

AD-A125 528

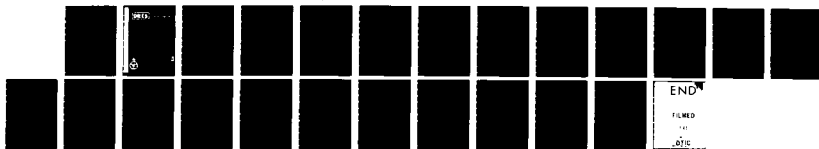
CURRENT TOXICOLOGY OF ETHYLENE OXIDE(U) DEFENCE
RESEARCH ESTABLISHMENT SUFFIELD RALSTON (ALBERTA)
C E MENDOZA ET AL. DEC 82 DRES-356

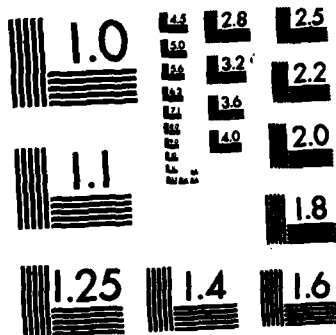
1/1

UNCLASSIFIED

F/G 6/20

NL





MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

UNCLASSIFIED

DRES

SUFFIELD REPORT

NO. 356

DISTRIBUTION
UNLIMITED

③

AD A 1 25528

CURRENT TOXICOLOGY OF ETHYLENE OXIDE (U)

by

C.E. Mendoza and I.W. Coleman

Project No. 13D10

December 1982

DTIC FILE COPY



DTIC
ELECTE
MAR 1 1 1983
S D E

DEFENCE RESEARCH ESTABLISHMENT SUFFIELD : RALSTON : ALBERTA

UNCLASSIFIED

DISTRIBUTION
UNLIMITED

DEFENCE RESEARCH ESTABLISHMENT SUFFIELD
RALSTON ALBERTA

SUFFIELD REPORT NO. 356

CURRENT TOXICOLOGY OF ETHYLENE OXIDE (U)

by

C.E. Mendoza and I.W. Coleman

Project No. 13D10

December 1982

Accession For	
NTIS GRA&I	☒
DTIC TAB	☐
Unannounced	☐
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A	

WARNING

The use of this information is permitted subject to recognition
of proprietary and patent rights.



UNCLASSIFIED

UNCLASSIFIED

DEFENCE RESEARCH ESTABLISHMENT SUFFIELD
RALSTON ALBERTA

SUFFIELD REPORT NO. 356

CURRENT TOXICOLOGY OF ETHYLENE OXIDE (U)

by

C.E. Mendoza and I.W. Coleman

ABSTRACT

The current toxicology of ethylene oxide is emphasized in this report. Studies such as acute toxicity, subacute toxicity, mutagenicity, reproductive toxicology and carcinogenicity are presented. The overall toxicological implications and a recommendation on the use of ethylene oxide are briefly discussed.

(U)

UNCLASSIFIED

ACKNOWLEDGEMENT

We would like to acknowledge Dr. T. Lewis and Dr. K. Anger of NTP, NIOSH, Cincinnati, Ohio, U.S.A., and Dr. W. Snelling of Union Carbide Corporation, Bushy Run Research Center, Export, Pennsylvania, U.S.A. for the most recent and unpublished toxicological information. We also acknowledge Capt W.M. Smith, Medical Officer, CFB Suffield, Ralston, Alberta, for his interest and cooperation in the preparation of this report. Likewise, we thank Miss Helena Walsh for typing the manuscript.

This report was prepared in response to the request of Dr. M.C. Hamblin, Director, Defence Sciences Division, DRES, on September 16, 1982.

UNCLASSIFIED

**DEFENCE RESEARCH ESTABLISHMENT SUFFIELD
RALSTON ALBERTA**

SUFFIELD REPORT NO. 356

CURRENT TOXICOLOGY OF ETHYLENE OXIDE (U)

by

C.E. Mendoza and I.W. Coleman

SUMMARY

✓ Ethylene oxide is used as a fumigant to sterilize surgical equipment and as a fungicide for agricultural commodities. It is a liquid at below 12°C and has a boiling point of 10.7°C. It is readily soluble in water and most organic solvents.

