List of Titles

Technical Information Report

AAMI TIR28:2001

Product adoption and process equivalency for ethylene oxide sterilization

AAMI
Association for the Advancement of Medical Instrumentation

AAMI Technical Information Report AAMI TIR28:2001

Product adoption and process equivalency for ethylene oxide sterilization

Approved 24 December 2001 by
Association for the Advancement of Medical Instrumentation

Abstract: This AAMI technical information report (TIR) provides guidance for the adoption of a new or modified product into an existing validated sterilization process and for the determination of equivalency of a sterilization process as conducted in different equipment. Its guidance is intended to augment ANSI/AAMI/ISO 11135:1994, *Medical devices—Validation and routine control of ethylene oxide sterilization,* and to expand on the areas of product adoption and process equivalency that are not addressed in ANSI/AAMI/ISO 11135:1994.

Keywords: adoption, equivalency, process equivalency, product adoption, product family

List of Titles

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List of Titles

Contents

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.

International designation	U.S. designation	Equivalency
IEC 60601-1-2:2001	ANSI/AAMI/IEC 60601-1-2:2001	Identical
IEC 60601-2-21:1994 and Amendment 1:1996	ANSI/AAMI/IEC 60601-2-21 & Amendment 1:2000 (consolidated texts)	Identical
IEC 60601-2-24:1998	ANSI/AAMI ID26:1998	Major technical variations
ISO 5840:1996	ANSI/AAMI/ISO 5840:1996	Identical
ISO 7198:1998	ANSI/AAMI/ISO 7198:1998/2001	Identical
ISO 7199:1996	ANSI/AAMI/ISO 7199:1996	Identical
ISO 10993-1:1997	ANSI/AAMI/ISO 10993-1:1997	Identical
ISO 10993-2:1992	ANSI/AAMI/ISO 10993-2:1993/(R)2001	Identical
ISO 10993-3:1992	ANSI/AAMI/ISO 10993-3:1993	Identical
ISO 10993-4:1992	ANSI/AAMI/ISO 10993-4:1993	Identical
ISO 10993-5:1999	ANSI/AAMI/ISO 10993-5:1999	Identical
ISO 10993-6:1994	ANSI/AAMI/ISO 10993-6:1995/(R)2001	Identical
ISO 10993-7:1995	ANSI/AAMI/ISO 10993-7:1995/(R)2001	Identical
ISO 10993-8:2000	ANSI/AAMI/ISO 10993-8:2000	Identical
ISO 10993-9:1999	ANSI/AAMI/ISO 10993-9:1999	Identical
ISO 10993-10:1995	ANSI/AAMI/ISO 10993-10:1995	Identical
ISO 10993-11:1993	ANSI/AAMI 10993-11:1993	Minor technical variations
ISO 10993-12:1996	ANSI/AAMI/ISO/CEN 10993-12:1996	Identical
ISO 10993-13:1998	ANSI/AAMI/ISO 10993-13:1999	Identical
ISO 10993-14:2001	ANSI/AAMI/ISO 10993-14:2001	Identical
ISO 10993-15:2000	ANSI/AAMI/ISO 10993-15:2000	Identical
ISO 10993-16:1997	ANSI/AAMI/ISO 10993-16:1997	Identical
ISO 11134:1994	ANSI/AAMI/ISO 11134:1993	Identical
ISO 11135:1994	ANSI/AAMI/ISO 11135:1994	Identical
ISO 11137:1995	ANSI/AAMI/ISO 11137:1994	Identical
ISO 11138-1:1994	ANSI/AAMI ST59:1999	Major technical variations
ISO 11138-2:1994	ANSI/AAMI ST21:1999	Major technical variations
ISO 11138-3:1995	ANSI/AAMI ST19:1999	Major technical variations

