STERILIZING GAS MIXTURE

FOR INDUSTRIAL USE IN COMMERCIAL GAS STERILIZERS

ACTIVE INGREDIENT
Ethylene Oxide . . 80 wt %
INERT INGREDIENT
Carbon Dioxide . . 20 wt %
NET CONTENTS 154 lbs.
E.P.A. REG. NO. 28472-4
E.P.A. EST. 28472-PA-1

[illegible]

DANGER: KEEP [illegible] Extremely flammable. [illegible] temperature above 125°F may cause bursting. Liquid and gas under [illegible] Keep away from heat, sparks and open flame. Breathing of vapor is harmful. Contact with skin or eyes may cause serious damage. Avoid contact. In case of contact, immediately remove all contaminated clothing and flush with plenty of water for at least fifteen minutes. If in eyes get medical attention. Instructions for use and other information are in Sterilizing Gas Brochure.

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Air Products

AIR PRODUCTS & CHEMICALS, INC. - SPECIALTY GAS DEPT.
P.O. BOX 351 - TAMAQUA, PENNSYLVANIA 18252

DANGER: KEEP OUT OF REACH OF CHILDREN

Extremely flammable. Exposure to temperatures above 125°F may cause bursting. Liquid and gas under pressure. Keep away from heat, sparks and open flame. Breathing of vapor is harmful. Contact with skin or eyes may cause severe damage. Avoid contact. In case of contact, immediately remove all contaminated clothing and flush with plenty of water for at least fifteen minutes, for eyes get medical attention. Instructions for use and other information are in Sterilizing Gas Brochure.

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GASEOUS STERILIZATION
with
80% ETHYLENE OXIDE/20% CARBON DIOXIDE

Air Products and Chemicals

INTRODUCTION

The primary purpose of this brochure is to provide an understandable semi-technical explanation of the principals of ethylene oxide sterilization. It is impossible to comprehensively cover the subject in a brochure of this nature because of the wealth of knowledge that has developed since the investigations of Phillips & Kaye in 1949[1], demonstrated the bactericidal activity of ethylene oxide.

PENETRATIVE PROPERTIES OF ETHYLENE OXIDE

The penetration or diffusion of ethylene oxide through various materials has been studied in full detail. Ethylene oxide itself is highly penetrative and will diffuse from most commonly used packaging materials. There are several reports published on the diffusion of various gases through plastic films. Waak, et al[2] determined the permeability constance of ethylene oxide and other gases through several polymer films. However, the sterilization of materials wrapped in polymeric films or paper require quite an extensive study to determine the exposure times and temperatures necessary to achieve sterilization.

FLAMMABILITY

One of the major drawbacks of the use of ethylene oxide has to do with its explosive flammability. The mixture of 80% ethylene oxide and 20% carbon dioxide is extremely flammable. The vapors explode on exposure to open flame, electric spark, or other detonating agents. Also, certain materials can catalyze ethylene oxide polymerization, which in a confined space may take place with explosive force. Keep this product away from heat, sparks, open flame, and detonating agents.

CONDITIONS FOR ETHYLENE OXIDE STERILIZATION

Sterilization with ethylene oxide and mixtures of ethylene oxide is essentially the function of four variables.

1. Concentration
2. Time
3. Temperature
4. Humidity

A change in any one of these variables normally requires a change in one or more of the other.

1. Concentration

Current literature offers littl information available to indicate exactly how much ethylene oxide is required to destroy a single bacterial cell. It is generally assumed that as the concentration of ethylene oxide is increased, it has a higher rate of lethal activity on the bacteria. For sterilization purposes, ethylene oxide concentrations of 450 to 1000 milligrams/liter of chamber space are required to effect a 100% kill (1 milligram/liter = 1 oz./1000 cu.ft.). As the concentration of ethylene oxide is increased, the time of exposure or time required for sterilization is usually reduced, doubling the concentration generally reduces the exposure time by one-half. It is also known that sterilization with gaseous ethylene oxide can be achieved in shorter periods when the ethylene oxide concentration is increased to higher levels. However, it should be mentioned that from a physical standpoint an increase in ethylene oxide concentration will usually result in an increase in chamber pressure. In this case, an increase in the temperature may be required in order to maintain the gas in the vapor state. Figure #1 shows ethylene oxide concentration in the sterilizing chamber as a function of chamber pressure at four different temperatures. These curves have been developed, assuming that the gas mixtures behave as ideal gases. Please note that the graph is indicated in psia meaning that the initial sterilizer absolute pressure must be added to the graph value to determine the final sterilizer pressure. The following equation[3], can be used to calculate the pounds of sterilizing gas mixture needed for any sterilizer.