✓ Its chemical properties make the compound very reactive on mucous membranes and cellular components. Symptoms of acute poisoning are irritation of the skin, mucous membranes and lungs; pulmonary edema; depression of the central nervous system; lacrimation; nausea or vomiting; and convulsion. Severe pulmonary edema could lead to death. Deaths after a few days are due to liver and kidney failure.

Adverse effects were demonstrated by some of the specific, standard toxicological studies such as acute, skin and eye irritation, mutagenicity, reproduction, and oncogenicity tests. Its LD₅₀ values of less than 500 mg/kg of body weight rank ethylene oxide among the dangerous poisons. It causes severe skin burns and eye irritation without apparent permanent damage. Moreover, this chemical is highly mutagenic in

(i)

UNCLASSIFIED

UNCLASSIFIED

SUMMARY (Cont'd)

microbiological and mammalian systems.) Reproductive impairment was observed in both male and female test animals that were exposed to ethylene oxide vapour. A single exposure of the male rats to vapour at 1000 ppm for 4 hours resulted in reproduction abnormalities corresponding to the effect on germinal cells after meiotic division. Recent oncogenicity studies on rats and cynomolgus monkeys indicated that ethylene oxide causes leukemia.

It should be noted also that ethylene oxide in the presence of water produces ethylene glycol. Subchronic and chronic exposures to ethylene glycol result in blood clotting abnormalities, reproductive failure as well as tumours in laboratory animals.

Considering the chemical nature, and the serious toxicological effects on the mammalian systems, ethylene oxide should be regarded as a dangerous compound. Therefore, it should be handled and used with utmost care. Monitoring of its residues and by-products must be conducted, particularly when it is used to sterilize equipment that will be used directly on humans. The threshold limit value (TLV) is 1 ppm or 2 mg/m³ of air.

(ii)

UNCLASSIFIED

UNCLASSIFIED

**DEFENCE RESEARCH ESTABLISHMENT SUFFIELD
RALSTON ALBERTA**

SUFFIELD REPORT NO. 356

CURRENT TOXICOLOGY OF ETHYLENE OXIDE (U)

by

C.E. Mendoza and I.W. Coleman

INTRODUCTION

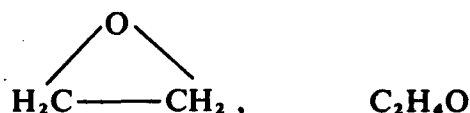
The present report briefly summarizes the toxicological data and clinical symptoms of ethylene oxide poisoning. It also attempts to give the most recent findings regarding the toxicological effects, including oncogenicity, of ethylene oxide. Highlights of the most recently completed but unpublished studies have been obtained through the courtesy of Dr. Trent Lewis (Project Leader for ethylene oxide studies and Contact Person for Pulmonary Toxicology, National Institute of Occupational Safety and Health (NIOSH), National Toxicology Program, Public Health Service, U.S. Department of Health and Human Services, Cincinnati, Ohio, U.S.A.).

The topics discussed in this report are chemistry, uses, symptomatology, and toxicological studies including skin and eye irritation, mutagenicity, reproduction, teratogenicity, oncogenicity, acute and subacute toxicity. Toxicological information on ethylene glycol, the product of ethylene oxide hydrolysis, is included in order to give a balanced perspective of the hazards due to the use of ethylene oxide.

UNCLASSIFIED

CHEMICAL NAME

Ethylene oxide, 1,2-epoxy ethane, oxidoethane, oxinane.

STRUCTURE**MOLECULAR WEIGHT**

44.06

PROPERTIES

Colourless flammable gas at ordinary temperature and pressure; liquid below 12°C, boiling point 10.7°C; freezing point - 111°C, specific gravity (at 0°C/4°C water) 0.891, (at 20°C/4°C water) 0.8694, (at 60°C/4°C water) 0.804; refraction index (for 20°C and sodium light) 1.3597. Soluble in water, alcohol, ether (Merck Index, 9th ed., 1976).