International designation	U.S. designation	Equivalency
ISO 11140-1:1995 and Technical Corrigendum 1:1998	ANSI/AAMI ST60:1996	Major technical variations
ISO 11607: 200x[1]	ANSI/AAMI/ISO 11607:2000	Identical
ISO 11737-1:1995	ANSI/AAMI/ISO 11737-1:1995	Identical
ISO 11737-2:1998	ANSI/AAMI/ISO 11737-2:1998	Identical
ISO TR 13409:1996	AAMI/ISO TIR13409:1996	Identical
ISO 13485:1996	ANSI/AAMI/ISO 13485:1996	Identical
ISO 13488:1996	ANSI/AAMI/ISO 13488:1996	Identical
ISO 14155:1996	ANSI/AAMI/ISO 14155:1996	Identical
ISO 14160:1998	ANSI/AAMI/ISO 14160:1998	Identical
ISO 14161:2000	ANSI/AAMI/ISO 14161:2000	Identical
ISO 14937:2000	ANSI/AAMI/ISO 14937:2000	Identical
ISO 14969:1999	ANSI/AAMI/ISO 14969:1999	Identical
ISO 14971:2000	ANSI/AAMI/ISO 14971:2000	Identical
ISO 15223:2000	ANSI/AAMI/ISO 15223:2000	Identical
ISO 15223/A1:2001	ANSI/AAMI/ISO 15223:2000/A1:2001	Identical
ISO 15225:2000	ANSI/AAMI/ISO 15225:2000	Identical
ISO 15674:2001	ANSI/AAMI/ISO 15674:2001	Identical
ISO 15675:2001	ANSI/AAMI/ISO 15675:2001	Identical
ISO TS 15843:2000	ANSI/AAMI/ISO TIR15843:2000	Identical
ISO TR 15844:1998	AAMI/ISO TIR15844:1998	Identical
ISO TR 16142:1999	ANSI/AAMI/ISO TIR16142:2000	Identical

[1] FDIS approved; being prepared for publication.

Committee representation

Association for the Advancement of Medical Instrumentation

AAMI Sterilization Standards Committee

This technical information report was developed by the AAMI Industrial Ethylene Oxide Sterilization Working Group under the auspices of the AAMI Sterilization Standards Committee. Approval of the TIR does not necessarily imply that all working group members voted for its approval.

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

Introduction

This document is part of a series of reports intended to be used in conjunction with ANSI/AAMI/ISO 11135:1994, *Medical devices—Validation and routine control of ethylene oxide sterilization*. The other reports in the series are:

— AAMI TIR14:1997, *Contract sterilization for ethylene oxide*

— AAMI TIR15:1997, *Ethylene oxide sterilization equipment, process considerations and pertinent calculations*

— AAMI TIR16:2000, *Process development and performance qualification for ethylene oxide sterilization—Microbiological aspects*, and

— AAMI TIR 20:2001, *Parametric release for ethylene oxide sterilization*.

This technical information report provides guidance for the adoption of new or modified products into an existing validated sterilization process and for the determination of equivalency of the sterilization process as conducted with different equipment. Although these areas are not specifically addressed by ANSI/AAMI/ISO 11135:1994 (AAMI, 1994), they are important industry practices that are used to reduce the expense and time associated with the validation process, and are based on accumulated process knowledge.

The adoption of a new or modified product into an existing validated sterilization process involves the determination that the product is no more of a challenge than the product that was used to validate the ethylene oxide (EO) sterilization process. Product adoption has been a longstanding practice in the industry. Although it has been addressed in individual papers (Lowery and DeRisio, 1982; Burgess and Reich, 1993) it has not been addressed in a guidance document. Therefore, this TIR will address how product can be adopted into an existing EO process.

The process equivalency section of this TIR will provide guidance on the level of validation testing required on the basis of the equivalence of the sterilization process and/or equipment. It will also provide guidance on how to determine the equivalence of the process and/or equipment.

NOTE—This TIR is considered “informative,” and the use of the terms “shall,” “should,” and so forth should be considered within the context of this TIR only. That is, if the decision is made to use a particular method presented in this TIR, then the method should be followed with adherence to the requirements (“shall”) and recommendations (“should”) as set forth in this TIR. The term “must” refers to regulatory requirements.

List of Titles

Product adoption and process equivalency for ethylene oxide sterilization

1 Scope

This TIR addresses medical devices that are processed by ethylene oxide sterilization using conventional or parametric product release. The document applies to the following situations for the sterilization of medical devices:

— a new product is being added to the previously validated process;

— changes to validated products are being evaluated;

— a previously validated process is being moved to a different facility and/or equipment; and

— equivalency of a sterilization process is being evaluated.

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. This document does not address the equivalency of two or more sterilization processes run in the same or different sterilization process equipment.

2 References and bibliography

ANSI/AAMI/ISO 10993-7:1995, *Biological evaluation of medical devices—Part 7: Ethylene oxide sterilization residuals, 2ed.*

ANSI/AAMI/ISO 11135:1994, *Medical devices—Validation and routine control of ethylene oxide sterilization, 3ed.*

ANSI/AAMI/ISO 11737-1:1995, *Sterilization of medical devices—Microbiological methods—Part 1: Estimation of population of microorganisms on products, 1ed.*

AAMI ST67:200X,[2] *Sterilization of medical devices—Requirements for products labeled 'STERILE.'* (In preparation.)

