INTERNATIONAL STANDARD

ISO 14160

First edition
1998-03-15

Sterilization of single-use medical devices incorporating materials of animal origin — Validation and routine control of sterilization by liquid sterilants

Stérilisation des dispositifs médicaux non réutilisables contenant des matières d'origine animale — Validation et contrôle de routine de la stérilisation par agents stérilisants chimiques liquides

Contents

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Printed in Switzerland

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.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75% of the member bodies casting a vote.

International Standard ISO 14160 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

Annexes A, B and C of this International Standard are for information only.

Introduction

A sterile product item is one which is free of viable microorganisms. International Standards require, when it is necessary to supply a sterile product item, that adventitious microbiological contamination of a medical device from all sources prior to sterilization be minimized by all practical means. Even so, product items produced under defined manufacturing conditions in accordance with the requirements for quality systems for medical devices (see ISO 13485 and ISO 13488) can, prior to sterilization, have microorganisms on them, albeit in low numbers. Such product items are non-sterile. The purpose of sterilization processing is to inactivate the microbiological contaminants and thereby transform the non-sterile items into sterile ones.

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

Generic requirements for the quality system for the design/development, production, installation and servicing are given in the ISO 9000 family of standards and in ISO 13485 and ISO 13488. The ISO 9000 series of standards designates certain processes used in manufacture as "special" if the results cannot be fully verified by subsequent inspection and testing of the product. Sterilization is an example of a special process because process efficacy cannot be verified by inspection and testing of the product. For this reason, sterilization processes have to be validated before use, the performance of the process monitored routinely and the equipment maintained.

It is important to be aware that the exposure to a properly validated and accurately controlled sterilization process is not the only factor associated with the provision of reliable assurance that the product is sterile and in this respect suitable for its intended use. Attention has also to be given to a number of factors, including the microbiological status (bioburden) of incoming raw materials and/or components, their subsequent storage, and to the control of the environment in which the product is manufactured, assembled and packaged.

The agents for sterilization used most frequently for medical devices are moist heat, dry heat, irradiation and ethylene oxide. While some devices containing animal tissues may be compatible with these commonly applied methods of sterilization (for example catgut sutures are usually sterilized by irradiation), other devices, such as biological heart valves or tissue patches, are not compatible with conventional sterilization processes. It has been recognized that other sterilizing agents might have to be used in these exceptional circumstances. Liquid chemical sterilants have been widely used in such instances and, in common with the other sterilization methods, the efficacy of the process needs to be demonstrated and recorded before it is adopted for routine use.

This International Standard contains requirements for the validation and routine monitoring of sterilization of single-use medical devices containing materials of animal origin by exposure to liquid chemical sterilants; guidance on the application of this International Standard is given in annex A. Manufacturing processes for medical devices containing animal tissues frequently include exposure to chemical agents which can in themselves reduce significantly the bioburden on the medical device. Following the manufacturing process, a medical device is exposed to a defined sterilization process; the requirements for validation and routine control described in this International Standard apply only to this defined sterilization process and do not take account of the lethal effects of other bioburden reduction steps.

NOTE — The guidance given in annex A is not obligatory and it is not provided as a check list for auditors.

Sterilization of single-use medical devices incorporating materials of animal origin — Validation and routine control of sterilization by liquid chemical sterilants

1 Scope

This International Standard specifies requirements for the development, validation, process control and monitoring of the sterilization, by the use of liquid chemical sterilants, of single-use medical devices comprising, in whole or in part, materials of animal origin.

This International Standard does not apply to material of human origin.

This International Standard does not describe a quality assurance system for the control of all stages of manufacture.

NOTE 1 Attention is drawn to the standards for quality systems (see ISO 9001 and ISO 13485 or ISO 9002 and ISO 13488) which can be used in the control of all stages of manufacture including the sterilization process.

This International Standard does not describe tests to establish the effects of any chosen sterilization method upon the fitness for use of the medical device.

