TECHNICAL ISO/TS

First edition
2017-12

Guidance on aspects of a risk-based approach to assuring sterility of terminally sterilized, single-use health care product that is unable to withstand processing to achieve maximally a sterility assurance level of 10^{-6}

Document d'orientation sur les aspects d'une approche, fondée sur l'appréciation du risque, permettant d'assurer la stérilité des produits de santé à usage unique, soumis à une stérilisation terminale y compris ceux ne pouvant pas supporter un traitement atteignant un niveau d'assurance de la stérilité maximal de 10^{-6}

Reference number
ISO/TS 19930:2017(E)

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

Introduction

A sterile health care product is one that is free of viable microorganisms. International Standards that specify requirements for validation and routine control of sterilization processes require, when it is necessary to supply a sterile health care product, that adventitious microbiological contamination of that health care product prior to sterilization be minimized. Even so, health care product produced under standard manufacturing conditions in accordance with the requirements for quality management systems (see, for example, ISO 13485) could, prior to sterilization, have microorganisms on them, albeit in low numbers. Such health care product is non-sterile. The purpose of sterilization is to inactivate or remove the microbiological contaminants and thereby transform the non-sterile health care product into sterile ones.

Compliance with the requirements of International Standards for development, validation and routine control of sterilization processes ensures that the sterilization process is both reliable and reproducible so that predictions can be made, with reasonable confidence, that there is a low probability of there being a viable microorganism present on a health care product after sterilization.

Specification of this probability is a matter for regulatory authorities and can vary from country to country.

For example, the European Standards Organization has published EN 556-1. EN 556-1 has been harmonized in the European Union and also been adopted in a number of countries outside Europe, for example Australia and China. EN 556-1 specifies that a sterility assurance level (SAL) of 10^{-6} or less (e.g. 10^{-7}) has to be achieved in order to designate a terminally sterilized medical device as sterile. EN 556-1 includes an explanatory note that specifies that permission for acceptance of a sterility assurance level of greater than 10^{-6} (e.g. 10^{-5}) may be sought through appropriate regulatory bodies and such permission requires consideration of the individual situation, including consideration of the risk assessment undertaken by the manufacturer of the medical device.

In the USA, the American National Standard ANSI/AAMI ST67 specifies that a maximal sterility assurance level of 10^{-6} is required for the majority of terminally sterilized health care product. ST67 also indicates that

a) there are circumstances for which a greater maximal sterility assurance level of 10^{-3} can be acceptable for certain product, e.g. product that does not contact breached skin or compromised tissue, and

b) when product cannot withstand a terminal sterilization process that achieves maximally a SAL of 10^{-6}, a greater sterility assurance level (e.g. 10^{-5}) might be acceptable for that product.

There is health care product that is unable to withstand a terminal sterilization process achieving maximally a SAL of 10^{-6}. This might be because some or all of the materials that constitute the product are sensitive to one or more traditional sterilization processes, for example cellular or biologically-based components.

The purpose of this document is to provide general guidance on the considerations to be taken into account in selecting a SAL for health care product that is unable to withstand terminal sterilization to meet the general requirement to achieve maximally a SAL of 10^{-6}. Particularly, the document gives advice in relation to fulfilling the EN 556-1:2001, Note to 4.1 and AAMI ST67:2011, 4.2.4.

It is recognized that this topic is contentious for some regulatory agencies, conformity assessment bodies, manufacturers, contract sterilizers and national standards bodies. Some see development of this document as a potential move to relax the current regulatory quality requirements to supply product as sterile. This is not the intention. This document states clearly that a decision to approve a SAL other than 10^{-6} for a specific product resides solely with the relevant regulatory agency. A cautious approach has been taken during development of this document and ongoing diligence is maintained to ensure that the spirit in which this document is intended is not misconstrued. The purpose of this document is to promote discussion between interested parties and to bridge a gap in existing standards and regulations. This document provides much-needed guidance on technical aspects when considering an

alternative SAL to 10^{-6} for identified high clinical need, terminally sterilized product that is unable to withstand the processing conditions necessary to achieve maximally a SAL of 10^{-6}.

This document is intended to be applied by process developers, manufacturers of health care product to be sterilized and organizations responsible for the sterilization of health care product.