AAMI TIR14:1997, *Contract sterilization for ethylene oxide, 1ed.*

AAMI TIR15:1997, *Ethylene oxide sterilization equipment, process considerations, and pertinent calculations, 1ed.*

AAMI TIR16:2000, *Process development for ethylene oxide sterilization—Microbiological aspects, 1ed.*

AAMI TIR19:1998, *Guidance for ANSI/AAMI/ISO 10993-7:1995, Biological evaluation of medical devices—Part 7: Ethylene oxide sterilization residuals, 1ed.*

EN550:1994, *Sterilization of medical devices—Validation and routine control of ethylene oxide sterilization.*

Burgess DJ and Reich RR. Industrial Ethylene Oxide Sterilization. In Morrissey RF and Phillips GB, eds. *Sterilization technology: A practical guide for manufacturers and users of health care products.* New York, NY: Van Nostrand Reinhold, 1993.

Gillis J and Schmidt WC. Scanning electron microscopy of spores on inoculated product surfaces. *Medical Device and Diagnostic Industry.* June 1983, vol. 5, no. 6, pp. 46–49.

Lowery A and DeRisio R. *Adopting a device into a validated sterilization system*. Text of presentation at HIMA conference, April 1982, by A. Lowery.

West KL. Ethylene oxide sterilization: *A study of resistance relationships*. In Gaughran E and Kereluk K, eds. *Sterilization of medical products.* New Brunswick, NJ: Johnson & Johnson,1977.

[2] AAMI expects to publish this standard in the second quarter of 2002 following completion of appropriate approval processes.

3 Terms and definitions

For the purposes of this AAMI TIR, the following terms and definitions apply.

3.1 candidate equipment: New or modified piece of equipment proposed for delivering the existing validated sterilization process.

3.2 candidate product: New or modified product, including the packaging system, proposed for inclusion into the existing validated sterilization process.

3.3 installation qualification (IQ): Obtaining and documenting evidence that equipment has been provided and installed in accordance with its specifications.

3.4 load configuration: Totality of attributes defining the presentation of the product to the sterilization process. This configuration includes 1) the orientation of the product within the primary package; 2) the quantity and orientation of the primary package(s) within the secondary and tertiary package; 3) the quantity, orientation, and placement of the tertiary packages on the sterilizer pallets (or within the carriers); and 4) the quantity and placement of the pallets (or carriers) within the vessel or area.

3.5 operational qualification (OQ): Obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with operational procedures.

3.6 packaging system: Entire packaging for a product that consists of the sterile barrier (primary package), the carton or shelf pack (secondary packaging), and the shipping container (tertiary packaging). Secondary and tertiary packaging might not be used in the packaging of all products.

3.7 performance qualification (PQ): Obtaining and documenting evidence that the equipment, as installed and operated in accordance with operational procedures, consistently performs in accordance with predetermined criteria and thereby yields a product that meets specifications.

3.8 process challenge device (PCD): Object that simulates the worst case of conditions as they are given for the sterilizing agent(s) in terms of the goods to be sterilized.

Note 1—The design of the process challenge device depends on the kind of goods to be sterilized and the sterilization procedure. The device should be so constituted that a biological indicator can be arranged in the place most difficult for the sterilant to reach. The biological indicator should not interfere with the function of the process challenge device.

Note 2—In some process challenge devices, an inoculated carrier may be used in place of a biological indicator.

3.9 process equivalency: Documented evaluation that the same sterilization process can be delivered by two or more pieces of sterilization process equipment.

3.10 processing group: Collection of products or product families that can be sterilized in the same EO sterilization process. All products within the group have been determined to present an equal or lesser challenge to the sterilization process.

3.11 product adoption: Process of formally including a candidate product into an existing validated sterilization process.

3.12 product family: Collection of products that are determined to be similar or equivalent for validation purposes.

3.13 sterility assurance level (SAL): Probability of a viable microorganism being present on a product unit after sterilization.

NOTE—SAL is normally expressed as 10^{-n}.

3.14 sterilization process equipment: Preconditioning area (if used), chamber/sterilizer and aeration area, and their respective ancillary equipment.

3.15 sterilization specialist: Person who is knowledgeable, by training and experience, of the science of sterilization.

4 Product adoption

4.1 Introduction

Product adoption is the process of determining whether a candidate product can be included in an existing validated sterilization process by performing a documented evaluation. The determination involves comparing the relative resistance to the sterilization process of the candidate product versus the existing PCD. A sterilization specialist

performs this determination. If the candidate product cannot be adopted into the existing validated process, refer to ANSI/AAMI/ISO 11135:1994.