EQUATION AND EXPLANATION

$$\text{LBS MIXTURE NEEDED} = \frac{.00624\ CV}{E}$$

C = Concentration of ETO in sterilizer space, mg/l

E = Percent ETO concentration in sterilizing mixture

V = Sterilizer volume, cu.ft.

2. Exposure Time

Some period of time is required for the ethylene oxide gas to react with and destroy microorganisms. As a result, ethylene oxide sterilization is not a rapid process. 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. The following table[3] illustrates relative exposure time to kill various types of organisms.

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	5X
Bacillus subtilis	5X

This time period, however, is dependent upon several factors including the level and degree of hydration present and the influence of all the other factors. A standard exposure period for ethylene oxide can not be formulated for all products or articles.

3. Temperature

It is known that sterilization can be affected with ethylene oxide at 70°F but rather long exposure periods are required. It is also well established that as the temperature is raised, the rate of sterilization for destruction of microorganisms is increased. With gaseous sterilization with ethylene oxide, the temperature also plays an important role in that it effects the permeability of ethylene oxide to the bacterial cell walls, as well as through the packaging materials. Function of the temperature to the ability of the ethylene oxide to sterilize was described in a report by Phillips & Kaye.[1]

Generally, ethylene oxide sterilization is conducted at temperatures of 120—150°F. There are some special instances where ethylene oxide sterilization is conducted at lower temperatures due to the heat stability of certain materials.

Generally, for every 30°F rise in temperature, time required for sterilization is halved.[3]

Phillips[1] demonstrated that the temperature effect concerning the ability of ethylene oxide to sterilize is increased by a factor of 2.74 for every 10° rise centigrade in temperature in the range of a complete kill of bacterial spores. The temperatures in the range of 120—150°F are usually employed.

4. Humidity

Humidity is an essential element in achieving sterility with ethylene oxide vapors. It has been shown[1] that relative humidity in the range of 20—50% is required for maximum sterilization efficiency. The influence which moisture has on gas sterilization has been the subject of many studies and reports and literature. It has also been found that humidity during the gas exposure period may not be sufficient in itself to make the ethylene oxide sterilizing procedure effective against dry spores. Preconditioning of the materials may be necessary.

Preconditioning

Dry bacteria spore are especially resistant to ethylene oxide sterilization and may require a preconditioning with water or humidity. Ethylene oxide will not kill dehydrated spores. Instruments must be precleaned to remove adhering tissue and serous exudates. All instruments or articles must be presoaked in water for a minimum of one (1) hour immediately prior to exposure with ethylene oxide. Articles that cannot be immersed in water must be sterilized in an ethylene oxide device with a built-in automatic moisture-vapor pretreatment rehydration system.

5. Residuals

Many materials readily absorb ethylene oxide and must be properly treated by aeration prior to reuse. However, one of the advantages of using ethylene oxide is its ability to rapidly dissipate from exposed materials on removal from a sterilizing chamber. The quantity of ethylene oxide retained in materials and the rate at which it dissipates from these materials following exposures is important. Adequate investigation of the residuals and the rate of dissipation is necessary.

ETHYLENE OXIDE STERILIZING EQUIPMENT

There is a number of competent companies specializing in the manufacturing of sterilizing equipment for the utilizing of ethylene oxide sterilizing gases. We suggest your contacting one of the following manufacturers for full information on sterilization equipment -

1. American Sterilizer Co.
   Erie, Pa.
2. Castle Corp.
   Rochester, N. Y.
3. Environmental Tectronics
   Southampton, Pa.
4. Griffith Laboratories
   Chicago, Ill.
5. Vacudyne Corp.
   Chicago Heights, Ill.

Articles that can be sterilized with ethylene oxide -

Ethylene oxide can be used in the sterilization of plastics, rubber, metals, leather, wood, wool, rayon, nylon, glass, and virtually all other materials.

