologic studies, both negative (Morgan et al. 1981) and positive (Hogstedt et al. 1986).

b.) Comment. The DHS staff has not conducted a "complete, scientific evaluation". Not all the available scientific information was considered, particularly "biochemical and biological mechanisms, metabolism and pharmacokinetics, and tumor types of relevance to man."

Response. DHS staff disagrees with this interpretation. (1) We have incorporated the data of Tyler and McKelvey (1983) on target site doses. (2) The consideration of metabolic and pharmacokinetic activity is not relevant since ethylene oxide reacts directly with DNA, requiring no

metabolic activation. (3) The tumor types observed in animals correspond to those observed in man. For these reasons DHS staff concludes that we must use the available data, validate our assessment based on all relevant available information, and provide our best plausible estimate using current scientific methods.

c.) Comment. Mathematical models for risk assessment are "statistical procedures or tools to assist the scientist in assessing risk."

Response. DHS staff agrees. This is exactly the purpose for which they have been used.

d.) Comment. "There are still many difficulties in using epidemiologic studies."

Response. DHS staff agrees. However, when observational studies use sound data collection procedures and apply correct statistical methods of analysis, the results can be illuminating. The Hogstedt studies provide the best available epidemiologic data. Newer studies will probably show smaller risks since occupational exposures have been reduced by government regulation.

e.) Comment. The 0.63 ppm ethylene oxide exposure in plant 1 of Hogstedt et al. (1986) should have been applied to all the workers at the plant.

Response. The lifetime ambient exposure of 0.63 ppm was applied to the 69 employees who were exposed all day. This yielded the 4.8 excess deaths predicted. Applying this high dose to workers who only passed through the area and thus received a much lower exposure is not appropriate. For all

three plants under study, using a lower, more appropriate, overall estimated exposure, DHS staff predicted a total leukemia mortality of 9.01 which agreed well with the observed number of 8.

f.) Comment. The various uncertainties associated with the process of risk assessment may cause the risk to be overestimated by several orders of magnitude.

Response. DHS acknowledges that health-conservative (protective) assumptions are used in the risk assessment. While it is true that data are extrapolated over 4 orders of magnitude, there is no ethical or practical way to directly obtain data on risks for doses closer to the predicted ambient level. In addition, DHS staff found that the risk estimates derived from the animal studies were consistent with the results of the occupational epidemiologic studies, which tends to diminish the concern that the risks have been vastly overestimated. ("... while absolute and undisputed scientific evidence may not be available to determine the exact nature and extent of risk from toxic air contaminants, it is necessary to take action to protect public health." H&SC 39650(e).)

3.) Comments from Environ Corporation dated 1/13/87

a.) Comment. The interpretation of the trend test for peritoneal mesotheliomas was an overinterpretation of a statistical test. The test only shows that the slope is significantly different from zero.

Response. The wording on p.28 in part B of the draft document only states that an increased incidence of mesotheliomas correlates with ethylene oxide exposure.

b.) Comment. The epidemiologic evidence is exaggerated in importance with regard to establishing the causation for EtO carcinogenesis in humans.

Response. As implied above, there is seldom a "smoking gun" in epidemiology, a high exposure to a single chemical leading to high relative risk. However, the Hogstedt studies strongly suggest an association of leukemia with ethylene oxide exposure. The original excess observed in first report of Hogstedt et al. (1979) was confirmed in further follow-up in two plants and in a separate study in a third plant. While DHS staff concurs with Environ that the epidemiologic studies are "limited in establishing causation", DHS considers animal carcinogens to be potential human carcinogens. The finding of leukemias, i.e., cancer in the same tissue, in both rats and humans, strengthens the evidence from either species alone.

c.) Comment. "The epidemiologic data are inadequate to derive an estimate of cancer risk from exposure to ethylene oxide."

Response. DHS staff agrees and did not use these data to derive an estimate of risk. This is discussed in our response to comments by EOIC.

d.) Comment. The unit cancer risk determined by DHS is eight-fold higher than that determined by Environ for McCormick.