4.2 Families

Validating every individual product for placement within a product family is not feasible in many cases. Therefore, products are traditionally grouped together into product families and processing groups on the basis of similarities in configuration, materials, density, packaging, or difficulty of sterilization compared against a worst-case representative. Often, products within a family can consist of various combinations of similar items. For example, kits may contain various combinations of sponges, bowls, instruments, towels, drapes, and other items. The only difference between kits in a chosen family may be the types, quantities, and sizes of items included within the kits. These are product families and should not be confused with processing groups. A processing group is a collection of product families that may be dissimilar in details of construction or packaging. Each of the product families will have been qualified in a common sterilization process. For example, various IV sets may constitute a product family, and may be placed in a processing group that includes a product family of blood collection sets. The following list provides guidance to the elements that may be considered when placing products into families:

— product design;

— product function (end use);

— manufacturing method;

— manufacturing environment/area;

— material of construction;

— packaging materials;

— primary and/or secondary packaging configuration;

— density;

— size and/or surface area; and

— bioburden.

4.3 Determination of adverse effects

Before determining whether a product or packaging system can be adopted into a validated EO process, it should be determined whether the product and packaging system will remain functional and effective. A system to evaluate these aspects should be addressed by the design and/or change control process. Consideration should be given to functionality, integrity, stability, biocompatibility, and residuals, with special consideration given to determining the effect the sterilization process might have on drugs that could be included in devices/components. For products (e.g., kits) that may contain presterilized components (e.g., drugs), the manufacturer should consider regulatory requirements with regard to safety and efficacy of these components.

NOTE—The candidate product and its packaging should be evaluated for EO residuals, and any changes to either should be evaluated for the impact on product release. ANSI/AAMI/ISO 10993-7 and AAMI TIR19 should be used as guidance for making this evaluation.

4.4 Determination of sterilization challenge

Within each family or processing group, a worst-case or representative member is selected for validation studies. The worst-case or representative member should be selected on the basis of characteristics described in annex A, as applicable. This list is not all-inclusive; there may be other factors that should be considered. Conversely, some of the items in this list might not apply, depending on the product being evaluated. Often, several dissimilar product families may be included within the same processing group. All products within this processing group should present an equivalent or lesser challenge to the sterilization process when compared to the worst-case or representative member.

4.4.1 Product

Perform a technical review of the candidate product compared to the currently validated product and/or PCD that was used to validate the existing EO process. The construction and configuration of the candidate product should be carefully examined for any areas that could present obstacles to EO/heat/humidity penetration. This comparison should also involve an examination of factors that could potentially affect the product bioburden, such as manufacturing, production methods, facilities, location, and raw material types and sources that could affect the desired SAL (see ANSI/AAMI/ISO 11737-1). Annex A is a guide that can be used to assist in these comparisons.

If the results of the technical review show that the products are similar and the differences between them are determined to be not significant or to be a lesser challenge than the currently validated product or PCD, then the candidate product may be adopted into the validated EO process without further study. The rationale for this decision should be made by a sterilization specialist and must be documented. When a product, kit, or component is proposed and the challenge cannot be determined by physical inspection, then a further evaluation must be made regarding the actions necessary to assign an effective sterilization process. One method to evaluate products that are not clearly equivalent or represent a lesser challenge may be to perform cycle lethality studies (see 4.4.3 and AAMI TIR16).

4.4.2 Packaging system

Changes in the design of primary, secondary, or tertiary packaging systems, or to load density and/or load configuration, should be evaluated for their impact on the sterilization process. The items should be compared to the existing packaging system (see annex A).

If the technical review finds that the packaging systems are similar and that the differences between them are clearly not significant, then the candidate packaging system may be adopted into the validated EO process without further study. If the density or load configuration of the candidate product and its packaging could present a greater sterility challenge to the sterilization process than the previously validated product, then temperature and relative humidity penetration studies and/or cycle lethality studies should also be conducted.

When load equivalency studies are required, they should be conducted in a production chamber to evaluate the effects of the candidate secondary and/or tertiary packaging, load configuration, and/or load density on temperature distribution, moisture penetration, and/or sterilant gas absorption/desorption.

4.4.3 Cycle lethality studies

Cycle lethality studies may be conducted with a challenge consisting of product inoculated directly or indirectly, a PCD, or natural product bioburden (see 3.3.1.1.1 of AAMI TIR16). The location of a microbial challenge should represent the worst-case location (i.e., that location which is judged to be most resistant to the penetration of heat, humidity, and EO within the candidate product).

NOTE—Direct inoculation of a product can result in variable resistance of the inoculum because of the occlusion of the spores on or in the product, surface phenomena, and/or other environmental factors. Therefore, it is important to validate this practice. See Gillis and Schmidt, 1983; West, 1977; and ANSI/AAMI/ISO 11737-1:1995 for additional information.