NOTE 2 Such testing is a crucial part of the design and development of a medical device.

This International Standard does not describe methods for the validation of the inactivation of viruses.

NOTE 3 In developing a method for processing medical devices containing materials of animal origin, consideration of the effects of liquid chemical sterilization on potential viral contaminants will also be necessary because of the source of materials used in the manufacture of these particular medical devices. The importance of validation of viral inactivation for processes within the scope of this International Standard is recognized. This aspect is excluded from this International Standard; a separate European Standard is in preparation (EN 12442-3).

NOTE 4 Liquid chemical sterilants traditionally employed to sterilize animal tissues in medical devices may not be effective in inactivating the causative agents of transmissable spongiform encephalopathies such as bovine spongiform encephalopathy (BSE), or scrapie. Satisfactory validation in accordance with this International Standard should not be assumed to demonstrate inactivation of infective agents of this type.

This International Standard does not cover the level of residual sterilant within medical devices.

NOTE 5 ISO 14538 is concerned with this issue.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, agreements based on this International Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 9001:1994, *Quality systems — Model for quality assurance in design, development, production, installation and servicing.*

ISO 9002:1994, *Quality systems — Model for quality assurance in production, installation and servicing.*

ISO 11138-1:1994, *Sterilization of health care products— Biological indicators — Part 1: General.*

ISO 11737-1:1995, *Sterilization of health care products — Microbiological methods — Part 1: Estimation of the population of microorganisms on product.*

NOTE — The relationship between International Standards and European Standards is given in annex B.

3 Definitions

For the purposes of this International Standard, the following definitions apply.

3.1
batch
defined quantity of bulk, intermediate, or finished product that is intended or purported to be uniform in character and quality, and which has been produced during a defined cycle of manufacture

3.2
bioburden
population of viable microorganisms on a product and/or a package

3.3
carrier
supporting material on which test organisms are deposited

3.4
commissioning
obtaining and documenting evidence that equipment has been provided and installed in accordance with its specifications and that it functions within predetermined limits when operated in accordance with operational instructions

3.5
decimal reduction value
D-value
time (expressed in minutes) or irradiation dose (expressed in kilograys) required to achieve inactivation of 90 % of a population of the test organism under stated exposure conditions

3.6
exposure time
time for which the medical device is exposed at the specified temperature and sterilant concentration

3.7
inactivation
process resulting in the loss of the ability of microorganisms to grow and/or multiply

NOTE — For the purpose of this International Standard, microorganisms comprise sporing and non-sporing bacteria, viruses, fungi and protozoa.

3.8
inoculated carrier
carrier on which a defined number of test organisms has been deposited

3.9
liquid chemical sterilant
defined formulation of chemicals in a solution or liquid form which is applied to achieve sterility

3.10
medical device
any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

— diagnosis, prevention, monitoring, treatment or alleviation of disease;

— diagnosis, monitoring, treatment, alleviation of, or compensation for an injury or handicap;

— investigation, replacement or modification of the anatomy or of a physiological process;

— control of conception;

and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means

3.11
performance qualification
obtaining and documenting evidence that the equipment as commissioned will produce acceptable product when operated in accordance with the process specification

3.12
presterilization count
viable count obtained prior to sterilization

3.13
product compatibility
ability of the sterilization process to achieve the intended results without detrimental effect on the product

3.14
process development
documented programme of studies which are performed in order to define the sterilization process based upon the product/packaging/loading pattern and/or equipment limitations

3.15
revalidation
repetition of part or all of the validation test requirements for the purpose of reconfirming process reliability

3.16
sterility
state of being free from viable microorganisms

NOTE — In practice no such absolute statement regarding the absence of microorganisms can be proven (see 3.18 sterilization).

3.17
sterile
free from viable microorganisms

NOTE — In practice no such absolute statement regarding the absence of microorganisms can be proven (see 3.18 sterilization).