Response. DHS followed the California Guidelines for Chemical Carcinogen Risk Assessments and Their Scientific Rationale (1985). DHS staff used the most sensitive sex, site and species, an interspecies conversion based on surface area, an upper confidence limit to determine the recommended unit risk values, and tumor incidences from all four exposure levels (0, 10, 33, and 100 ppm) of the Snellings et al. (1984) data. The values for mononuclear cell leukemia in female rats were the same as EPA's Carcinogen Assessment Group's numbers. On the other hand, Environ did not use the data from the 100 ppm dose group, used maximum likelihood estimates and used body weight as the interspecies conversion factor. Thus, some of Environ's assumptions and procedures were different from those used by DHS staff. However, Environ's methodology is not demonstrably more scientifically valid. Furthermore, the McCormick document is a nonpublic document; we do not know if it has been subjected to independent review.

e.) Comment. The Gaylor-Kodell model was not applied appropriately.

Response. DHS staff acknowledges that the value was calculated using a 95% UCL on the actual incidence data at the lowest dose and thus was not calculated properly. We also note that several p-values in Table 7.2 should be lower than originally reported. The best fit was for the probit model, which was slightly better than the logit model. The risk calculated using the Gaylor-Kodell approach as suggested by Environ with all the data and the probit model was 1.9×10^{-5} (for an ambient level of 50 ppt). It should be noted that the Gaylor-Kodell model was used by DHS staff only for comparison with the results obtained with the multistage model.

REFERENCES FOR DHS RESPONSE TO PUBLIC COMMENTS

CDHS (1985) Guidelines for Chemical Carcinogen Risk Assessments and their Scientific Rationale. State of California, Health and Welfare Agency.

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Hemminki K, Mutanen P, Saloniemä I, Niemi ML, Vainio H (1982) Spontaneous abortions in hospital staff engaged in sterilizing with chemical agents. Br Med J 285:1461-1463.

Hogstedt C (1986) Reply to letter of Divine and Amanollahi. JAMA 256:1727.

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Hogstedt C, Malmvist N, Wadman B (1979) Leukemia in workers exposed to ethylene oxide. JAMA 241:1132-1133.

Lynch DW, Lewis TR, Moorman WJ, Burg JR, Groth DH, Khan A, Ackerman LJ, Cockrell BY (1984) Carcinogenic and toxicologic effects of inhaled ethylene oxide and propylene oxide in F344 rats. Toxicol Appl Pharmacol 76:69-84.

Morgan RW, Claxton KW, Divine BJ, Kaplan SD, Harris VB (1981) Mortality among ethylene oxide workers. J Occup Med 23:767-770.

OSHA (1984) Occupational exposure to ethylene oxide (29 CFR Part 1910). Fed Reg 49:25734-25809.

Snellings WM, Weil CS, Maronpot RR (1984) A two-year inhalation study of the carcinogenic potential of ethylene oxide in Fischer 344 rats. Toxicol Appl Pharmacol 75:105-117.

Tyler TR, McKelvey JA (1983) Dose-dependent disposition of ¹⁴C labeled ethylene oxide in rats. Carnegie-Mellon Institute of Research, Pittsburgh, PA.

**IV. Air Resources Board
Letters to Commenters**

IR RESOURCES BOARD

STREET
BOX 2815
CRAEMENTO, CA 95812



April 10, 1987

Ronald Van Mynen
Chairman
Ethylene Oxide Industry Council
2501 M Street, N.W., Suite 200
Washington, D.C. 20037

Dear Mr. Van Mynen:

Thank you for your comments on Part B of the Draft Report on Ethylene Oxide. Your comments have been forwarded to the California Department of Health Services. I understand their staff has prepared responses which will be incorporated into Part C of the Final Draft Report, which should be released to the public within a month.

Sincerely,

A handwritten signature in cursive script that reads "William V. Loscutoff".

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

AIR RESOURCES BOARD

1102 Q STREET

BOX 2815

SACRAMENTO, CA 95812



April 20, 1987

Dr. Malcolm G. Ridgway, Vice President
HRI Engineering Services
Center of Health Resources
6666 Valjean Avenue
Van Nuys, CA 91406

Dear Dr. Ridgway:

Comment on Preliminary Draft on Ethylene Oxide

Thank you for your comments on the ethylene oxide report. My staff appreciates your statement that it did "a good job in developing emission data from hospitals."

