Technical Information Report

AAMI TIR16: 2017

Microbiological aspects of ethylene oxide sterilization

AAMI
Advancing Safety in Health Technology

AAMI Technical Information Report

AAMI TIR16:2017
(Revision of AAMI TIR16:2013)

Microbiological aspects of ethylene oxide sterilization

Approved 17 November 2017 by
Association for the Advancement of Medical Instrumentation

Abstract: Addresses various microbiological aspects of the development and validation of an ethylene oxide sterilization process. Does not address the various factors that can have an effect on the bioburden of the product and on the sterilization process. Provides additional guidance to ANSI/AAMI/ISO 11135:2014 for medical device manufacturers, including those that use contract sterilization facilities or contract sterilization operations.

Keywords: sterilization, microbiological aspects, validation, ethylene oxide, bioburden, performance qualification

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Published by

AAMI
4301 N. Fairfax Drive, Suite 301
Arlington, VA 22203-1633
www.aami.org

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Printed in the United States of America

ISBN 978-1-57020-691-7

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www.aami.org/standards/glossary.pdf

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Committee representation

Association for the Advancement of Medical Instrumentation

Industrial Ethylene Oxide Sterilization Working Group

This technical information report (TIR) was developed by the Association for the Advancement of Medical Instrumentation (AAMI) Industrial Ethylene Oxide Sterilization Working Group under the auspices of the AAMI Sterilization Standards Committee. Working Group approval of the TIR does not necessarily imply that all committee members voted for its approval.

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NOTE Participation by federal agency representatives in the development of this technical information report does not constitute endorsement by the federal government or any of its agencies.

Foreword

This document is part of a series of technical information reports (TIRs) intended for use in conjunction with ANSI/AAMI/ISO 11135:2014. The other reports in the series are listed below:

— AAMI TIR14:2009, *Contract sterilization using ethylene oxide*

— AAMI TIR15:2009, *Physical aspects of ethylene oxide sterilization*

— AAMI TIR28:2009/(R)2013, *Product adoption and process equivalence for ethylene oxide sterilization*

— AAMI TIR39:2009, *Guidance on selecting a microbial challenge and inoculation sites for sterilization validation of medical devices*

— AAMI TIR56:2013, *Guidance for the development, validation and routine control of an ethylene oxide sterilization process utilizing flexible bag systems for the sterilization of medical devices*

The original TIR16, along with other AAMI TIRs, provided additional guidance to the 1994 edition of the industrial EO sterilization standard 11135, which was revised in 2007 under a new designation, ANSI/AAMI/ISO 11135-1:2007, *Sterilization of health care products—Ethylene oxide—Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*. In 2008, ISO published its own guidance document for the 11135 standard, ISO/TR 11135-2:2008*, Sterilization of health care products—Ethylene oxide—Part 2: Guidance on the application of ISO 11135-1*, which was based to a great extent on the earlier AAMI technical information reports. ANSI/AAMI/ISO 11135-1:2007 and ISO/TIR 11135-2:2008 were revised into a single document: ISO 11135:2014.

This TIR provides guidance related to the microbiological aspects of EO sterilization that is typically not covered in depth, or at all, in the existing guidance documents for EO sterilization. It is designed to provide information that will assist in design, qualification, and routine processing of EO sterilization processes. This TIR condenses pertinent information that may be available in a variety of sources in one location and is based on practices that have been found to be used successfully within the United States. This TIR contains guidelines that are not intended to be absolute or to apply in all circumstances. One should use judgment in applying the information in this TIR.

As used within the context of this document, “should” indicates that among several possibilities one is recommended as particularly suitable without mentioning or excluding others, or that a certain course of action is preferred but not necessarily required, or that (in the negative form) a certain possibility or course of action should be avoided but not prohibited. “May” is used to indicate that a course of action is permissible within the limits of the TIR. “Can” is used as a statement of possibility and capability. “Must” is used only to describe “unavoidable” situations, including those mandated by government regulations. See also the NOTE on Page 1.

Suggestions for improving this technical information report are invited. Comments and suggested revisions should be sent to AAMI, 4301 Fairfax Drive, Suite 301, Arlington, VA 22203.

NOTE This foreword does not contain provisions of AAMI TIR16:2017, *Microbiological aspects of ethylene oxide sterilization*, but it does provide important information about the development and intended use of the document.

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Microbiological aspects of ethylene oxide sterilization

NOTE This technical information report is not a standard, and the material contained herein is not normative in nature. The committee has used the term "shall" in a few instances, based on their knowledge of requirements contained in relevant standards and regulatory requirements.