Inflammable at concentrations greater than 3% in air (Spencer, 1982).

USES

As a fumigant for food stuffs and textiles; to sterilize surgical instruments; as an agricultural fungicide. In syntheses, especially in the production of ethylene glycol. In manufacture of acrylonitrile and nonionic surfactants (Merck Index, 9th ed., 1976).

SYMPTOMATOLOGY

Intense irritation of skin (blisters), mucous membranes, and lungs, with production of pulmonary edema. Irritation and pain usually act as adequate warnings but **not always**. Prompt deaths are thought to be the result of central depression with respiratory arrest; in delayed deaths for several hours, deaths are due to pulmonary edema; those after a few days are due to liver and kidney damage (Gosselin *et al.*, 1976). Lacrimation, nausea or vomiting, convulsion, hyperactivity of the gastro-intestinal system are observed in human exposures (Lewis and Tatken, 1982).

TOXICOLOGICAL DATA

I. Skin and eye irritation data

A. Lewis and Tatken, 1982:

- Human skin — 1%/7 seconds exposure, no results given.
- Rabbit eye — 18 mg/6 hours exposure, moderate irritation.

B. Grant, 1974:

- Rabbit eye — a drop of ethylene oxide caused intense conjunctivitis but cleared in 4 days.

II. Mutation data

A. Lewis and Tatken, 1982:

- *Salmonella typhimurium* — 40 μ mol/plate.
- *Escherichia coli* — 3500 μ mol/10 hours.
- *Neurospora crassa* — 140 mmol/L/10 minutes.
- *Drosophila melanogaster*, cytogenetic analysis, (parenteral) — 55 mmol/L.
- *D. melanogaster*, sex chromosome loss and nondisjunction, (parenteral) — 5 mmol/L.
- Human fibroblast, sister chromatid exchange — 36 ppm/24 hours.
- Rat bone marrow, cytogenetic analysis, (*in vitro*) — 30 μ g/L/2 days.
- Rat, cytogenetic analysis (inhalation) — 1 μ g/L for 17 weeks.
- Rat, cytogenetic analysis (p.o.) — 9 mg/kg.
- * — Rat, micronucleus test on "lymphocytes?" (i.v.) — 200 mg/kg.
- ** — Rat dominant lethal test (inhalation) — 1000 ppp/4 hours.

* Mammalian, *in vivo*, studies; perhaps "lymphocytes?", since they are commonly used in this type of test.

** Most relevant mammalian, *in vivo*, study to acute exposure of humans to ethylene oxide (see also Embree *et al.*, 1977).

- *— Mouse micronucleus test on "lymphocytes?" (i.p.) — 150 mg/kg.
- *— Mouse micronucleus test on "lymphocytes?" (i.v.) — 200 mg/kg.
- Mouse unscheduled DNA synthesis test on "skin fibroblast or primary hepatocytes" (inhalation) — 300 ppm.
- Mouse dominant lethal test (inhalation) — 500 ppm for 80 hours, intermittent dosing.
- Mouse dominant lethal test (i.p.) — 150 mg/kg.
- Mouse lymphocyte or mammalian somatic cell mutation (*in vitro*) — 5 μ mol/L.
- Mouse fibroblast heritable translocation test (i.p.) — 30 mg/kg for 25 days, intermittent dosing.

B. Embree *et al.*, 1977:

- Dominant lethal study on male Long-Evans rats exposed once to 1000 ppm of ethylene oxide for 4 hours, mated each week to groups of 2 females for 10 weeks, using trimethylenemelamine as the positive control.
- Results:
 - a) Significant increase in post-implantation foetal deaths.
 - b) Significant increase during the first 5 weeks of the experiment, corresponding to residence time of germinal cells exposed to ethylene oxide after their meiotic division (cell division that results in the formation of gametes).

III. Reproduction effects data

A. Lewis and Tatken, 1982:

- Foetotoxicity in rat (inhalation), lowest effect dose or concentration (LDLo) 100 ppm, 6 hours per day at 6 – 15 days of pregnancy.

* Mammalian, *in vivo*, studies; perhaps "lymphocytes?", since they are commonly used in this type of test.