I note your comments that the amount of ethylene oxide to which the public may be exposed, and the risk of additional cancer deaths attributable to hospital-released ethylene oxide, are both "extremely small." The report includes numerical estimates for exposure and risk. ARB staff does not believe it is appropriate to characterize these with adjectives. Such a judgement is appropriate for our Board.

Your comments regarding overall public health benefits of alternatives to sterilization with ethylene oxide, costs of control, and possible exemptions have been noted. However, ethylene oxide is being considered now only for possible identification as a toxic air contaminant. Your comments will be appropriately considered during a possible subsequent risk management phase.

Thank you for your interest. Please contact Gary Murchison at (916) 322-8521, if you have additional questions.

Sincerely,

A handwritten signature in cursive script that reads "William V. Loscutoff".

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

AIR RESOURCES BOARD

1102 Q STREET

BOX 2813

SACRAMENTO, CA 95812



April 27, 1987

Mr. W. Thomas Schipper, Regional Director
Plant, Technology and Safety Management
Kaiser Permanente, Walnut Center
Pasadena, CA 91188

Dear Mr. Schipper:

Comment on Preliminary Draft Report on Ethylene Oxide

Thank you for your comments on the ethylene oxide report. We appreciate the commendation regarding hospital emission characterization.

Your comments regarding control equipment and possible exemptions from control requirements are noted. However, this report only recommends the identification of ethylene oxide as a toxic air contaminant. If ethylene oxide is so identified by our Board, your comments would be appropriately considered during a subsequent risk management phase.

Thank you for your interest. Please contact Gary Murchison at (916) 322-8521, if you have questions regarding our response.

Sincerely,

A handwritten signature in cursive script that reads "William V. Loscutoff".

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

AIR RESOURCES BOARD

1102 Q STREET

BOX 2815

SACRAMENTO, CA 95812



April 27, 1987

Mr. Paul Lewandowski
Assistant Product Mgr.
ARC Chemical Division
Balchem Corporation
Box 180
Slate Hill, NY 10973

Dear Mr. Lewandowski:

Thank you for your January 8 letter with comments on our Draft Report on Ethylene Oxide (November, 1986). Your comments regarding the health effects data were forwarded to the California Department of Health Services, which has prepared responses that will be in the Final Draft Report on Ethylene Oxide. All of your comments appropriate for this part of the process have been considered. I have summarized our action below. Your comments on control or restrictions for the health industry will be considered if ethylene oxide is identified as a toxic air contaminant and we start the risk management part of the process.

Regarding your comments on our assumptions for emissions from ethylene oxide blenders, my staff has had discussions with two distributors of ethylene oxide with blending facilities in California, and has prepared responses to their written comments for the Final Draft Report. Also, my staff will analyze newly obtained information to determine if further changes should be made to the report.

In your letter, you stated that, our original data on emissions may be misleading because facilities will shortly introduce further emission controls to reduce present emission levels. We agree that emissions are changing, therefore, our Final Draft Report clarifies that emission estimates are for 1985. We have included footnotes to indicate all more recent changes in emissions of which my staff is aware.

Mr. Paul Lewandowski

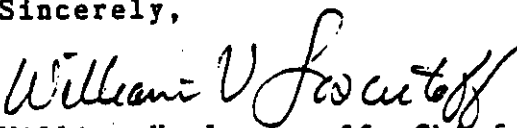
-2-

April 27, 1987

Your Attachment 1 concerning ethylene oxide control, and Attachments 5 and 6 concerning benefits of ethylene oxide use, will be considered during a possible subsequent risk management phase. Your attachments 2, 3 and 4, concerning health effects of ethylene oxide, were forwarded to the California Department of Health Services for review.

Thank you for the valuable information. Please contact Gary Murchison at (916) 322-8521, if you have questions regarding our response.

Sincerely,



William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

AIR RESOURCES BOARD

1102 O STREET
P.O. BOX 2815
SACRAMENTO, CA 95812



April 27, 1987

Dr. Robert G. Tardiff, Principal
Environ Corporation
The Flour Mill, 1000 Potomac St., NW
Washington, DC 20007

Dear Dr. Tardiff:

Thank you for your comments on the Draft Report on Ethylene Oxide (November 1986). Your submissions on assessment of possible health risks associated with exposure to ethylene oxide released to the atmosphere from the Salinas plant of McCormick and Company, Inc. have been forwarded to the California Department of Health Services (DHS). The DHS has prepared responses to your health risk comments that will soon be made available to the public in the Final Draft Report on Ethylene Oxide.