1 Scope

This technical information report (TIR) addresses various microbiological aspects of the development and validation of an ethylene oxide (EO) sterilization process. It does not cover the various factors that can have an effect on the bioburden of the product and on the sterilization process. This TIR provides additional guidance to ANSI/AAMI/ISO 11135:2014 for medical device manufacturers, including those that use contract sterilization facilities or contract sterilization operations.

Although the information presented was developed for application to medical devices, the content of this guideline may also be applied to other relevant products or materials.

Products that have been used in a healthcare setting and are being presented for resterilization in accordance with the manufacturer's instructions (see ANSI/AAMI/ISO 17664) are a special case. There is the potential for such products to possess a wide range of contaminating microorganisms and residual inorganic and/or organic contamination in spite of the application of a cleaning process. Hence, it is important to pay particular attention to the validation and control of the cleaning and disinfection processes used during reprocessing. Healthcare facilities are encouraged to review AAMI ST35, TIR30, and TIR34 for additional information on handling reusable or non-sterile devices requiring sterilization processing.

2 Terms and definitions

For the purposes of this TIR, the terms and definitions in ANSI/AAMI/ISO 11135: 2014 and the following apply.

2.1 **compromised tissue**: Skin or mucous membrane that has been intentionally or accidentally opened, exposed, or breached

2.2 **inoculated carrier:** Supporting material on or in which a defined number of test organisms has been deposited

3 Process and equipment characterization

3.1 Sterilization equipment

Guidelines for equipment selection can be found in AAMI TIR15 and EN 1422. Careful selection of the sterilizing equipment and development of the facility design will enable a manufacturer to process a product safely and effectively.

3.2 Process characterization—Physical parameters

3.2.1 Introduction

The variables that have a significant effect on the lethality of an ethylene oxide (EO) sterilization process are EO concentration, temperature, EO exposure time, and often relative humidity (RH). These variables are interrelated and a change in one can often be compensated for by a change in another. Other aspects that might affect lethality are the actual depth and rate of evacuations during the sterilant-removal phases as evacuations can be affected by chamber temperature, humidity, sterilant levels, vacuum pump performance, and/or product load configuration.

3.2.2 EO concentration

Common practice is to develop and qualify cycles using an EO concentration ranging from 400 to 650 milligrams per liter (mg/L), because concentrations in this range have been found to achieve microbiological lethality for most products within a reasonable and practical exposure time. When lower EO concentrations are necessary due to product or process considerations, the exposure time might need to be increased to achieve the same lethality; however, the time increase can be mitigated if the temperature of the process can be increased sufficiently.

Using a gas mixture other than 100 % EO can result in some differences in lethality due to a relief of the vacuum by a mixture of diluent gas and EO, potentially resulting in a lower EO concentration at locations within the product. These effects can also be seen in situations where an inert gas is used to maintain the pressure of the chamber during EO exposure. These effects can be minimized by the use of recirculation and compensating for the lower concentration of EO with an increase in the initial concentration or an increase in temperature.

When an inert gas is used to maintain the chamber pressure, it is important that the chamber recirculation system be sufficient to minimize risk and magnitude of stratification of the inert gas (e.g., nitrogen) and EO gas. In mixed sterilant gas processes, the makeup gas will replace only a fraction of the EO absorbed, and the EO concentration in the chamber could decrease with time.

The minimum gas concentration or partial pressure used in process definition should be considered for microbiological performance qualification (MPQ) to challenge the tolerance for lethality. If the MPQ is successful, this parameter may be used to establish the lower limit for routine sterilization. EO concentration and RH can be calculated as prescribed in AAMI TIR15, or they can be directly measured.

NOTE Using a gas mixture other than 100 % EO might result in some differences in lethality.

3.2.3 Relative humidity

The resistance of microorganisms to deactivation by EO is affected by available water activity. At low levels of humidity, below 30 %, process lethality might be reduced, which might be expressed as a tailing effect on the lethality curve. RH in excess of 30 % in the chamber is commonly used to help moisture adsorption on difficult-to-sterilize regions of the product. Preconditioning is a means of increasing the humidity of the load, which might allow for less conditioning in the chamber during the sterilization cycle. If a preconditioning process is conducted outside the chamber, a maximum transfer time to the chamber should be established to minimize humidity loss (e.g., typical transfer time is 60 minutes or less to minimize humidity loss within the product load).

Cycles that result in very high levels of humidity in the product should be taken into consideration during process definition, because excessive moisture can compromise the product, the packaging, or both, and can adversely affect EO transfer to product surfaces.

The use of dry inert gases during the initial vacuum and conditioning can desiccate the product and thus reduce process effectiveness. The use of humidified inert gas or steam injection before and/or after inert gas addition can help minimize desiccation of the product, package, and bioburden.