- Live birth litter size — rat (inhalation), LDLo 100 ppm, 6 hours per day; males treated for 60 days pre-mating, 1 – 19 days of pregnancy.
- Testes, sperm ducts, epididymis; pre-implantation mortality, LDLo 3600 $\mu\text{g}/\text{m}^3$ for 24 hours per day; males treated for 60 days pre-mating.
- Post implantation mortality in mouse (i.v.), LDLo 225 mg/kg at 10 – 12 days of pregnancy.
- Musculo-skeletal system in mouse (i.v.), LDLo 450 mg/kg at 8 – 10 days of pregnancy.
- Before birth ("caesarian section") litter size; foetotoxicity in mouse (i.v.), LDLo 450 mg/kg at 10 – 12 days of pregnancy.

B. Snelling, *et al.*, 1982a:

- Male and female Fischer rats were exposed to ethylene oxide vapour for 6 hours per day, 5 days per week for 12 weeks. Animals were mated and the females were continued on exposure from Day 0 through Day 19 of gestation for 6 hours per day, 7 days per week.
- Results:
 - a) The major treatment-related adverse effect was significantly fewer pups born per litter in the highest exposure level only.
 - b) There were fewer implantation sites per pregnant female, and a smaller ratio of the number of foetuses born to the number of implantation sites per pregnant female in the highest level group than in any other groups.
 - c) The gestation period was significantly longer in the 100-ppm group than in the control group.
 - d) Fertility indices for the treated males and females were not statistically different from the control group.
 - e) No significant adverse effects were observed in terms of body weight gain, survival and other toxic signs in the F_0 and F_1 generations.

C. National Center for Toxicological Research (NCTR), Food and Drug Administration (FDA), Jefferson, Arkansas study (under the direction of Dr. Carole Kimmel), personal communication September 20, 1982 with Dr. T. Lewis, NTP:

- No detail protocol or schedule of the study was obtained.
- Teratogenicity study on rabbits exposed to ethylene oxide.
- Results:
 - Increased incidence of foetotoxicity, no teratogenicity observed.

IV. Oncogenic data

A. Lewis and Tatken, 1982:

- Neoplasma (benign or lacking complete description) in mouse (s.c.), LDLo 1090 mg/kg for 91 weeks, intermittent dosing.
- Currently being tested for the National Toxicology Program (NTP), Public Health Service, U.S. Department of Health and Human Services, by Battelle Northwest Laboratory.

B. Personal communication, September 20, 1982, with Dr. Trent Lewis, National Toxicology Program (NTP), NIOSH, Department Health and Human Services, Cincinnati, Ohio:

1. NTP, NIOSH (being conducted by Battelle Northwest Lab., monitored by Tracor-Jitco for NTP under the direction of Dr. T. Lewis).
 - Chronic inhalation study on mice, male and female, exposed to 0, 50, or 100 ppm of ethylene oxide for 6 hours per day, 5 days per week for 2 years.
 - The study was started in late August, 1981, is in progress as of September 20, 1982. There is no progress report available.
2. NIOSH study (terminated in 1981, final report in preparation)

- Chronic inhalation study on Fischer 344 rats, females only, exposed to 0, 50, or 100 ppm of ethylene oxide for 6 – 7 hours (or approximately 6.8 hours) per day, 5 days per week for 2 years.
- Results:
 - Increased incidence of leukemia that is treatment-related.
- 3. NIOSH study (terminated in 1981, final report in preparation)
 - Chronic inhalation study on *Macaca fascicularis* (cynomolgus monkey), males only, exposed to 0, 50 or 100 ppm of ethylene oxide for 6 – 7 hours per day, 5 days per week for 2 years.
 - Results:
 - a) Treatment-related increase in chromosomal aberration and sister chromatid exchange in the circulating lymphocytes.
 - b) Treatment-related significant decrease in sperm motility and counts.
 - c) Histopathological abnormality of the nucleus gracilis of the dorsal column, central nervous system, related to tactile sensory; also increased axonal bodies. Histopathology was conducted by Dr. H. Spring, Midwest Research Institute and Kansas University, Kansas City, Missouri (Project Officer for histopathological and behavioural studies, Dr. Kent Angers of NIOSH at Cincinnati, Ohio, personal communication, September 21, 1982).