We also appreciate your submitting copies of the three 1986 reports by Environ which evaluated McCormick emissions of ethylene oxide and population exposure. ARB staff was earlier provided copies of these reports, and considered them in the Draft Report.

Because none of these reports provides a discussion of how the emissions were determined, my staff contacted your staff by telephone regarding the derivation of the 0.3498 g/second average total emission rate which you provided in your letter. Apparently, for a sterilizer chamber charged with 56 pounds of ethylene oxide, McCormick accounted for 11.48 pounds of emissions via the primary exhaust vent, auxiliary air vent, and secondary air vent. McCormick also determined that 24.79 pounds was accounted for in water; leaving 19.73 pounds in the spice products, drums, pallets, and unaccounted for.

ARB staff agrees that if the 11.48 pounds of direct air emissions were the only emissions to air, then the Schilling plant would emit 6.1 tons/year. ARB had assumed, however, that the 19.73 pounds was subsequent emitted to the atmosphere. Because the reactivity of ethylene oxide is quite low, and no

April 27, 1987

other fates of ethylene oxide are known, ARB staff considers it likely that virtually all of the ethylene oxide accounted for in spice products, drums, and pallets will off-gas at the facility. Therefore, in the absence of documentation showing that the 19.73 pounds is not subsequently emitted to the atmosphere, ARB staff believes it should be included in total emissions. Also, ARB staff reports cited in the Draft Report provide a somewhat lower figure of ethylene oxide in water. Furthermore, much of this ethylene oxide could be re-emitted to the atmosphere near the facility. Therefore, ARB staff has not changed the 20 tons/year emission estimate.

With respect to your comment on page 3, 3.a., "...the exposure concentrations represent maximum rather [than] average concentrations." the Draft Report on Ethylene Oxide always provides annual average concentrations. Maximum annual concentrations were provided, but only annual average isopleths in conjunction with census tract data were used to estimate public exposure. We agree with your subsequent statement, "the correct expression of inhaled concentration is the daily average and not the maximum concentration."

Thank you for your comments.

Sincerely,

William V. Loscutoff
William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

AIR RESOURCES BOARD

1102 Q STREET
P.O. BOX 2815
SACRAMENTO, CA 95812



April 27, 1987

Mr. James F. Jorkasky
Director, Environmental, Occupational
and Small Business Programs
Health Industry Manufacturers Assoc.
1030 Fifteenth Street, NW
Washington, DC 20005-1598

Dear Mr. Jorkasky:

Comments on Preliminary Report on Ethylene Oxide

Thank you for your comments on the ethylene oxide report. We agree with your recommendation that the California Air Resources Board (CARB) review EPA's database and conclusions on ethylene oxide (ETO) use and emissions control. My staff has been in contact with Mr. David Markwordt in EPA's Office of Air Quality Planning and Standards. On Jan. 31, 1987, he sent me a comparison of EPA's and CARB's ethylene oxide databases. My staff has had follow-up discussions with his contractor for this work, Midwest Research Institute. The emissions estimates in the Final Draft Report on Ethylene Oxide have been revised to reflect this information, which became available since the November 1986 release of the Preliminary Draft Report.

My staff has also revised these estimates based upon recent information obtained from the South Coast Air Quality Management District (SCAQMD).

We have also revised our emission estimates based on the fact that emission reductions have occurred at various California facilities, and note that others have closed down. However, we have also identified companies that emit ethylene oxide. Overall we have revised downward our estimate of statewide emissions from almost 400 tons/year to about 370 tons/year, or about a seven percent decrease.

Mr. James F. Jorkasky

-2-

April 20, 1987

We trust that you will find that the data in our Final Draft Report reflects the most current data available on emission sources. Please contact Gary Murchison at (916) 322-8521, if you have additional questions.

Sincerely,

A handwritten signature in cursive script that reads "William V. Loscutoff". The signature is written in dark ink and is positioned above the typed name.

