Microbiological aspects of ethylene oxide sterilization

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 11135:2007 and ANSI/AAMI/ISO TIR11135–2:2008 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
AAMI Technical Information Report

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## Glossary of equivalent standards

International Standards adopted in the United States may include normative references to other International Standards. For each International Standard that has been adopted by AAMI (and ANSI), the table below gives the corresponding U.S. designation and level of equivalency to the International Standard. NOTE: Documents are sorted by international designation.

Other normatively referenced International Standards may be under consideration for U.S. adoption by AAMI; therefore, this list should not be considered exhaustive.

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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 11135-1:2009. 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, Product adoption and process equivalence for ethylene oxide sterilization; and

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. Correspondingly, the AAMI Industrial EO sterilization working group is updating its TIRs to take into account changes to the 11135 standard as well as to avoid redundancy with ANSI/AAMI/ISO TIR11135-2:2008.

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 TIR16:2009, Microbiological aspects of ethylene oxide sterilization, but it does provide important information about the development and intended use of the document.
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 11135-1:2007 and ANSI/AAMI/ISO TIR11135-2:2008 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.

2 Terms and definitions

For the purposes of this TIR, the terms and definitions in ANSI/AAMI/ISO 11135–1 and ANSI/AAMI/ISO TIR11135–2 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 TIR15:2009 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 ethylene oxide (EO) concentration, relative humidity (RH), temperature, and EO exposure time.

EO concentration and RH may be calculated as prescribed in AAMI TIR15:2009, or they may be directly measured. It is recommended that evacuation and injection rates be established to define their effect on the cycle lethality throughout the program. The use of controlled evacuation and injection rates minimizes the potential for package and product damage. These rates should be incorporated in the final process specifications as appropriate for chamber parameters. It is also important to remember that the actual depth and rate of evacuations might be different for the air-removal versus the sterilant-removal phases, because the product and packaging have been exposed to increased temperature, humidity, and sterilant levels prior to the sterilant-removal phase.

3.2.2 EO concentration

Common practice is to develop and validate 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 may need to be increased to achieve the same lethality; however, the time increase may be mitigated if the temperature of the process can be increased sufficiently.