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7256-2

FORM 40N

STERILIZING GAS MIXTURE

ACTIVE INGREDIENT ETHYLENE OXIDE 20%
(18% CARBON DIOXIDE) INERT INGREDIENT 80%

THIS CYLINDER IS THE
PROPERTY OF THE
MATHESON CO., INC.

THIS CYLINDER IS
EQUIPPED WITH
VALVE OUTLET
CGA 350

DO NOT
REFILL

Cameraman's Note
Poor Copy

KEEP COOL

CAUTION

STERILIZING
GAS MIXTURE

DO NOT DROP

This is to certify that the contents of this package are properly described by name and are packed and marked and are in proper condition for transportation according to the regulations prescribed by the Interstate Commerce Commission.

THE MATHESON CO., INC.
EAST RUTHERFORD,
NEW JERSEY

ACTIVE INGREDIENT ETHYLENE OXIDE 20%
(80% CARBON DIOXIDE) INERT INGREDIENT 80%

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USDA REG. NO. _____

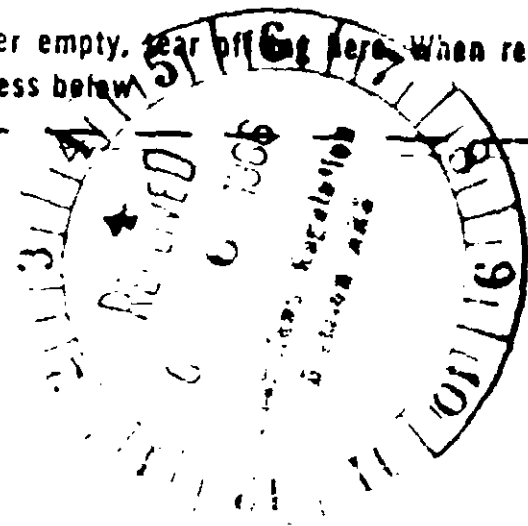
Use and store in cool, dry, well ventilated place. Keep cylinder temperature from exceeding 125° F. Close valve when not in use. Never refill cylinder. Handle cylinder with care. Discharge in normal vertical position. After discharge close cylinder valve to prevent suck-back of contaminants. Ethylene oxide is subject to polymerization use within 2 months after receipt.

READ STERILIZING GAS
MIXTURES BROCHURE BEFORE
USING.

When Empty Return to Nearest Location
THE MATHESON CO., INC., EAST RUTHERFORD, N. J.
NEWARK, CALIF. • JOLIET, ILL. • LAPORTE, TEX. • MORROW, GA.

WHEN RETURNING this cylinder empty, tear off tag here. When returning full cylinder, leave tag intact, but deface address below.

TO:



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U.S. PATENT NO.
2,891,838

STERILIZING GAS MIXTURES

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STERILIZING GAS MIXTURES

DESCRIPTION — Sterilizing gas mixtures as provided by The Matheson Company are composed of Ethylene Oxide, which is the active sterilizing agent, plus a diluent such as Carbon Dioxide, or a halogenated hydrocarbon or combination of halogenated hydrocarbons.

Ethylene Oxide is a true bactericidal agent. It acts as a germicide on both bacterial and vegetable molds. ~~It also destroys all forms of insect life.~~ The addition of proper diluents acts to increase the volatility of the sterilizing gas and decrease the flammable hazard associated with the handling of Ethylene Oxide.

Penetrative Properties

Sterilizing gases containing Ethylene Oxide have high penetrative qualities. They are capable of readily diffusing through paper, clothing and blankets. Penetration of powders, dried drugs, vegetable gums, etc. depends on the method of packaging and the density of the material itself. Sterilization of pre-packaged material is possible through proper use of packing materials. The gas is known to penetrate polyethylene and plioilm.

Types of Sterilizing Gases Available

The following typical Ethylene Oxide mixtures are available from all branches of The Matheson Company, Inc.:

- 10% Ethylene Oxide—90% Carbon Dioxide
- 20% Ethylene Oxide—80% Carbon Dioxide
- 11% Ethylene Oxide—35% "Freon-12"^{*}, 54% "Freon-11"^{**}
- 12% Ethylene Oxide—88% "Freon-12"^{*}

Mixtures containing 10% by weight or less of Ethylene Oxide in Carbon Dioxide, or 11% by weight or less of Ethylene Oxide in halogenated hydrocarbons are completely non-flammable in any proportions with air. The use of mixtures containing higher Ethylene Oxide concentrations introduces a flammability hazard, requiring special handling procedures and equipment design.