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division

PART C ADDENDUM
PUBLIC COMMENTS AND RESPONSES TO THE
FINAL DRAFT ETHYLENE OXIDE REPORT

Prepared by the Staff of the Air Resources Board

June 1987

(Part C Addendum reflects the comments received from the public during the April 28, 1987 to May 29, 1987 public review period for the Final Draft Report. The responses of the Air Resources Board staff to those comments are contained in Part C Addendum.)

ADDENDUM TO PART C - CONTENTS

- I. Comment Received from Chemrox, Inc.
- II. Air Resources Board Response to Chemrox, Inc.
- III. Air Resources Board Letter to Chemrox, Inc.

I. Comment Received from Chemrox, Inc.

CHEMROX, INC. 4695 MAIN STREET,
BRIDGEPORT, CT 06606-203-372-5455

DEOXX™ Systems for
• Commercial Sterilizers
• Hospital Sterilizers
• Chemical Process Industry

May 28, 1987

Mr. William V. Loscutoff, Chief
Toxic Pollutants Branch
Air Resources Board
Attn: Ethylene Oxide
P.O. Box 2815
Sacramento, CA 95812

Subject: Final Draft Report on Ethylene Oxide

Dear Mr. Loscutoff:

With respect to subject report prepared by the state of California Air Resources Board, we would like to offer the following comments:

- Overview and Recommendations, page 9

The use of water-sealed, once-through vacuum pumps on sterilizers results in fugitive EtO emissions. However, this problem can be easily resolved by replacing once through vacuum pumps with closed-loop systems. In a closed loop system, the seal liquid leaving the gas/liquid separator is recycled back to the pump inlet. This completely eliminates EtO discharges to the sewer system and associated fugitive emissions of EtO. It should be noted that a number of companies in the state of California have already installed closed loop systems and many others are in the process of doing so.

- Part A, page 11-4

The rate constant for hydration of ethylene oxide to ethylene glycol under acidic conditions reported in Figure 11-3 suggests that the reaction follows second order kinetics. However, the experimental data developed by Chemrox indicates that hydration of EtO to ethylene glycol is a first-order reaction with respect to ethylene oxide in the presence of excess water. Also, the report does not provide a pH value associated with the reported rate constant. We have found that the rate constant is strongly dependent upon pH.

May 28, 1997
page 2 of 2

We appreciate the opportunity to comment on subject report and hope these comments will be helpful to you. If you have any questions, please do not hesitate to call.

Very truly yours,

Pankaj R. Desai

Pankaj R. Desai, Ph.D.
Vice President
Sales and Marketing

PRD: JS

II. Air Resources Board Response to Chemrox, Inc.

III. Air Resources Board Letter to Chemrox, Inc.

AIR RESOURCES BOARD

102 Q STREET
BOX 2815
SACRAMENTO, CA 95812



June 8, 1987

Pankaj R. Desai, P.E.
Vice President
Sales and Marketing
Chemrox, Inc.
4695 Main Street
Bridgeport, CT 06606

Dear Mr. Desai:

Comments on Final Report on Ethylene Oxide

Thank you for submitting comments on ARB's Final Draft Report on Ethylene Oxide.

In response to your first comment, statements have been inserted into the report on page 9 of the overview and on page II-5 of Part A, to the effect that some companies have recently installed closed-loop vacuum pump systems which can eliminate ethylene oxide discharges to the wastewater. Your letter has been cited as the reference for this information. I trust that this change satisfies your request for a note to be added to the report on this topic.

In response to your second comment, you are correct that the rate constant for hydration of ethylene oxide to ethylene glycol under acidic conditions reported in Figure II-3 suggests that the reaction follows second-order kinetics. In fact, the reaction rate is dependent upon the concentrations of both ethylene oxide and hydrogen ions. If the hydrogen ion concentration is fixed (fixed pH), then the hydration would be a pseudo-first-order reaction with respect to ethylene oxide as your data suggests. Page II-16 of the report includes a tabulation of half-lives calculated for ethylene oxide at pH values ranging from 2 to 11, and these times vary greatly relative to pH. Because your comments are consistent with the cited statements in the report, no change was made in the report.

Thank you for your helpful comments. If you have questions, please do not hesitate to call Gary Murchison of my staff at (916) 322-8521.

Sincerely,

A handwritten signature in cursive script that reads "William V. Loscutoff".

William V. Loscutoff, Chief
Toxic Pollutants Branch
Stationary Source Division