C. Snelling *et al.*, 1982b:

- Chronic inhalation study on Fischer 344 rats, male and

female, exposed to 0, 10, 33, or 150 ppm of ethylene oxide for 6 hours per day, 5 days per week for 2 years.

— Results:

- a) Depression of body weight and increase in mortality at the 33 and 150 ppm levels.
- b) No consistent pattern of association of histologically confirmed organ damage with any alteration in urinalysis, hematology, serum clinical chemistry, or organ weights.
- c) Skeletal muscle atrophy in both sexes at 150 ppm at 24 months.
- d) Increased prevalence of mononuclear leukemia, treatment-related in females at the 10, 33 or 150 ppm level.
- e) Increased incidence of more than two neoplasms per rat in the three treatment groups.
- f) Increased incidence of malignant neoplasm in females at the 33 or 150 ppm level.
- g) Treatment-related increase in peritoneal mesothelioma in the male rats at the 33 or 150 ppm level.
- h) Incidence of mononuclear leukemia and peritoneal mesothelioma in the control group comparable to historical published background.
- i) The possible contribution of sialodacryoadenitis viral outbreak (which occurred during the 15th exposure month) to the ethylene dioxide exposure related tumors is unknown.

D. Reyniers *et al.*, 1964:

- Male and female mice (ALBM-2, colony 101-F) were exposed to the corncob bedding sterilized with ethylene oxide

up to 900 days. They were observed for blood dyscrasia, reproductive capacity and tumour incidence.

- Mice that were accidentally exposed to the ethylene oxide-treated bedding prior to the intentional exposure experiment mentioned in the preceding paragraph were observed for reproductive failure.
- Results:
 - a) Female mice exposed to corncob bedding treated with ethylene oxide experienced reproductive failure.
 - b) Survivors (90%), 400 to 900 days old mice, developed tumours of various kinds and in various sites.
 - c) Graafian follicles and corpora lutea rarely found; abnormal ovaries in almost all animals.
 - d) No tumours in either males or females up to 600 days old that were exposed to non-treated corncob bedding.
 - e) Males exposed for less than 50 days to the toxic bedding lived longer, had markedly lengthened blood-clotting time, and died of hemorrhage.
 - f) Only one female showed extensive hemorrhages.
 - g) Attempts to breed surviving males failed.

V. Toxicity data

A. Lewis and Tatken, 1982:

- Convulsion, nausea or vomiting, changes in lungs, thorax or respiration in adult woman (inhalation), LDLo 500 ppm for 2 minutes.
- Lacrimation, changes in structure and function of salivary glands, hypermotility of the gastro-intestinal tracts, diarrhea in rat (inhalation), LDLo 72 mg/kg; in dog (inhalation), LC₅₀ = 960 ppm for 4 hours exposure.
- Irritation in human (inhalation), LDLo 12500 ppm for 10 seconds.

- Rat (p.o.) LD₅₀ = 72 mg/kg.
- Mouse (inhalation) LD₅₀ = 836 ppm for 4 hours.
- Mouse (i.p.), LDLo 100 mg/kg.
- Mouse (i.v.), LD₅₀ = 290 mg/kg.
- Rabbit (i.v.), LDLo 175 mg/kg.
- Guinea pig (p.o.), LD₅₀ = 270 mg/kg.
- Guinea pig (inhalation), LDLo 7000 ppm for 150 minutes (2.5 hours).
- *— Rat (inhalation), LD₅₀ = 1462 ppm for 4 hours.
- *— Rat (p.o.), LD₅₀ = 330 mg/kg.