Typical items which can be sterilized by ethylene oxide are as follows -

1. Pharmaceutical processors -

   Plastic vials, plastic tubing and droppers, intravenous injection sets, antibiotics and other drugs, rubber materials, hypodermic needles and syringes.

2. Medical supply manufacturers -

   Rubber materials, plastic bandages, plastic vials and tubing.

3. Hospitals and laboratories -

   Hospital items, catheters, surgical instruments, intravenous injection sets, hypodermic needles and syringes, rubber gloves, telescopic instruments, mattresses, clothing, heart/lung machines.

4. Laboratory items -

   Glassware, petri dishes, animal bedding.

5. Hospital equipment -

   Face masks, suction catheters, reservoir bags, scalpel blades.

While the list of materials that can be sterilized with ethylene oxide is endless, these are just a few of the materials that are presently being sterilized with ethylene oxide.

USE INSTRUCTIONS

This particular mix, much richer in ethylene oxide than the usual mixes, is intended for commercial or industrial sterilization use. It is not adaptable to the type of gas sterilizer commonly used in hospitals. It can be considered as a replacement for pure ethylene oxide in its commercial applications, rather than a replacement for mixes containing a high (90% or slightly less) amount of carbon dioxide or one of the fluorinated hydrocarbons. In these mixes the large amount of diluent acts to reduce or eliminate flammability, as well as acting as a propellent. With only 20% carbon dioxide in this mix the flammability is essentially the same as that of pure ethylene oxide gas. As little as 3% of ethylene oxide vapor by volume in air will support combustion if confined.

While ethylene oxide is a gas at most ambient temperatures, boiling at 51.3°F or 10.7°C, it has a vapor pressure of only 7.3 psig at 70°F. As the vapor expands in propelling the liquid from its container, it quickly cools to its boiling point or below, and is expelled and vaporized quite slowly. The 20% carbon dioxide will make the transfer and vaporizing of the ethylene oxide much simpler and more rapid.

The chambers used in industrial sterilization are usually specially designed and constructed. Because of the flammability of this mix the air must be evacuated before the mix is added, and provision must exist for venting the gas mixture safely outdoors before air is readmitted and the chamber is opened. This means that the chamber must be strong enough to withstand not only a high vacuum, but also the desired operating gas pressures with sufficient margins of safety. As with all ethylene oxide sterilization procedures, provision for moisture control must be provided. This is even more important with vacuum chambers since water vapor as well as air is removed during the evacuation process, and the ethylene oxide-carbon dioxide mix contains no moisture. If the sterilization process is to be carried out at higher than ambient temperatures, heating provisions and controls must also be provided. One convenient method is to inject low pressure steam to the chamber to both raise temperature and add moisture before the gas is admitted.

There are two methods by which the ethylene oxide concentration within the chamber can be regulated. With the internal dimensions of the chamber known and the volume taken up by the load subtracted, the amount of gas admitted can be controlled by the weight loss of the container. A second method, which is independent of the void volume inside the chamber, is to measure the pressure within the chamber. With any gas the concentration is directly related to the pressure it exerts. The concentration of ethylene oxide in milligrams per liter is given for various pressures and temperatures ranging from ambient to 130°F, graphically in Figure I and numerically in Table I. As can be seen the ethylene oxide pressure-concentration values do not vary greatly over this range. These values are given in psia terms, but it must be remembered that they are the absolute pressures over and above the residual pressure after the vacuum has been pulled. This will probably be around 4 psia.

The sterilization rate is no different than with any other ethylene oxide process, remembering that the bactericidal action is dependent upon the ethylene oxide only. While the pressures with this mix, as with other mixes, are largely dependent upon the diluent concentration, carbon dioxide and other diluents have no effect on the sterilization process. Sterilization times are primarily dependent upon ethylene oxide concentration, temperature and, as is not so well recognized, the contamination level. The destruction of microorganisms is a logarithmical process, similar to radiological decay. It is usually measured as a decimal reduction time, or D value. That is the time required for the number of survivors to be reduced to 1/10 of their previous value.

