
**Sterilization of health care products —
Low temperature steam and
formaldehyde — Requirements for
development, validation and routine
control of a sterilization process for
medical devices**

*Stérilisation des produits de santé — Formaldéhyde et vapeur à faible
température — Exigences pour le développement, la validation et
le contrôle de routine d'un procédé de stérilisation pour dispositifs
médicaux*

ISO 25424:2018

<https://standards.iteh.ai/catalog/standards/iso/52ec2627-f1fe-40c8-9690-5bbf067bbbd1/iso-25424-2018>



iTeh Standards
(<https://standards.itih.ai>)
Document Preview

ISO 25424:2018

<https://standards.itih.ai/catalog/standards/iso/52ec2627-f1fe-40c8-9690-5bbf067bbbd1/iso-25424-2018>



COPYRIGHT PROTECTED DOCUMENT

© ISO 2018

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Page

Foreword	v
Introduction	vi
1 Scope	1
2 Normative references	2
3 Terms and definitions	2
4 Quality management system elements	8
4.1 General	8
4.2 Documentation	8
4.3 Management responsibility	8
4.4 Product realization	9
4.5 Control of non-conforming product	9
5 Sterilizing agent characterization	9
5.1 General	9
5.2 Sterilizing agent	9
5.3 Microbicidal effectiveness	9
5.4 Material effects	10
5.5 Environmental considerations	10
6 Process and equipment characterization	10
6.1 General	10
6.2 Process	10
6.3 Equipment	11
7 Product definition	11
8 Process definition	12
9 Validation	13
9.1 General	13
9.2 Installation qualification	14
9.2.1 General	14
9.2.2 Installation	14
9.2.3 Equipment	14
9.3 Operational qualification	15
9.4 Performance qualification	15
9.4.1 General	15
9.4.2 Performance qualification — Physical	16
9.4.3 Performance qualification — Microbiological	16
9.4.4 Performance qualification — Desorption and drying	17
9.5 Review and approval of validation	17
10 Routine monitoring and control	18
10.1 General	18
10.2 Biological indicators	18
10.3 Chemical indicators	18
10.4 Records	18
11 Product release from sterilization	19
12 Maintaining process effectiveness	19
12.1 General	19
12.2 Maintenance of equipment	19
12.3 Requalification	19
12.4 Assessment of change	20
Annex A (normative) Process definition based on inactivation of reference microorganisms and knowledge of bioburden on product items to be sterilized	21

Annex B (normative) Process definition based on inactivation of reference microorganisms	22
Annex C (informative) Guidance on application of this document	25
Annex D (informative) Environmental aspects regarding development, validation and routine control of low temperature steam and formaldehyde processes.....	35
Bibliography	40

iTeh Standards
(<https://standards.itih.ai>)
Document Preview

[ISO 25424:2018](https://standards.itih.ai/catalog/standards/iso/52ec2627-f1fe-40c8-9690-5bbf067bbbd1/iso-25424-2018)

<https://standards.itih.ai/catalog/standards/iso/52ec2627-f1fe-40c8-9690-5bbf067bbbd1/iso-25424-2018>

Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

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).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

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*.

This second edition cancels and replaces the first edition (ISO 25424:2009), which has been technically revised. The main changes compared to the previous edition are as follows:

— alignment with EN 14180:2014; [ISO 25424:2018](https://standards.iteh.ai/catalog/standards/iso/52ec2627-f1fe-40c8-9690-5bbf067bbbd1/iso-25424-2018)

— alignment with ISO 14937:2009;

— alignment of definitions with ISO 11139:2018;

— addition of relevant literature.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

A sterile medical device 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 medical device, that adventitious microbiological contamination of a medical device prior to sterilization be minimized. Even so, medical devices 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 medical devices are non-sterile. The purpose of sterilization is to inactivate the microbiological contaminants and thereby transform the nonsterile medical devices into sterile ones.