3.18
sterilization
validated process used to render a product free of all forms of viable microorganisms

NOTE — In a sterilization process, the nature of microbial death is described by an exponential function. Therefore, the presence of viable microorganisms on any individual item can be expressed in terms of probability. While this probability may be reduced to a very low number, it can never be reduced to zero. The probability can be expressed as a sterility assurance level (SAL), normally expressed in the form 10^{-n}

3.19
storage solution
liquid in which a medical device in its final form is presented for use

3.20
validation
documented procedure for obtaining, recording and interpreting the data required to show that a process will consistently yield product complying with predetermined specifications

NOTE — For sterilization by liquid chemical sterilants, validation is considered as a total programme which consists of commissioning and performance qualification.

3.21
viable count
number of microorganisms estimated by growth of discrete colonies under the stated culture condition

NOTE — A discrete colony may not necessarily originate from a single viable microorganism.

4 General

4.1 Control of manufacturing

The manufacturing process shall be established and controlled to maintain the presterilization count below a specified limit.

NOTE 1 Employing a quality system complying with ISO 13485 or ISO 13488 meets this requirement.

A documented system shall be established and maintained to control the sourcing of raw materials of animal origin.

NOTE 2 A European Standard on sourcing, controls, collection and handling (EN 12442-2) is under preparation.

The documented procedures and instructions required by this International Standard shall be implemented effectively. Documentation and records shall be reviewed and approved by designated personnel (see 4.2).

4.2 Personnel

Responsibility for the maintenance of equipment (see 4.4), for the validation (see clause 5) and routine control (see clause 6) of sterilization by exposure to liquid chemical sterilants and for the release of product shall be assigned to qualified personnel as specified in ISO 9001 or in ISO 9002.

4.3 Calibration

An effective system shall be established, documented and maintained for the calibration of all controlling, indicating and recording instruments used for validation and routine control of the sterilization process. This system shall comply with the requirements of either ISO 9001 or ISO 9002.

4.4 Maintenance of equipment

Preventative maintenance shall be planned and performed in accordance with documented procedures. The procedure for each planned maintenance task and the frequency at which it is to be carried out shall be specified and documented.

Equipment shall not be used to process medical devices unless all maintenance tasks have been satisfactorily completed and recorded.

Records of maintenance shall be retained as specified in ISO 9001 or ISO 9002.

The maintenance scheme, maintenance procedures and maintenance records shall be reviewed periodically by a designated person (see 4.2).

4.5 Process development and product compatibility

4.5.1 Prior to the introduction of a new or altered product, package, loading pattern or sterilization process, the sterilization process to be validated shall be defined and documented.

A demonstration of equivalence to previously validated product, package or loading pattern shall be considered to meet this requirement. Any demonstration of equivalence shall be documented.

NOTE — The specified sterilization process may comprise separate treatments with more than one liquid chemical sterilant.

4.5.2 Product and packaging shall be designed to allow contact with liquid chemical sterilant and so that residues of the liquid chemical sterilant are below levels as specified by the manufacturer. The location within the product at which sterilization is most difficult to achieve shall be identified.

4.5.3 It shall have been demonstrated and documented that the sterilization process does not affect adversely the fitness for use of the product or its packaging. If resterilization is to be permitted, the effects of such processing shall be evaluated and documented.

5 Validation

5.1 General

Procedures for validation shall be documented and records of each validation shall be retained (see 5.4.1).

5.2 Commissioning

Commissioning shall demonstrate that the specifications for equipment used for the sterilization process are met.

5.3 Performance qualification

5.3.1 The performance qualification shall demonstrate that the sterilization process has:

a) appropriate lethal activity against a representative range of microorganisms (see 5.3.5, 5.3.6 and A.5);

b) defined processing parameters (e.g., time, temperature, liquid chemical sterilant concentration, pH) which are capable of control throughout the process.

5.3.2 For the performance qualification, the part of the product which is most difficult to sterilize, as defined according to 4.5.2, shall be taken into consideration during the performance qualification.