Sublethal cycles may be performed with replicates of the candidate product and PCD according to the recommendations of ANSI/AAMI/ISO 11135:1994 (see 7.2.1.1 and 7.2.1.2). If the resistance of the candidate product is such that the desired SAL is still attainable under the validated cycle conditions, then the candidate product can be adopted into the existing EO cycle.

NOTE—Comparative resistance studies associated with the candidate product and PCD may be performed in a pilot chamber. Comparative resistance studies associated with load configurations should be performed in the production chamber.

It is desirable to compare the candidate product with the current PCD used to validate the sterilization cycle; doing so allows one to identify which is the worst-case challenge. The worst-case challenge should then be used in subsequent validation studies. The sterilization cycle can be shown to deliver the desired SAL to the candidate product without directly comparing it to the PCD. This determination might require that additional comparison of D-values be done during subsequent studies to establish whether the candidate product or PCD is the worst case.

Further information on the performance of lethality studies and SAL can be found in AAMI TIR16 and AAMI ST67.

4.5 Documentation

All decisions related to the outcome of the analysis to determine if a candidate product may be adopted into the EO process must be documented. At a minimum, this documentation package should include the following:

a) The complete specification for the candidate product which fully describes the product configuration and how it is to be presented to the EO process (packaging and load configuration). The specification should also include or reference the required SAL.

b) Evidence or assessment of the compatibility of the product with the process.

c) Result of the comparison between the candidate product and the existing validated product(s). This result should clearly demonstrate that product complexity, materials, packaging, and load configuration were assessed.

d) Evidence or assessment of the bioburden of the candidate product and its resistance relative to the PCD.

e) The documented conclusion that the candidate product is suitable for adoption into the product family/processing group specifically referenced in the current validation study to achieve the specified SAL. This conclusion should include or reference any additional test results performed to supplement the existing validation study and any further testing performed for confirmation/qualification for routine release of product from the existing validated cycle (residual testing, functional testing, etc.).

f) Approval by the sterilization specialist and other individuals as required by the normal change control practices within the organization.

g) A list of applicable sterilizer operating procedures and specifications issued or changed to authorize sterilization of the adopted product in the current cycle.

5 Process equivalency

5.1 General

Process equivalency can be established for a sterilization process through design/engineering analysis and by analysis of data. The data should demonstrate that the sterilization equipment is performing within an acceptable range of control (i.e., process parameters can be attained and reproduced). The data analysis should also identify the acceptable range and the level of variability for each phase of the specific process. The sterilization process equipment used to deliver a sterilization process commonly consists of a chamber, rooms, and ancillary control systems. Sterilization process equipment may be located within a given processing facility or among several facilities. This equipment can be used independently to deliver the same process conditions and may be exactly the same or may differ in size and/or extent of ancillary equipment. The design/engineering analysis should provide information on the extent of these differences.

According to ANSI/AAMI/ISO 11135:1994, sterilization process equipment that has been qualified and shown to be equivalent during installation qualification (IQ), operational qualification (OQ) (IQ and OQ are commissioning), and physical performance qualification (PQ) may use a reduced microbiological PQ during revalidation of the sterilization process. Initial validation of a sterilization process in candidate equipment that performs in an equivalent manner to qualified equipment may also be accomplished using a reduced microbiological PQ if the candidate equipment has been fully validated (IQ, OQ, and PQ) already.

5.2 Introduction

Process equivalency can be established when equipment is located either in the same facility or at different facilities. The requirements that shall be met prior to the establishment of a process equivalency program are the following:

a) Full validation of the sterilization process in at least one existing system according to the requirements of ANSI/AAMI/ISO 11135:1994.

b) Performance of the IQ and OQ studies that demonstrate and document that all equipment has been installed in accordance with engineering specification requirements and operates in accordance with those requirements.

5.3 Determination of process equivalency

The equivalency of a specific sterilization process can be established by comparing the data obtained when the process is run in the candidate equipment to that obtained from the same sterilization process in the existing equipment. This comparison should include an evaluation of the candidate equipment's capability to deliver the desired specifications reproducibly with a worst-case product load. These specifications should be those that were previously validated in the performance qualification of the sterilization process in the existing equipment. The sterilization process equipment should also be compared to the existing equipment to determine how significant the differences are between the equipment. This comparison should be performed initially to establish the basis for the remainder of the process equivalency study. The IQ and OQ for all candidate equipment should be reviewed to ensure that it is applicable to the sterilization process.