B. Allan *et al.*, 1962:

- Blood clotting study on mice, male and female, exposed to either pine shavings (bedding), sterilized with ethylene oxide, for 6 months; by gavage administration of 0.25 mg or 2.5 mg of ethylene oxide in olive oil per day for 4 weeks; or by i.v. administration of 2.5 µg or 2.5 µg of ethylene oxide in saline solution per day for 4 weeks. An untreated control group was also observed.
- Ethylene glycol (HOCH₂CH₂OH) was also administered to the mice at 10⁻², 10⁻³, and 10⁻⁴ dilutions by gavage each weekday (interpreted as 5 days/week) for 12 weeks.
- Extracts of the control shavings, or the shavings sterilized with ethylene oxide, were also administered to the mice at 10⁻¹, 10⁻², and 10⁻³ dilutions.
- Results:
 - a) Unautoclaved ethylene oxide administered by gavage (0.25 mg or 2.5 mg/day) or i.v. (2.5 µg or 25 µg/day) produced no clotting abnormality in the mice.

* Data from Sax, 1979.

- b) Haemothorax, bleedings at various body sites, jaundice and subsequent deaths observed on males only reared in bedding sterilized with ethylene oxide.
- c) Both ethylene glycol and extracts of shavings that had been autoclaved with ethylene oxide produced increased specific clotting abnormalities, which appeared predominantly in male mice.
- d) Autoclaved ethylene oxide in the presence of water produced ethylene glycol, which is responsible in the production of blood clotting abnormalities.
- e) Ethylene glycol administered by gavage at 1:5 to 1:10 dilutions produced the same blood clotting abnormalities in mice.

VI. Threshold limit value — time weighted average or TLV-TWA (Amer. Confer. Gov. Ind. Hyg., 1982)

- Intended changes for 1982, 1 ppm or 2 mg/m³ air, with a warning that it may be a carcinogen.

GENERAL COMMENTS

Mackel (1974) of the Public Health Service, U.S. Department of Health, Education and Welfare (now Department of Health and Human Services) recommended that ethylene oxide gas autoclaving be used on all non-steamable-autoclavable reusable equipment. It was recommended that biological sterility controls be used during the sterilization operation and that all materials must be adequately aerated before use. The use of a heated aerator which circulates and continuously vents air at 50 to 60°C for 8 to 12 hours.

In 1977, the National Institute for Occupational Safety and Health (NIOSH) issued a special occupational hazard review and recommendations for the use of ethylene oxide as a sterilant in medical facilities (Glaser, 1977). The report includes reviews of effects of ethylene oxide in animals, lower biological systems and humans. Haemolysis has been reported with ethylene oxide sterilized devices used for blood perfusion, and with devices used for i.v. administration in patients. Subsequent studies in dogs treated with ethylene oxide gave conflicting results. Perhaps these conflicting results were obtained since haemolysis may be more associated with ethylene glycol than ethylene oxide, the test material used. Ethylene glycol has been implicated with internal haemorrhages and other blood dyscrasia in experimental animals (Allen *et al.*, 1962; Reyniers *et al.*, 1964).

Leukemia observed in mice, rats and monkeys parallels that observed in three industrial workers exposed to ethylene oxide for a long period of time (Hogstedt *et al.*, 1979). It should be emphasized that leukemia was observed after a prolonged chronic exposure. However, with a single or short experimental exposure, it should be noted that the test animals were not observed long enough for the development of leukemia or other diseases with long latent period.

CONCLUSION

The reports reviewed indicated that ethylene oxide is highly mutagenic in animals, in microbial systems, and in isolated animals and humans cells. Reproductive failures in both male and female test animals exposed to ethylene oxide were also observed. Recently completed and unpublished chronic toxicity studies indicated that it causes leukemia in rodents and cynomolgus monkeys.

Since ethylene oxide reacts with water to produce ethylene glycol, particularly under heat and pressure, secondary hazard due to ethylene glycol can be expected. Ethylene glycol causes internal haemorrhages and other blood dyscrasia in the laboratory animals. It is a very stable compound, with a boiling point of 197.6°C at 760 mm Hg pressure to 20°C at 0.06 mm Hg pressure. Evacuation of ethylene glycol will be very difficult particularly from charcoal-containing cannisters.