As is generally known, when the concentration of ethylene oxide is doubled the exposure time can generally be halved. In other words the product of the concentration and the time to reach sterility is approximately a constant. This relationship does not hold however at very short exposure times. Apparently some time must elapse for penetration to occur both to the microorganisms and through the cell wall, and this time is not particularly affected by concentration.

At 25°C the concentration-time product to drop the number of surviving microorganisms six D values, or from an initial contamination load of one million (the number usually present on spore strips) to one survivor or less, is about 1,000 milligrams/liters x hours. At 130°F this value drops to around 350 to 400 mg/l x hr. Thus at this temperature and a concentration of 350 mg/l sterile spore strips can be expected in one hour. However to provide a suitable margin of safety these values are usually doubled or tripled in operating instructions, especially for hospital use.

With this mix the usual recommended sterilization times may not necessarily be so long at any particular concentration and temperature because of the following reasons. In repetitive industrial operations, the average contaminate levels, and the type of contamination, can usually be rather well controlled on the objects being sterilized. This can usually be kept far below the one million highly resistant organisms found on spore strips. Moreover in industrial practice better control can be maintained since monitoring is usually done by sterility testing on a predetermined number of items removed from each sterilization lot. Thus more realistic safety factors can be set.

This is brought out because it is not advisable to over-treat. Not only is it wasteful in time and the amount of gas used, but may result in more adsorbed gas with certain materials, and greater aeration residue problems.

HANDLING AND STORAGE OF ETHYLENE OXIDE CYLINDERS

The following general rules should apply to the handling and storage of ethylene oxide and ethylene oxide sterilizing gas mixtures cylinders. Further details concerning the handling and storage of flammable gases and all other gases are available through Air Products.

1. Do not use open flame heaters, exposed element electric heaters, or any spark producing electrical equipment such as electrical motors with exposed brushes. Use fans with induction type or seal type motors. Cylinders should be stored in a well ventilated area. When discharged from a cylinder in a confined space, the gas replaces the air and may be harmful. Do not breathe vapors.

2. Cylinder valve opens by turning to left or counterclockwise. Always open the cylinder valve wide when discharging contents. Do not retard flow of gas from cylinder by throttling cylinder valve or by using pressure regulators.

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

4. Never tamper with the safety devices and valves or cylinders.

5. Avoid dragging, rolling or sliding cylinders even for a short distance. They should be moved safely using a suitable hand truck. Cylinders should be stored in a specific area. The area should be dry, cool, well ventilated, and preferably fire resistant. Keep

the cylinders protected from excessive temperature rise by storing them away from sources of heat. Storage conditions should comply with local and state regulations, as well as good manufacturing practices.