Therefore, the evaluation of equivalency is a three-phase process consisting of:

Phase 1—Design and engineering evaluation,

Phase 2—Process analysis and evaluation, and

Phase 3—Microbiological evaluation.

5.3.1 Phase 1—Design and engineering evaluation

The design and engineering evaluation consists of a comparison of the equipment used in the candidate sterilization process system to that used in the existing validated sterilization process system. Annex B is a general guide for the sterilization specialist to the items that may be considered in the evaluation. The guide is not all-inclusive; there may be other factors that should be considered. Conversely, some of the items in this list may not apply, depending on the system being evaluated.

The outcome of this evaluation is a basis for determining the extent of further qualification testing in the second and third phases. If the evaluation shows that the equipment is not similar, it is still possible to establish process equivalency on the basis of the results of the second and third phases. Typically, the greater the similarity between the candidate equipment and the existing equipment, the less testing would be required in these phases.

5.3.2 Phase 2—Process analysis and evaluation

The second phase in establishing equivalency is an analysis of all process data associated with a validated process in the candidate equipment. This data should be compared to the specification limits for that specific sterilization process. The specification limits are those established in the initial validation for the sterilization process (including all process requirements identified in ANSI/AAMI/ISO 11135:1994) in the existing equipment. The specifications, acceptance criteria, and pallet/load configuration shall be as defined for the initial process validation studies. Statistical methods that evaluate both the central tendencies of the test data and the degree of variability of the data may be used to assist in this evaluation.

If the process analysis and evaluation do not meet the acceptance criteria, then it is not possible to demonstrate process equivalency even though the results of the other phases may be equivalent.

5.3.2.1 Evaluation of preconditioning or aeration areas

The requirements for establishing equivalency are the same for preconditioning or aeration areas, with the exception that relative humidity usually does not apply to aeration.

An evaluation that compares the load temperature and humidity profiles within each environment should be performed. At a minimum, temperature and humidity uniformity within the load and the relationship of the uniformity with the corresponding set points and recorded control variables should be evaluated.

Process equivalency can be established if analysis of performance data concludes that conditions within the load meet the specification limits at the end of preconditioning and/or throughout aeration.

5.3.2.2 Evaluation of sterilization chamber performance

An evaluation that compares the load profiles within each candidate chamber shall be performed. This evaluation should be performed using the existing process parameters and gas mixture. The critical process parameters should be defined for the sterilization process before the evaluation is performed. These parameters will be unique for each sterilization process but may include:

a) vacuum depth and rate throughout the sterilization process;

b) humidification time and steam injection rate;

c) gas injection temperature, rate, and amount of gas used (weight, concentration, and/or pressure); and

d) air and/or nitrogen injection rate.

In addition, the following should be evaluated:

1) Product temperature range—Distribution and control within the load throughout the cycle. See ANSI/AAMI/ISO 11135:1994 and/or EN 550 for the number of sensors that should be used.

2) Product humidification—Distribution and control within the load at the end of conditioning. See ANSI/AAMI/ISO 11135:1994 and/or EN 550 for the number of sensors that should be used.

A comparison of the process from the chamber runs shall indicate that the processes are equivalent in their ability to meet the existing process specification limits and any additional acceptance criteria. If the analysis of the data meets the acceptance criteria, then a reduced microbiological PQ with product may be performed (see Table 1) to validate the candidate chamber(s). The data generated should be analyzed and compiled in a format that will allow for its use in future process equivalency determinations.

5.3.3 Phase 3—Microbiological evaluation

The third phase in the analysis of process equivalency is the performance of a microbiological evaluation. This evaluation consists of the consideration given to any factors that would affect the lethality of the sterilization process.

The factors that should be evaluated include any changes to the sterilization location or manufacturing location that may have an impact on the bioburden level of the product as presented for sterilization. Increased distances between the manufacturing facility and sterilization site may result in higher bioburden levels, especially if the product will support microbial growth. Differences in manufacturing environments may lead to the production of product with higher bioburden levels than previously validated, even if the product does not support microbiological growth.

5.3.4 Results evaluation

The results of the microbiological evaluation, in conjunction with the results of Phase 1 and Phase 2, are used to determine if a microbiological PQ should be performed (see Table 1). If the conclusions of the design and engineering evaluation (Phase 1), the process analysis and evaluation (Phase 2), and the microbiological evaluation (Phase 3) are that the processes are equivalent, then the performance of a microbiological PQ is not necessary.

If Phase 2 and either Phase 1 or Phase 3 conclude that the processes are equivalent, or if only Phase 2 concludes that the processes are equivalent, then at least one microbiological PQ run should be performed (see Table 1). This run should be sufficient to demonstrate that the desired SAL of the process is achieved, even if the equipment and/or the microbiological evaluation is not equivalent.