We recommend, therefore, that ethylene oxide should not be used to sterilize equipment such as cannisters, particularly if they contain adsorbents. Adequate venting of enclosed cannisters and adsorbed gas may not be achieved unless specially tested procedures are followed. In addition, the hydrolysis product, ethylene glycol, has a very low vapour pressure which makes it difficult to be completely evacuated from the cannisters containing absorbents.

REFERENCES

- Allen, R.C., Meier, H., and Hoag, W.G. Ethylene glycol produced by ethylene oxide sterilization and its effect on blood-clotting factors in an inbred strain of mice. *Nature* **193**, 387, 1962.
- Anonymous. TLVs Threshold Limit Values for Chemical Substances in Workroom Air Adopted by ACGIH for 1982. American Conference of Governmental and Industrial Hygienists, 1982.
- Embree, J.W., Lyon, J.P., and Hine, C.H. The mutagenic potential of ethylene oxide using the dominant-lethal assay in rats. *Toxicol. Appl. Pharmacol.* **40**, 261, 1977.
- Glaser, Z.R. Special occupational hazard review with recommendations for the use of ethylene oxide as a sterilant in medical facilities, U.S. Department Health, Education and Welfare, Public Health Service, Center for Disease Control, NIOSH, PB-274 795, pp. i - v; 1 - 58, 1977.
- Gosselin, R.E., Hodge, H.C., Smith, R.P. and Gleason, M.N. *Clinical Toxicology of Commercial Products. Acute Poisoning.* 4th ed., Williams and Wilkins Co., Baltimore, p. 68, 1976.
- Grant, W.M. *Toxicology of the Eye.* 2nd ed. C.C. Thomas, Springfield, pp. 478 - 480, 1974.
- Hogstedt, C., Malmquist, N. and Wadman, B. Leukemia in workers exposed to ethylene oxide. *J. Amer. Med. Assoc.* **241**(11), 1132, 1979.
- Lewis, Sr., R.J. and Tatken, R.L. Registry of Toxic Effects of Chemical Substances. U.S. Dept. Health Human Services, NIOSH, Publication No. 81-116-4. Grids J03 and K03, Fiche 26, Jan., 1982.
- Mackel, D.C. Sterilization and disinfection of respiratory therapy equipment. *APIC Newsletter* **2**(3), pp. 1, 3 and 4, 1974.
- Reyniers, J.A., Sacksteder, M.R., and Ashburn, L.L. Multiple tumors in female germfree inbred albino mice exposed to bedding treated with ethylene oxide. *J. Nat. Cancer Inst.* **32**, 1045, 1964.
- Sax, N.I. *Dangerous Properties of Industrial Materials.* 5th ed., Van Nostrand Reinhold Co., New York, p. 662, 1979.
- Snelling, W.M., Weil, C.S., and Maronpot, R.R. Ethylene oxide vapor two-year inhalation study on rats. *The Toxicologist* **2**(1), 12, 1982b.

REFERENCES (Cont'd)

Snelling, W.M., Zelenak, J.P., and Weil, C.S. Effects on reproduction in Fischer 344 rats exposed to ethylene oxide by inhalation for one generation. *Toxicol. Appl. Pharmacol.* **63**, 382, 1982a.

Spencer, E.Y. Guide to the Chemicals Used in Crop Protection. Agriculture Canada Publication 1093, 7th ed., p. 277, 1982.

Windholz, M. Budavari, S., Stroumtsos, L.Y. and Fertig, M.N. The Merck Index. Merck and Co. Inc., Rahway, Index No. 3738, p. 500, 1976.

DOCUMENT CONTROL DATA - R & D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall document is classified)

1. ORIGINATING ACTIVITY DRES		2a. DOCUMENT SECURITY CLASSIFICATION Unclassified	
		2b. GROUP	
3. DOCUMENT TITLE Current Toxicology of Ethylene Oxide (U)			
4. DESCRIPTIVE NOTES (Type of report and inclusive dates) Suffield Report			
5. AUTHOR(S) (Last name, first name, middle initial) Mendoza, C.E. and Coleman, I.W.			
6. DOCUMENT DATE December 1982		7a. TOTAL NO. OF PAGES 18	7b. NO. OF REFS 15
8a. PROJECT OR GRANT NO. 13D10		8a. ORIGINATOR'S DOCUMENT NUMBER(S) SR356	
8b. CONTRACT NO.		8b. OTHER DOCUMENT NO.(S) (Any other numbers that may be assigned this document)	
10. DISTRIBUTION STATEMENT Unlimited			
11. SUPPLEMENTARY NOTES		12. SPONSORING ACTIVITY	
13. ABSTRACT The current toxicology of ethylene oxide is emphasized in this report. Studies such as acute toxicity, subacute toxicity, mutagenicity, reproductive toxicology and carcinogenicity are presented. The overall toxicological implications and a recommendation on the use of ethylene oxide are briefly discussed. (u)			