The cylinder pressures of sterilizing mixtures will vary with the concentrations of the various constituents. A higher proportion of diluents having higher vapor pressures will cause the final mixture to have a higher vapor pressure. The vapor pressures at 70 F. (cylinder pressures) of the above mixtures are as follows:

MIXTURE	VAPOR PRESSURE (p.s.i.g.)
10% Ethylene Oxide— 90% Carbon Dioxide	720
20% Ethylene Oxide— 80% Carbon Dioxide	640
11% Ethylene Oxide—35% "Freon-12" [*] , 54% "Freon-11" ^{**}	26
12% Ethylene Oxide—88% "Freon-12" [*]	52

Trademark "Freon" — E. I. du Pont de Nemours & Co. (Inc.)

^{*}Licensed and sold under Ben Venue Laboratories, Inc., U. S. Patent No. 2,891,838

^{**}Although penicillin can be effectively sterilized with no harmful effects, there is evidence that streptomycin suffers a loss of potency.

^{***}It is suggested that the user consult the literature of the Food and Drug Administration for information on the sterilization of pharmaceuticals.

Vapor pressure or cylinder pressure should not be confused with sterilizer pressure. Sterilizer pressure is dependent on the amount of sterilizing mixture that appears solely in the gas phase in the sterilizer; however, cylinder pressure is of value in determining whether or not enough head pressure is available to force the sterilizing mixture into the sterilizer, or associated sterilizer equipment.

ADVANTAGES OF STERILIZING GAS MIXTURES

These mixtures have been used to sterilize heat and moisture sensitive materials, ~~and for fumigation purposes.~~ ~~They are particularly useful for fumigating large, tightly packed containers, such as drums, kegs, crates, and rooms.~~ Gas sterilization can substantially increase the life of equipment normally subjected to steam or high temperature sterilization processes.

Among the items effectively sterilized and fumigated by Ethylene Oxide mixtures are the following:

PHARMACEUTICAL
Plastic vials, tubing and droppers
Antibiotics and other suitable drugs*
Rubber materials

~~**FOODSTUFFS***
Spices
Vegetable gums
Log Cabin
Eggs
Peanuts
Dried Fruits~~

MEDICAL
Clothing
Mattresses
Surgical Instruments
Intravenous injection sets
Rubber tubing
Glassware
Culture media

OTHER
Soil
Straw
Books
Leather
Paper
Electrical equipment
Motor oil
Vaseline
~~Root control~~

Below are general descriptions of sterilization ~~and fumigation~~ processes. The information presented does not refer to specific operations and it is suggested that all factors be weighed carefully prior to their adoption.

GAS STERILIZATION Sterilization with Ethylene Oxide mixtures has been practiced for some time. Because of its effectiveness and its advantages it is now commonly used by the surgical dressing and pharmaceutical industries. Some of the mixtures' more important advantages are as follows:

STERILIZING GAS MIXTURES

1. They have rapid action.
2. They have a low moisture requirement.
3. They are non-corrosive.
4. They are not harmful to most materials.
5. They have high penetrative properties.
6. They are readily purged by aeration.
7. They destroy all forms of organisms.
8. They are readily available.
9. They are convenient to store and handle.

Conditions of Sterilization

Sterilization by Ethylene Oxide mixtures is essentially a function of time of exposure, concentration of Ethylene Oxide in the sterilizer space, temperature and humidity.

A. TIME OF EXPOSURE

In general, non-spore forming bacteria are killed with relative ease, while a longer exposure is required for a 100% kill of spore-forming bacteria; generally, exposure time is a function of the Ethylene Oxide concentration in the sterilizer space. The following table illustrates relative exposure times to kill various types of organisms:

TABLE 1

SPECIES OF BACTERIA	RELATIVE TIME (X=UNIT TIME)
Bacillus globigii (spores)	5X
Staphylococcus aureus	3X
Mycobacterium phlei	3X
Gaffka tetragena	3X
Serratia marcescens	2X
Erberthella typhosa	X
Klebsiella pneumonia	X
Escherichia coli	X
Clostridium	0.5X
Bacillus subtilis	0.5X

B. CONCENTRATION

For sterilization purposes, Ethylene Oxide concentrations of 450-1000 mg./l. of chamber space are required to effect a 100% kill. (1 mg./l. = 1 oz./1000 cu. ft.) The higher the concentration of Ethylene Oxide, the shorter the time of exposure required for sterilization; usually doubling the concentration reduces the exposure time by one-half. The "Freon" mixtures have the added advantage of giving a higher volume percent of Ethylene Oxide in the gas phase (while still remaining non-flammable), compared with Carbon Dioxide mixtures of similar weight per cent, thus offering more rapid sterilization at low chamber pressures.

