INTERNATIONAL STANDARD

ISO 11137-1

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Sterilization of health care products — Radiation —

Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices

Stérilisation des produits de santé — Irradiation —
Partie 1: Exigences relatives à la mise au point, à la validation et au contrôle de routine d'un procédé de stérilisation pour les dispositifs médicaux

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. 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.

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.

ISO 11137-1 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care product*.

This first edition, together with ISO 11137-2 and ISO 11137-3, cancels and replaces ISO 11137:1995.

ISO 11137 consists of the following parts, under the general title *Sterilization of health care products — Radiation*:

— *Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices*

— *Part 2: Establishing the sterilization dose*

— *Part 3: Guidance on dosimetric aspects*

Introduction

A sterile medical device is one that is free of viable microorganisms. International Standards, which 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) may, 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 non-sterile 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 can generally best be described by an exponential relationship between the numbers 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 may survive 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 part of ISO 11137 describes requirements that, if met, will provide a radiation sterilization process intended to sterilize medical devices, that has appropriate microbicidal activity. Furthermore, compliance with the requirements ensures that this activity 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 product after sterilization. Specification of this probability is a matter for regulatory authorities and may 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 the products are sterile and, in this regard, suitable for its intended use. Attention is therefore given to a number of considerations 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 product;

c) the control of the environment in which the product 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 product is packaged;

g) the conditions under which product is stored.

This part of ISO 11137 describes the requirements for ensuring that the activities associated with the process of radiation sterilization are performed properly. These activities are described in documented work programmes designed to demonstrate that the radiation process will consistently yield sterile products on treatment with doses falling within the predetermined limits.

The requirements are the normative parts of this part of ISO 11137 with which compliance is claimed. The guidance given in the informative annexes 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 complying with the requirements. Methods other than those given in the guidance may be used, if they are effective in achieving compliance with the requirements of this part of ISO 11137.

The development, validation and routine control of a sterilization process comprise a number of discrete but interrelated activities; e.g. calibration, maintenance, product definition, process definition, installation qualification, operational qualification and performance qualification. While the activities required by this part of ISO 11137 have been grouped together and are presented in a particular order, this part of ISO 11137 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 may be iterative. It is possible that performing these different activities will involve a number of separate individuals and/or organizations, each of whom undertake one or more of these activities. This part of ISO 11137 does not specify the particular individuals or organizations to carry out the activities.

Sterilization of health care products — Radiation —

Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices

1 Scope

1.1 This part of ISO 11137 specifies requirements for the development, validation and routine control of a radiation sterilization process for medical devices.

NOTE Although the scope of this part of ISO 11137 is limited to medical devices, it specifies requirements and provides guidance that may be applicable to other products and equipment.

This part of ISO 11137 covers radiation processes employing irradiators using,

a) the radionuclide ^{60}Co or ^{137}Cs,

b) a beam from an electron generator

or

c) a beam from an X-ray generator.

1.2 This part of ISO 11137 does not specify requirements for development, validation and routine control of a process for inactivating the causative agents of spongiform encephalopathies such as scrapie, bovine spongiform encephalopathy and Creutzfeld-Jakob disease. Specific recommendations have been produced in particular countries for the processing of materials potentially contaminated with these agents.

NOTE See, for example, ISO 22442-1, ISO 22442-2 and ISO 22442-3.

1.2.1 This part of ISO 11137 does not detail specified requirements for designating a medical device as sterile.

NOTE Attention is drawn to regional and national requirements for designating medical devices as “sterile.” See, for example, EN 556-1 or ANSI/AAMI ST67.

1.2.2 This part of ISO 11137 does not specify a quality management system for the control of all stages of production of medical devices.

NOTE It is not a requirement of this part of ISO 11137 to have a complete quality management system during manufacture, but the elements of a quality management system that are the minimum necessary to control the sterilization process are normatively referenced at appropriate places in the text (see, in particular, Clause 4). Attention is drawn to the standards for quality management systems (see ISO 13485) that control all stages of production of medical devices, including the sterilization process. Regional and national regulations for the provision of medical devices might require implementation of a complete quality management system and the assessment of that system by a third party.