KEY WORDS

Ethylene Oxide
 Toxicology
 Acute Toxicity
 Mutagenicity
 Reproductive Toxicology
 Carcinogenicity
 Ethylene Glycol
 Symptomatology

INSTRUCTIONS

1. **ORIGINATING ACTIVITY** Enter the name and address of the organization issuing the document.
- 2a. **DOCUMENT SECURITY CLASSIFICATION:** Enter the overall security classification of the document including special warning terms whenever applicable.
- 2b. **GROUP** Enter security reclassification group number. The three groups are defined in Appendix 'M' of the DRB Security Regulations.
3. **DOCUMENT TITLE** Enter the complete document title in all capital letters. Titles in all cases should be unclassified. If a sufficiently descriptive title cannot be selected without classification, show title classification with the usual one-capital-letter abbreviation in parentheses immediately following the title.
4. **DESCRIPTIVE NOTES** Enter the category of document, e.g. technical report, technical note or technical letter. If appropriate, enter the type of document, e.g. interim, progress, summary, annual or final. Give the inclusive dates when a specific reporting period is covered.
5. **AUTHOR(S):** Enter the name(s) of author(s) as shown on or in the document. Enter last name, first name, middle initial. If military, show rank. The name of the principal author is an absolute minimum requirement.
6. **DOCUMENT DATE** Enter the date (month, year) of Establishment approval for publication of the document.
- 7a. **TOTAL NUMBER OF PAGES:** The total page count should follow normal pagination procedures, i.e., enter the number of pages containing information.
- 7b. **NUMBER OF REFERENCES** Enter the total number of references cited in the document.
- 8a. **PROJECT OR GRANT NUMBER** If appropriate, enter the applicable research and development project or grant number under which the document was written.
- 8b. **CONTRACT NUMBER** If appropriate, enter the applicable number under which the document was written.
- 9a. **ORIGINATOR'S DOCUMENT NUMBER(S)** Enter the official document number by which the document will be identified and controlled by the originating activity. This number must be unique to this document.
- 9b. **OTHER DOCUMENT NUMBER(S):** If the document has been assigned any other document numbers (either by the originator or by the sponsor), also enter this number(s).
10. **DISTRIBUTION STATEMENT:** Enter any limitations on further dissemination of the document, other than those imposed by security classification, using standard statements such as:
 - (1) "Qualified requesters may obtain copies of this document from their defence documentation center."
 - (2) "Announcement and dissemination of this document is not authorized without prior approval from originating activity."
11. **SUPPLEMENTARY NOTES:** Use for additional explanatory notes.
12. **SPONSORING ACTIVITY:** Enter the name of the departmental project office or laboratory sponsoring the research and development. Include address.
13. **ABSTRACT:** Enter an abstract giving a brief and factual summary of the document, even though it may also appear elsewhere in the body of the document itself. It is highly desirable that the abstract of classified documents be unclassified. Each paragraph of the abstract shall end with an indication of the security classification of the information in the paragraph (unless the document itself is unclassified) represented as (TS), (S), (IC), (R), or (U).

The length of the abstract should be limited to 20 single-spaced standard typewritten lines; 7/8 inches long.
14. **KEY WORDS:** Key words are technically meaningful terms or short phrases that characterize a document and could be helpful in cataloging the document. Key words should be selected so that no security classification is required. Identifiers, such as equipment model designation, trade name, military project code name, geographic location, may be used as key words but will be followed by an indication of technical context.

3-83

TI