Fig. 1 shows the variation of chamber pressure for three typical gas mixtures at a few commonly used temperatures, as a function of Ethylene Oxide concentration in the sterilizer space. These curves have been developed assuming the mixtures behave as ideal gases. This graph assumes complete evacuation of the sterilizer before addition of the sterilizing gas. Initial sterilizer absolute pressure should be added to the graph value to determine final sterilizer pressure. The use of the chart is shown by the following example:

What sterilizer pressure is required to utilize a 20% Ethylene Oxide-80% Carbon Dioxide mixture at a concentration of 600 mg./l. of Ethylene Oxide and 130°F, assuming initial sterilizer pressure of 2 p.s.i.a.?

Follow vertically from 600 on the horizontal scale to the line representing 130°F. in the group of lines representing 20% Ethylene Oxide-80% Carbon Dioxide mixture. At this intersection, follow horizontally to the left to the pressure scale noting the pressure of approximately 27 p.s.i.a. Add to this the initial pressure of 2 p.s.i.a. = total of 29 p.s.i.a. Subtracting 14.7 p.s.i. gives the sterilizer final gauge pressure of 14.3 p.s.i.g.

The following equation (1) can be used to calculate the lbs. of sterilizing gas mixture needed for any sterilizer:

$$\text{lbs. mixture needed} = \frac{.00624CV}{E} \quad (1)$$

C = Concentration of Ethylene Oxide in Sterilizer space, mg./l.

E = Percent Ethylene Oxide concentration in sterilizing mixture.

V = Sterilizer volume, cu. ft.

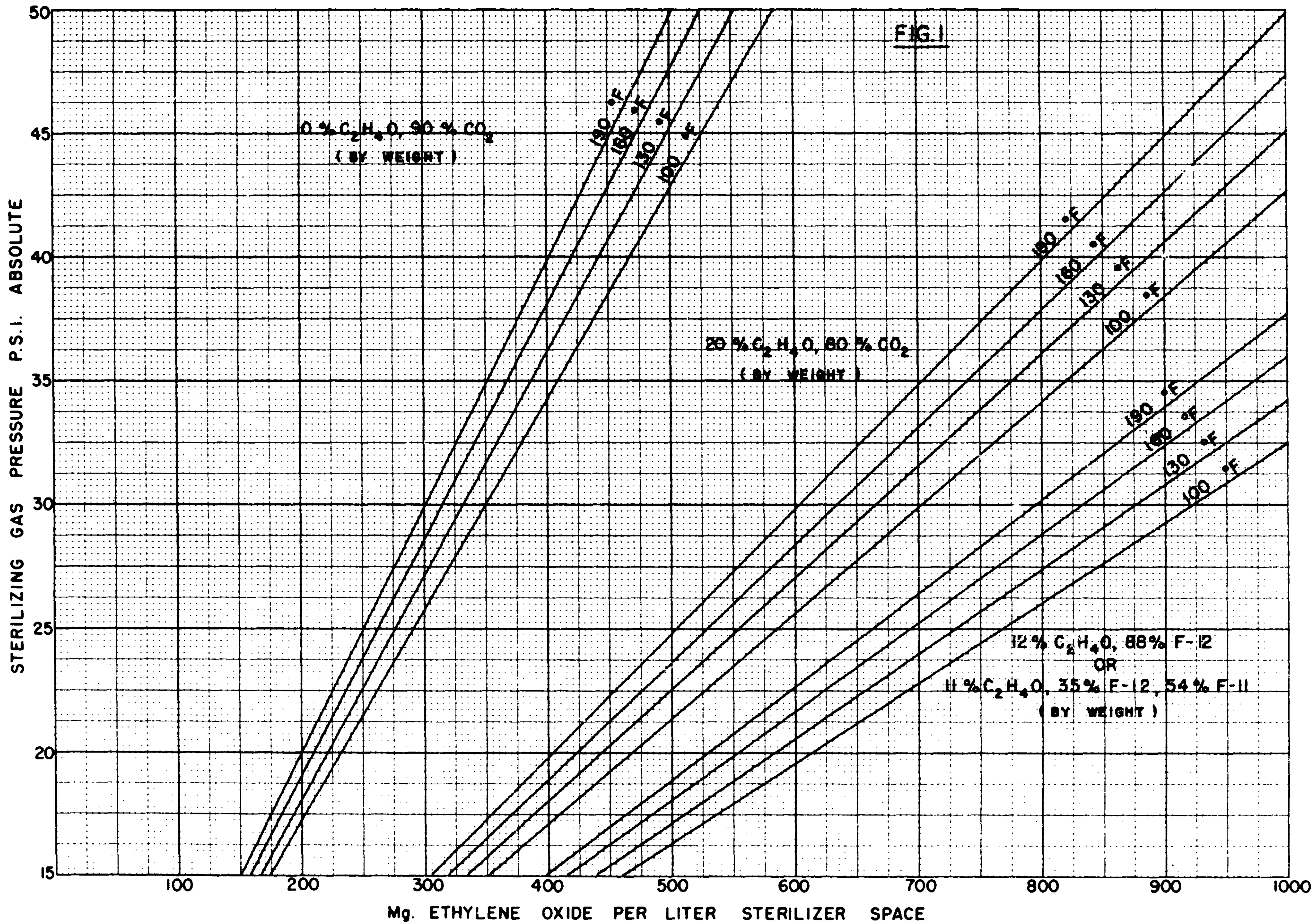
For example: How many pounds of 11% Ethylene Oxide in halogenated hydrocarbon mixture are required for a 10 cubic foot sterilizer per sterilizing cycle, assuming a final Ethylene Oxide concentration of 800 mg./l. in the sterilizer space?