If the conclusion of Phase 2 is that the processes are not equivalent, then the process should be declared “not equivalent” and should be fully validated according to the requirements of ANSI/AAMI/ISO 11135:1994 before the candidate equipment is used. The results of Phase 1 or 3 do not change this declaration of “not equivalent.”

Table 1—Evaluation results

Phase 1—Design and engineering evaluation	Phase 2—Process analysis and evaluation	Phase 3—Microbiological evaluation	Minimum number of microbiological PQ runs
Equivalent	Equivalent	Equivalent	None
Not equivalent	Equivalent	Equivalent	1
Equivalent	Equivalent	Not equivalent	1
Not equivalent	Equivalent	Not equivalent	1
Equivalent or not equivalent	Not equivalent	Equivalent or not equivalent	3

NOTE—To perform the microbiological evaluation referred to in Table 1, Phase 3, consider the factors stated in 5.5 f) of this TIR, and information on potential product bioburden changes discussed in AAMI TIR16.

If the performance of one or more microbiological PQ runs is required, then the type of cycle (fractional, half, etc.), specification limits, and lethality requirements established in the validation of the existing process are to be used to evaluate the candidate equipment performance. The specification limits, lethality requirements, and acceptance criteria shall be defined before the microbiological PQ is performed.

5.4 Process requalification and maintenance of equivalency

According to ANSI/AAMI/ISO 11135:1994, the established process equivalency program must define the requirements for the equipment to produce repeatable performance characteristics annually. All sterilization process equipment must be included in the annual requalification program. The analysis should define what is an acceptable range and what level of variability in performance is required to maintain equivalency from year to year.

To guard against unreported or inadvertent changes, one should also consider periodic repetition of all or part of the performance qualification. The interval between periodic requalifications should be determined by the nature of the

sterilization process and by the amount of process data documented. The interval may be varied, taking into account historical data that demonstrates process reproducibility and conformance with established specifications for process parameters. The decision to perform requalification may be event-related or time-related and should be documented.

It is also necessary to review changes to each piece of equipment, the manufacturing process, and the sterilization process to ensure that changes do not compromise the overall determination of equivalency. This review should be conducted before changes are made and should be part of the change control process.

5.5 Documentation

All decisions related to the outcome of the analysis to determine if candidate equipment may be declared equivalent to the existing sterilization process equipment must be documented. At a minimum, this documentation package should include:

a) The complete specification for the candidate equipment, which fully describes the equipment, operating specifications and tolerances, and reference to or a list of applicable operating procedures, calibration procedures, and maintenance schedules. This should include or reference the current IQ per ANSI/AAMI/ISO 11135:1994.

b) Evidence or assessment of the ability of the equipment to deliver the intended process. Include or reference the current OQ per ANSI/AAMI/ISO 11135:1994.

NOTE—OQ is part of commissioning in ANSI/AAMI/ISO 11135:1994.

c) The result of the comparison between the candidate process equipment and the existing validated process equipment. This comparison should clearly demonstrate that all major systems and critical parameters were assessed, including statistical analysis, if used.

d) Evidence or assessment of the product conditions during processing within the candidate equipment to demonstrate equivalence to the existing process.

e) Results of evaluation of additional factors that could affect the lethality of the sterilization process.

f) The documented conclusion that the candidate equipment is equivalent to the equipment specifically referenced in the current validation study to achieve the specified SAL. This conclusion should include or reference any additional tests performed to supplement the existing validation study and any further testing performed for confirmation/qualification for routine release of product from the existing validated cycle (residual testing, functional testing on first three lots, etc.).

g) Approval by the sterilization specialist and other individuals as required by the normal change control practices within the organization.

h) A listing of applicable sterilizer operating procedures and specifications issued or changed to authorize use of the candidate equipment for routine processing of product.

Annex A
(informative)

Guide for evaluation of a product for adoption

This guide is not an all-inclusive list.

If the answer to any of the following questions is yes, further evaluation of the candidate product might be required to determine if the candidate product is more difficult to sterilize than the existing validated product.

A.1 Products within a family should have a similar configuration

1) Does the candidate product have more restricted passageways or inner chambers than the existing validated product?
2) Does the candidate product have fewer openings than the existing validated product?
3) Does the candidate product have more internal surfaces than the existing validated product?
4) Does the candidate product have more mated surfaces than the existing validated product?
5) Does the candidate product have more closures than the existing validated product?