3.2.4 Temperature

The temperature of the sterilization process has a significant effect on its microbiological lethality. A temperature increase of 10 °C can result in an approximate doubling of the lethality of the process. See information on Q_{10} or temperature coefficient in *Harper's Illustrated Biochemistry* (Murray, Rodwell, Bender, Botham, Weil, and Kennelly, 2009) and Parisi and Young in Block (1991). A higher sterilization temperature will allow a shorter exposure time and might also allow for a reduction in the EO concentration. However, many products (including their packaging) have temperature limitations. This may limit the sterilization parameters that affect product temperature, such as chamber temperature and steam injection. The minimum temperature of the product load entering the sterilization process should be established during process definition or validation to ensure that the appropriate minimum load conditions for lethality can be achieved during routine processing. Preconditioning is a means of increasing the load temperature, which reduces the amount of in-chamber conditioning required.

If a preconditioning process is conducted outside the chamber, the effect of transfer time on the load temperature should be considered in determining the transfer time to be used for development and qualification studies. The maximum transfer time should be established to minimize heat loss (e.g., typical transfer time is 60 minutes or less to limit temperature loss within the product load). A long loading time could allow additional heat migration to the center of the load if the load temperature has not stabilized before transfer from preconditioning. A long chamber loading time could result in the loss of heat and humidity from the exterior of the load. If preconditioning is not conducted outside the chamber, then in-chamber conditioning should be used to achieve the minimum product temperature and humidity before the gas exposure time is initiated.

During the performance qualification (PQ), the product temperature should be measured to verify that the specified product temperature can be reproduced during the exposure phase in the cycle. Sterilization cycle lethality could be evaluated at the low end of the process temperature range and minimum tolerances of the preconditioning process time.

3.2.5 EO exposure time

Process definition should determine the EO exposure time requirements that are necessary to provide the required sterility assurance level (SAL) throughout the sterilization load.

NOTE Lethality occurs not only during the defined exposure time but also during the sterilant injection time; the inert blanket injection time, if used; and the sterilant removal time. When optimizing certain cycles, these effects should be taken into consideration to determine an accurate Spore Log Reduction (SLR), *D*-value, or SAL. Lethality that occurs during the aeration phase of the process (if used) might also need to be considered.

4 Process definition

The purpose of this activity is to define the entire sterilization process and the equipment necessary to deliver the sterilization process reproducibly to meet the required SAL.

4.1 Considerations for process definition

The goal of process definition is to establish detailed specifications for the sterilization process to be used in the PQ of the defined product. Selection of the process definition method is based on many factors, including the nature of product bioburden, product design, packaging, manufacturing conditions, sterilizing equipment, and cost. The parameters necessary to deliver the required SAL for the product are generally developed using methods discussed in ANSI/AAMI/ISO 11135, ANSI/AAMI/ISO 14161, Pflug (2007), Block (2000), and other AAMI TIRs.

4.1.1 Ethylene oxide exposure parameters

Ethylene oxide cycle exposure time is calculated using the process definition information and taking into account the SAL for the product involved. The more commonly recognized SALs include the following:

a) SAL of 10^{-6} for products that come into contact with compromised tissue or normally sterile parts of the body; and

b) SAL of 10^{-3} for products that *do not* come into contact with compromised tissue or normally sterile parts of the body.

NOTE The SAL for products labeled “sterile” is typically 10^{-6}. If further information is desired on sterility assurance levels for products in the United States, please see ANSI/AAMI ST67. The SAL requirement for products labeled sterile could be different outside the United States.

Products with more than one SAL ─ some products have multiple items or components that are designed to be used for different purposes. In kits, items that are to be used on intact skin or mucous membranes or that are not intended to have patient contact might have different SAL requirements from those components that are intended to have internal tissue, neural, or blood contact. The sterilization process should deliver the required lethality to each component on the basis of the intended use of the device.

4.1.2 Product packaging

The packaging should allow removal of air and penetration of heat, humidity and EO and be capable of tolerating vacuum/pressure differentials and evacuation/pressurization rates. The use of adhesive labels on the breathable portion of the packaging could adversely affect the delivered lethality, as well as restrict the ability of the package to withstand the pressure and vacuum changes.

4.1.3 Load configuration

The load configuration should be designed to facilitate air removal, EO/heat/RH penetration, and subsequent removal of EO during the sterilization process.

4.1.4 Process development method

The selection of the method utilized for process definition might depend on the level and types of bioburden on the product to be sterilized, as well as on the product limitations and desired efficiency for the process. The overkill half cycle method typically results in longer exposure times and/or more rigorous cycle parameters, while the overkill