$$\text{lbs. mixture needed} = \frac{.00624 \times 800 \times 10}{11} = 4.53 \text{ lbs.}$$

This assumes neither leakage loss nor absorption. From a practical standpoint some excess should be used.

C. TEMPERATURE

While sterilization can be effected with Ethylene Oxide at 70°F., rather long exposure periods are required. As temperature is raised, the rate of sterilization is increased.



STERILIZING GAS MIXTURES

Generally, for every 30 F. rise in temperature, the time required for sterilization is halved. Phillips has demonstrated the temperature effect in his studies on the sterilization of bacterial spores at 80 C., 25 C., and 37 C., in which the increase in temperature afforded a considerable reduction of exposure time. He showed that the ability of Ethylene Oxide to sterilize is increased by a factor of 2.4 for each 10 C. rise in temperature in this range for a complete kill of the bacterial spores. Temperatures in the range of 150-180 F. are usually employed.

D. HUMIDITY

Humidity is definitely related to the sterilizing efficiency for Ethylene Oxide. It has been shown that relative humidity in the range of 20-30% is required for maximum sterilization efficiency. However, water vapor during the gas exposure period is not sufficient in itself to render the gas mixtures effective against dry spores. Pretreatment by soaking in water or exposure to very high humidities prior to the gas exposure intervals prescribed herein may be essential for assured sterilization.

E. RESIDUAL GAS

Many materials such as rubber, plastics or leather when sterilized with Ethylene Oxide, readily absorb the gas and must be properly treated by aeration prior to re-use. See Section on Toxicity for more detailed information regarding the effects of Ethylene Oxide.

Dispensing of the Gas for Sterilization

In dispensing the gas mixture, either a complete single charge cylinder may be used, or a large cylinder from which measured quantities are removed, may be used. The sterilizing mixtures are withdrawn from the cylinders as a liquid, either by inverting small cylinders or through the use of eductor tubes in large cylinders, permitting discharge of the liquid with the cylinder in a normal, upright position. The liquid partially vaporizes to a gas during its discharge into the sterilization chamber where, upon contact with the warm surfaces, it completely vaporizes. In order to prevent damage to material in the sterilizer that might possibly be caused by the liquid prior to vaporization, and for greater control in dispensing with assurance of a homogeneous mixture, the use of an auxiliary gas storage tank is employed. The liquid sterilizing mixture is discharged to this auxiliary storage tank and converted completely to a gas. The gas then may be introduced into the sterilizer, usually automatically, to maintain the desired mixture proportions.

Equipment

A number of companies specialize in the manufacture of sterilizing equipment for sterilization of pharmaceuticals. The equipment is capable of automatic dosage automation controls such as temperature, concentration, exposure time, temperature, and humidity. Write for literature contacting

either the American Sterilizer Company of Erie, Pennsylvania or Wilmot-Castle Company of Rochester, New York for full information on sterilization equipment.