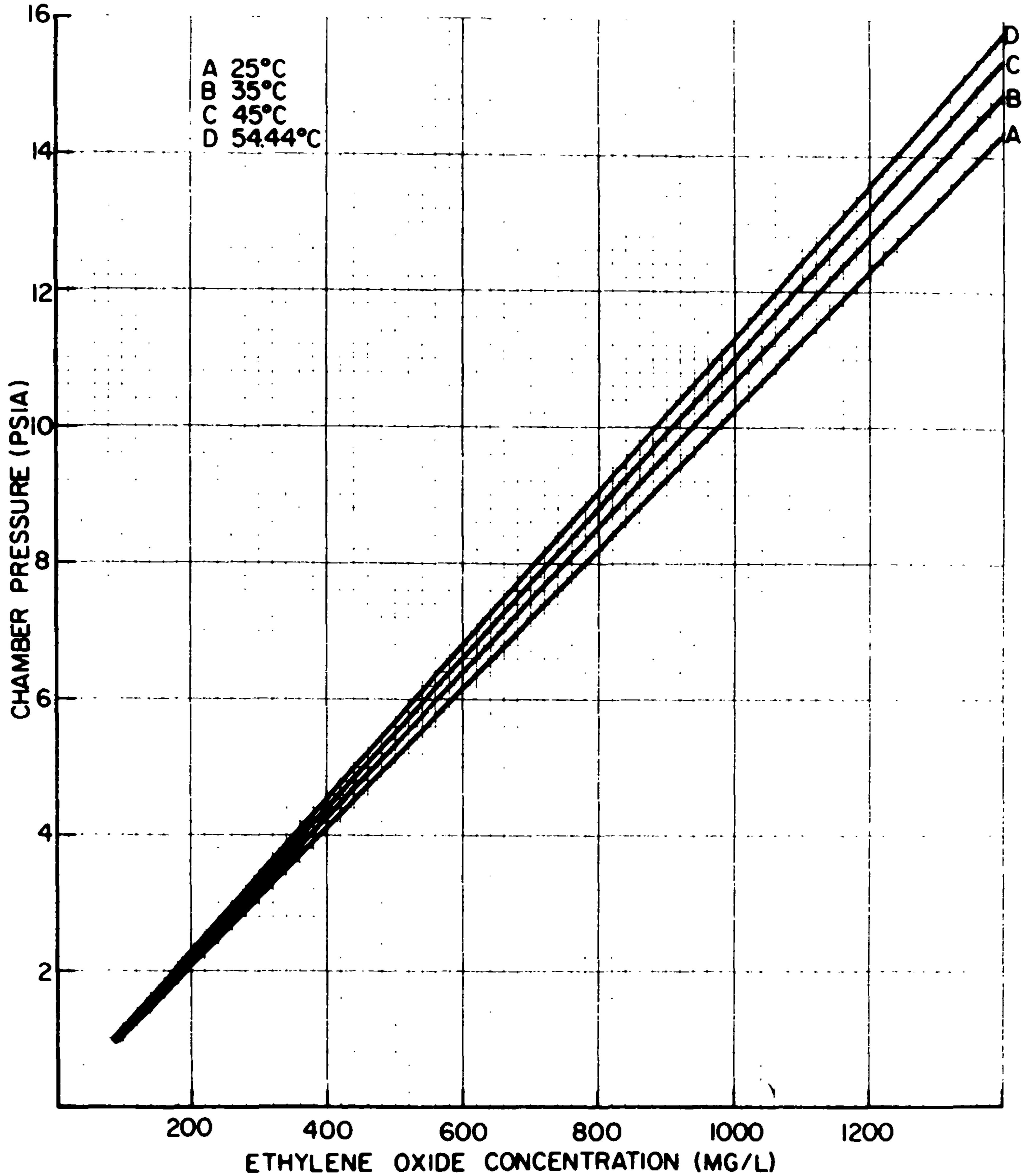
6. No part of the cylinder should be subject to a temperature higher than 125°F. Temperatures in excess of this figure may cause the cylinder to become liquid full, resulting in excessive hydrostating pressure buildup. Never permit a flame to come in contact with any part of a compressed gas cylinder. Use only metal connections and piping capable of withstanding the working pressure of the gas. Never use rubber tubing hose or gaskets.

7. Cylinder must be secured in an upright position when discharging and must be grounded before discharging in order to avoid static sparks.

8. Cylinder valves comply with all insurance requirements, laws, and regulations pertaining to fumigation and vacuum sterilization.

FIGURE I

ETHYLENE OXIDE CONCENTRATIONS VS CHAMBER PRESSURE 80% ETO/20% CO_2



ETO CONCENTRATION

80% ETO/20% CO_2

Chamber Pressure PSIA	ETO Conc. (Mg./L) 25°C 77°F	35°C 95°F	45°C 113°F	54.44°C 130°F
1	97.9	94.8	91.8	89.0
2	195.9	189.6	183.6	178.5
3	293.8	284.4	275.5	268.0
4	391.8		367.3	357.0
5	489.9	474.0	459.1	446.2
6	587.9	568.8	550.9	535.1
7	685.9	663.6	642.8	624.3
8	783.9	758.5	734.6	713.5
9	881.9	853.3	826.5	802.7
10	979.9	948.1	918.3	889.6
15	1470.0	1422.1	1377.4	1338.6
20	1959.8	1898.1	1836.6	1784.3
25	2449.6	2370.2	2295.7	2231.0
30	2939.6	2844.2	2754.9	2674.1

REFERENCES

1. Phillips, Charles R., and Kaye, Saul: "The Sterilizing Action of Gaseous Ethylene Oxide", Am. J. Hyg. 50: 270-306, 1949

2. Waak, R., Alex, H. H., et al., "Permeability of Polymer Films to Gases and Vapors", Indus. and Eng. Chem. 47: 2524-2527, Dec. 1955

3. Gabel, Hospital Topics, 1958