The kinetics of inactivation of a pure culture of microorganisms by physical and/or chemical agents used to sterilize medical devices generally can best be described by an exponential relationship between the number of microorganisms surviving and the extent of treatment with the sterilizing agent; inevitably this means that there is always a finite probability that a microorganism survives regardless of the extent of treatment applied. For a given treatment, the probability of survival is determined by the number and resistance of microorganisms and by the environment in which the organisms exist during treatment. It follows that the sterility of any one medical device in a population subjected to sterilization processing cannot be guaranteed and the sterility of a processed population is defined in terms of the probability of there being a viable microorganism present on a medical device.

This document describes requirements that, if met, will provide a sterilization process with appropriate microbicidal activity intended to sterilize medical devices. Furthermore, conformity with the requirements ensures that the sterilization process is both reliable and reproducible so that predictions can be made, with reasonable confidence, that there is a low level of probability of there being a viable microorganism present on a medical device after sterilization. Specification of this probability is a matter for regulatory authorities and can vary from country to country (see, for example, EN 556-1 and ANSI/AAMI ST67).

Generic requirements of the quality management system for design and development, production, installation and servicing are given in ISO 9001 and particular requirements for quality management systems for medical device production are given in ISO 13485. The standards for quality management systems recognise that, for certain processes used in manufacturing, the effectiveness of the process cannot be fully verified by subsequent inspection and testing of the product. Sterilization is an example of such a process. For this reason, sterilization processes are validated for use, the performance of the sterilization process is monitored routinely and the equipment is maintained.

Exposure to a properly validated, accurately controlled sterilization process is not the only factor associated with the provision of reliable assurance that a processed medical device is sterile and, in this regard, suitable for its intended use. Attention is also given to a number of factors including:

- a) the microbiological status of incoming raw materials and/or components;
- b) the validation and routine control of any cleaning and disinfection procedures used on the medical device;
- c) the control of the environment in which the medical device is manufactured, assembled and packaged;
- d) the control of equipment and processes;
- e) the control of personnel and their hygiene;
- f) the manner and materials in which the medical device is packaged;
- g) the conditions under which the medical device is stored.

The type of contamination on a medical device to be sterilized varies, and this influences the effectiveness of a sterilization process. Medical devices that have been used in a health care setting and that are being presented for resterilization in accordance with the manufacturer's instructions

(see ISO 17664) should be regarded as special cases. There is the potential for such medical devices 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, particular attention has to be given to the validation and control of the cleaning and disinfection processes used during reprocessing.

The requirements are the normative parts of this document with which conformity is claimed. The guidance given in [Annex C](#) is not normative and is not provided as a checklist for auditors. The guidance provides explanations and methods that are regarded as being a suitable means for conforming with the requirements. Methods other than those given in the guidance can be used if they are effective in achieving conformity with the requirements of this document.

The development, validation and routine control of a sterilization process comprise a number of discrete but interrelated activities, for example, calibration, maintenance, product definition, process definition, installation qualification, operational qualification and performance qualification. While the activities required by this document have been grouped together and are presented in a particular order, this document does not require that the activities be performed in the order that they are presented. The activities required are not necessarily sequential, as the programme of development and validation can be iterative. The responsibility for carrying out the activities required by this document will vary from case to case. This document requires that the responsibilities of the various parties be defined (see [4.3](#)) but does not specify to whom the responsibilities are allocated. [Annex C](#) provides guidance on allocation of responsibility.

Activities required by this document could also give rise to an environmental burden that can be considered and minimized, e.g. by utilizing flexibility in planning. Environmental aspects are addressed in [Annex D](#) of this document.

iTeh Standards (<https://standards.iteh.ai>) Document Preview

ISO 25424:2018

<https://standards.iteh.ai/catalog/standards/iso/52ec2627-f1fe-40c8-9690-5bbf067bbbd1/iso-25424-2018>