FUMIGATION WITH STERILIZING MIXTURES—In the past, fumigation with 90% Carbon Dioxide, 10% Ethylene Oxide has been practiced very effectively. It is an effective industrial fumigant capable of daily use without occupational hazards or damage to property. The gas mixture will effectively kill insect pests in all stages of life in various types of transportation equipment, such as railroad cars, ships, buses, and aircraft, and in storerooms. It is widely used in the daily routine of fumigation of many food products, tobacco and cotton from which seed has been removed. Recent rulings by the Food and Drug Administration have set residue limits for the use of Ethylene Oxide as a food sterilizing agent. These Food and Drug Administration regulations should be thoroughly investigated before consideration of Ethylene Oxide for food sterilization or fumigation.

Some of the features of fumigation with 10% Ethylene Oxide, 90% Carbon Dioxide are as follows:

1. It is non-flammable in all proportions with air.
2. It is non-corrosive.
3. It leaves no residues, odors or taste.
4. It has no effect on most materials of construction and fabric.
5. It effects a 100% kill of all insects if used properly.
6. It has excellent penetrative properties.
7. It is economical to use.
8. It is easy to apply.

For effective fumigation with 10% Ethylene Oxide, 90% Carbon Dioxide, it is necessary to accomplish the following:

1. Determine the dosage. Quantity of gas must be sufficient to allow for leakage and absorption by the contents of the area. Generally, a dosage of 6-8 pounds per 1000 cubic feet of space for a 3-5 hour period provides satisfactory treatment at temperatures above 70 F.

2. Keep the temperature at 70-80 F. or higher for more effective and rapid results.

3. Seal all openings gas tight. To avoid waste of gas and to maintain a killing concentration during the time of exposure, all openings to the outside should be made as gas tight as possible. Some openings, such as drains, can be sealed with vermiculite and water, or by stuffing with wadded wet news paper and taping. Other such openings of doors and windows can be sealed with mastic tape.

4. Open up all communications openings, doors, closets, basements, etc. to permit free circulation and penetration of the gas.

STERILIZING GAS MIXTURES

5. Discharge the gas as rapidly as possible by opening each cylinder valve all the way, while working away from the gas as it is being discharged. The cylinder or cylinders should be supported to prevent them from falling and the valve outlet should point into a cleared area so that the stream of spray of the cylinders does not come into contact with a painted, lacquered or varnished surface or upholstery or woodwork. Although the gas vapor is not injurious to the above mentioned items, the liquid spray has a tendency to soften paint or varnish and may damage fabrics.

After all cylinder valves are opened and the operator has left the compartment, the last exit is then closed and sealed with masking tape. After three to five hours of exposure, the doors and windows are opened, preferably from the outside and the area ventilated. Practical tests should be conducted to develop a simple standardized procedure for sealing the area to be fumigated and to determine the minimum lethal dosages for a 100% kill of the pests to be eliminated.

Care should be exercised to avoid inhaling the gas. Gas masks are not usually worn, but must be worn if the operator is exposed for considerable periods. In the event of overexposure, evidenced by such symptoms as headache, dizziness, difficulty in standing or walking, nausea, vomiting or fainting, the victim should immediately get to fresh air. He should not be permitted to exercise or continue to work, but must be kept quiet and warm. A physician should be called and the first-aid procedures recommended herein should be administered.

HANDLING AND STORAGE OF CYLINDERS — The following general rules should apply in the handling and storage of sterilizing gas mixtures.

1. Never drop cylinders or permit them to strike each other violently.

2. Cylinders should be assigned a definite area for storage. The area should be dry, cool, well-ventilated, and preferably, fire-resistant. Keep cylinders protected from excessive temperature rise by storing them away from radiators or other sources of heat. Storage conditions should comply with local and state regulations.

3. The valve protection cap should be left in place until the cylinder has been secured against a wall or bench, or placed in a cylinder stand and is ready to be used.

4. Avoid dragging, rolling or sliding cylinders, even for a short distance. They should be moved by using a suitable hand truck.

5. Never tamper with safety devices in valves or cylinders.

6. As soon as a cylinder has been discharged, close the cylinder valve. Replace any valve outlet or protective cap originally shipped with the cylinder. Mark or label the cylinder **EMPTY**.