A.2 Products within a family should have similar materials and characteristics

1) Are there changes or differences that may reduce the transfer of heat, moisture, or sterilant gas?
2) Are the materials known to retain higher EO residual levels than the existing validated product materials?
3) Is the candidate product manufactured with more materials from biological sources than the existing validated product?
4) Does the candidate product have temperature, pressure, or moisture limitations that the existing EO process cannot meet?
5) Does the candidate product have a significantly different bioburden with regard to types, numbers, and resistance?
6) Is the candidate product manufactured or assembled in a less-controlled environment than the existing validated product?
7) Does the candidate product have less in-process cleaning than that of the existing validated product?
8) Does the manufacture of the candidate product involve more handling than the existing validated process?

A.3 Products within a family should have a similar primary package configuration

1) Do the positions of any impermeable protective plastic sheets restrict or interfere with vents?
2) Is the nonpermeable CSR wrap different in type, number of layers, basis weight, coating, or treatment from the existing wrap?
3) Is there a difference in the type of venting material (e.g., paper instead of nonwoven polyolefin)?
4) Is there a decrease in the porosity of the venting material (e.g., basis weight, coating, treatment, application of secondary labels, etc.)?
5) Is there a decrease in the surface area of the venting material or underlying opening?
6) Does the packaging material(s) increase the bioburden level of the product?
7) Has a second (double) primary package been added?
8) Does the arrangement of the product within the package cause vents to be more occluded by the product, CSR wrap, and so forth?

9) Does the arrangement of individual packages in the shipping carton cause vents to be more occluded by nonvented surfaces of other products in the carton or by the secondary or tertiary packaging?

10) Does the product placement or primary package make it harder to heat the product?

11) Does the sterilization process damage or cause degradation of the packaging materials or seals?

12) Do the package design or materials reduce heat penetration or gas flow in the product?

A.4 Products within a defined family should have similar package density and should present a similar thermodynamic response to the process

1) Was there an addition or change in case polyliner(s), or an increase in the number of inner shelf packs?

2) Was the packaging changed to add double casing?

3) Is the stretch/shrink wrap used to hold pallet loads during processing of a greater thickness or density than in the existing configuration?

4) Was there an addition or change in any wrap-around product cartons before processing?

5) Was there a change in the composition, density, or thickness of the secondary or tertiary packing material(s)?

6) Was there an addition or change in protective or insulation materials that may be barriers to EO, water vapor, air, or heat transfer?

7) Were there other additions or changes in secondary or tertiary packaging materials that might make it harder to heat the product contained within the primary package?

8) Were there other additions or changes in secondary or tertiary packaging materials that might reduce flow and/or diffusion of EO, moisture, or air to or from the primary package?

9) Were there other additions or changes in secondary/tertiary packaging that reduce heat transfer or air flow and could impact EO residuals of the product?

10) Was there a change in the density of the overall pallet or load?

11) Is the pallet configuration more dense, or are there fewer exposed box surfaces?

12) Has the use of chimneys or other air spaces in the pallet been reduced?

13) Has the overall loading of the chamber increased?

14) Were there changes in configuration that reduce heat transfer or gas flow and that could affect EO residuals of the product?

Annex B
(informative)

Guide for design and engineering evaluation of candidate equipment

A greater number of yes responses to the following questions will lead to a conclusion that the candidate equipment is not equivalent to the existing equipment.

B.1 Preconditioning or aeration areas

1) Does the candidate area allow more loads than the existing area?
2) Is the volume of the candidate area larger than that of the existing area?
3) Does the heat source for the candidate area have less BTU/ft^3 available than that for the existing area?
4) Does the candidate area have less circulation and/or exhaust than the existing area?
5) Does the candidate area have a longer recovery time than the existing area?
6) Are the temperature and/or humidity in the candidate area less uniform than those in the existing area?
7) Is the candidate area farther from the sterilizer than the existing area?
8) Is the temperature in the candidate area less than that in the existing area?
9) Is the humidity level (if used) in the candidate area less than that in the existing area?
10) Are the utilities used to support the candidate area significantly different from those of the existing area?

B.2 Sterilization chamber

1) Is the volume of the candidate chamber different from that of the existing chamber?
2) Is the volume used in the candidate chamber different from that of the existing chamber?
3) Does the heat source for the candidate chamber have less BTU/ft^3 available than that for the existing chamber?
4) Does the candidate chamber have less circulation than the existing chamber?
5) Does the candidate chamber have a longer equilibration time than the existing chamber?
6) Are the temperature and humidity in the candidate chamber less uniform than those in the existing chamber?
7) Is the overall cycle time considerably shorter in the candidate chamber than in the existing chamber?
8) Are there differences in the configuration of the EO and steam distribution headers?
9) Are there differences in the EO vaporizing capability?