Inspections, Compliance, Enforcement, and Criminal Investigations

Ethylene Oxide Sterilization 1 Calculation of Initial Gas Concentration

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DEPT. OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION *ORA/ORO/DEIO/IB*

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ITG SUBJECT: ETHYLENE OXIDE STERILIZATIONS I.

Calculation of Initial Gas Concentration

Introduction

During investigations of firms that sterilize medical products with ethylene oxide, there is a frequent need to verify process data as furnished by the firm. It is important to make check calculations and report the ethylene oxide (ETO concentrations inside the sterilizers. In this ITG, we provide two elementary methods for determining this concentration a) by means of weight, and b) by means of the Ideal Gas Law. A third method for gas mixtures requires graphical aids, and will be provided in another ITG issue.

Calculation by Weight

A quick method for estimating the initial gas concentration can be shown as follows: given 600 1bs. of Benvicide {{Registered Trademark}}, a commercial gas mixture containing 11% ETO, in a 1348 ft 3 sterilizer, one can use a conversion factor \a\ of 16,000 to convert this concentration to units commonly expressed in mg/L.

$$\text{Concentration} = \frac{\text{Wt (1bs)} \times \text{(ETO fraction)} \times \text{(factor)}}{\text{Volume (ft 3)}}$$

$$= \frac{600 \times 0.11 \times 16{,}000}{1348\ \text{mg/L}} = 785$$

This is an accurate method when careful weights are taken for the drums (or cylinders) before and after "charging" the sterilizer.

Calculation by Ideal Gas Law

In the event that 100% ETO is used, and temperatures and pressures are known, the concentration can be estimated by the Ideal Gas Law (PV=nRT) \b\. Given a pressure differential (i.e., that increase in the chamber pressure due to addition of 100% ETO) of 16 in. Hg., at a 41 C temperature, the calculation is as follows:

$$n = \frac{P\ (\text{Atm}) \times V\ (\text{L})}{} = \frac{16/29.9 \times 1}{} = 0.0208\ \text{mols ETO in one Liter}$$

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R x T ( K)          0.082 x 314
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The molecular weight of ETO is 44 gm. Then each mol contains 44,000 mg. The concentration for each liter is 0.0208 mol/L x 44,000 mg/mol = 915 mg/L ETO.

Discussion

Use of ethylene oxide gas requires an additional degree of sterility assurance above that required by steam processes. For example, the USP XVIII places this procedure in category II requiring more sterility test units per se o the use of biological indicators in each batch to be sterilized. More emphasis is directed to monitoring the sterilizing parameters of gas concentration, time of exposure, temperature of reaction, moisture, barriers to gas penetration, and the degree of microbial resistance to the process.

The FDA has not established official guidelines or limiting parameters for ETO concentrations as of this date. Althoug Perkins \c\ has stated that ETO concentrations of 450 to 1,000 mg/L are required to effect a 100% kill of bacterial contaminants, it is emphasized that a process cannot be sanctioned or condemned by comparison with ETO concentration ranges found in the literature.

The customary inspectional approaches are still necessary to gather the data for full evaluation of the sterilization cycles. It is hoped that a knowledge of suggested concentration ranges will help in judging the reasonableness of th concentrations which are encountered.

In practice, exposure is determined experimentally for each product using test results from appropriate microbiologica studies. During production, spore strips or other biological indicators are useful in addition to regular production testing, when placed into the innermost portions of the product.

_____ \a\ This conversion factor is derived as follows:

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454 g/1b x 1,000 mg/g x 1,000 ml/L          ft 3 mg


--------------------------------- = 16,000 ------- (Rounded off)

1728 cu in/ft 3 x 16.39 ml/cu in            1b L
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\b\ P = Pressure differential (29.9 in. Hg. = 1 Atm.) T = Kelvin or (273 + C) V = Volume. Assume 1 L R = Ideal Gas Constant (0.082 L Atm. deg. -1 mole -1)*\

*\Daniels, Farrington; Outlines of Physical Chemistry, John Wiley & Sons, Inc. (1948), p. 9. \c\ Perkins, John J.; Principles and Methods of Sterilization in Health Sciences, Charles C. Thomas Co., (1969), p. 508.

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