7. No part of the cylinder should be subjected to a temperature higher than 125 F. Temperatures in excess of this figure may cause the cylinder to become liquid full resulting in excessive hydrostatic pressure buildup. Never permit a flame to come in contact with any part of a compressed gas cylinder.

8. Contact the gas supplier if any part of the cylinder or valve develops leakage that cannot be simply repaired, for example, the tightening of a packing nut to prevent leakage through valve packing.

TOXICITY — The toxic effects of sterilizing mixtures stem mainly from the Ethylene Oxide since the diluents used are inert in the physiological sense and act mainly as simple asphyxiants, displacing air when present in large amounts, thus preventing Oxygen from getting to the lungs. The recommended maximum allowable concentration of Ethylene Oxide for daily eight-hour exposure is 100 p.p.m. The first warning of Ethylene Oxide in the air is irritation of the eyes and nose. This irritation must be taken as warning of a dangerous atmosphere to avoid serious injury. Exposure to low concentrations of vapor over extended periods of time may result in delayed nausea and vomiting. Exposure to low concentrations, if continuous, will result in a numbing of the sense of smell, and harmful concentrations may be tolerated without warning. High concentrations of Ethylene Oxide can produce edema of the lungs and irritation of the eyes and mucous membranes. Ethylene Oxide is not cumulative in the body and therefore, chronic poisoning due to Ethylene Oxide does not occur. Ethylene Oxide can act as a vesicant and cause blisters if its vapors are in contact with the skin for a period of time. The pure liquid, if spilled on the skin, evaporates too quickly to cause any harm, but if confined by clothing or shoes, blisters will appear. Rubber and leather articles, in particular, should be aired for about 24 hours after being exposed to a spill or high concentration of Ethylene Oxide vapors.

Liquid Ethylene Oxide or solutions may cause severe eye burn.

Protective clothing should be worn when working directly with liquid Ethylene Oxide or mixtures. Such clothing should be removed promptly when exposed to the liquid, as skin irritations and burns occur only as a delayed reaction. When working with the gas, no special precautions are required, other than to insure adequate ventilation.

FIRST AID — Because of the nature and use of Ethylene Oxide sterilization mixtures, the probability of being over-

STERILIZING GAS MIXTURES

come or excessively exposed to the vapors of the mixture is unlikely. However, the following first aid suggestions are given for cases where severe exposure has occurred and are based on those recommended for Ethylene Oxide.

The suggestions herein are believed to be common practice in industry. Their adoption in any specific case should be subject to prior endorsement by a competent medical adviser. Summon a physician at once for anyone who has been overcome by Ethylene Oxide, or who has been burned as a result of skin contact with it. Prior to the physician's arrival, first aid measures should be started immediately.

Inhalation

In case breathing has stopped, artificial respiration should be started at once. After a severe exposure, pure Oxygen should be administered as soon as possible by trained personnel. The patient should breathe pure Oxygen under positive exhalation pressure for one-half hour periods every hour for at least three hours. If there are no signs of lung congestion at the end of this period, and if breathing is easy and the color of the skin and mucous membranes is good, Oxygen inhalation may be discontinued. Throughout this time, the patient should be kept comfortably warm, but not hot.

Skin Contact

All clothing contaminated with liquid Ethylene Oxide or exposed to high concentrations of Ethylene Oxide vapors should be removed at once. Clothing, including shoes, should not be worn again until thoroughly aerated. Shoes

can seldom be decontaminated, and it is suggested that they be not worn again. All affected areas of skin should be thoroughly washed with soap and water.

Eyes

Ethylene Oxide, as liquid or vapor, is capable of producing eye damage. Should it reach the eyes, the eyes should be irrigated copiously with water for fifteen minutes.

The eyelids should be held apart during the irrigation, to insure contact of the water with all tissues of the surface of the eyes and lids. Should eye irritation persist, the eyes should be irrigated for a second period of fifteen minutes, and a physician, preferably an eye specialist, should be called in attendance.

ECONOMICS: Attached is a price list showing various typical sterilizing gases, prices for the various cylinder sizes available and prices for multiple cylinder orders.

Once the concentration of Ethylene Oxide is established from Fig. 1 or otherwise, calculation by equation (1) will then supply the information of the quantity of any sterilizing gas shown in the listing required for any sterilizer space. Knowing the total requirements and prices quoted herein, the economics of gas sterilization versus other known forms of sterilization can be compared.

All The Matheson Company, Inc. branches are equipped to supply all types of sterilizing gas mixtures and will be very happy to quote on special custom-made mixtures meeting your requirements.

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