1.2.3 This part of ISO 11137 does not require that biological indicators be used for validation or monitoring of radiation sterilization, nor does it require that a pharmacopoeial test for sterility be carried out for product release.

1.2.4 This part of ISO 11137 does not specify requirements for occupational safety associated with the design and operation of irradiation facilities.

NOTE Attention is also drawn to the existence, in some countries, of regulations laying down safety requirements for occupational safety related to radiation.

1.2.5 This part of ISO 11137 does not specify requirements for the sterilization of used or reprocessed devices.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 10012-1, *Quality assurance requirements for measuring equipment — Part 1: Metrological confirmation system for measuring equipment*

ISO 11137-2:2006, *Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose*

ISO 11737-1, *Sterilization of medical devices — Microbiological methods — Part 1: Determination of a population of microorganisms on products*

ISO 11737-2, *Sterilization of medical devices — Microbiological methods — Part 2: Tests of sterility performed in the validation of a sterilization process*

ISO 13485:2003, *Medical devices — Quality management systems — Requirements for regulatory purposes*

3 Terms and definitions

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

3.1
absorbed dose
dose
quantity of ionizing radiation energy imparted per unit mass of a specified material

NOTE 1 The unit of absorbed dose is the gray (Gy) where 1 Gy is equivalent to the absorption of 1 J/kg.

NOTE 2 For the purposes of this part of ISO 11137, the term dose is used to mean “absorbed dose”.

3.2
bioburden
population of viable microorganisms on or in the product and/or sterile barrier system

[ISO/TS 11139:2006]

3.3
biological indicator
test system containing viable microorganisms providing a defined resistance to a specified sterilization process

[ISO/TS 11139:2006]

3.4
calibration
set of operations that establish, under specified conditions, the relationship between values of a quantity indicated by a measuring instrument or measuring system, or values represented by a material measure or a reference material, and the corresponding values realized by standards

[VIM:1993, definition 6.11]

3.5
change control
assessment and determination of the appropriateness of a proposed alteration to product or procedure

[ISO/TS 11139:2006]

3.6
correction
action to eliminate a detected nonconformity

NOTE A correction can be made in conjunction with corrective action (3.7).

[ISO 9000:2005]

3.7
corrective action
action to eliminate the cause of a detected nonconformity or other undesirable situation

NOTE 1 There can be more than one cause for a nonconformity.

NOTE 2 Corrective action is taken to prevent recurrence whereas "preventive action" (3.24) is taken to prevent occurrence.

NOTE 3 There is a distinction between correction and corrective action.

[ISO 9000:2005]

3.8
***D* value**
D_{10} value
time or radiation dose required to achieve inactivation of 90 % of a population of the test microorganism under stated conditions

NOTE For the purpose of the ISO 11137 series, the *D* value refers to the radiation dose necessary to achieve the 90 % reduction.

[ISO/TS 11139:2006]

3.9
development
act of elaborating a specification

[ISO/TS 11139:2006]

3.10
dose mapping
measurement of dose distribution and variability in material irradiated under defined conditions

3.11
dosimeter
device having a reproducible, measurable response to radiation, which can be used to measure the absorbed dose in a given system

[ISO/TS 11139:2006]

3.12
dosimetry
measurement of absorbed dose by the use of dosimeters

3.13
establish
determine by theoretical evaluation and confirm by experimentation

[ISO/TS 11139:2006]

3.14
fault
one or more of the process parameters lying outside of its/their specified tolerance(s)

[ISO/TS 11139:2006]

3.15
health care product(s)
medical device(s), including *in vitro* diagnostic medical device(s), or medicinal product(s), including biopharmaceutical(s)

[ISO/TS 11139:2006]

3.16
installation qualification
IQ
process of obtaining and documenting evidence that equipment has been provided and installed in accordance with its specification

[ISO/TS 11139:2006]

3.17
irradiation container
holder in which product is transported through the irradiator

NOTE The holder can be a carrier, cart, tray, product carton, pallet or other container.

3.18
irradiator operator
company or body responsible for irradiation of product

3.19
maximum acceptable dose
dose given in the process specification as the highest dose that can be applied to a defined product without compromising safety, quality or performance

3.20
medical device
instrument, apparatus, implement, machine, appliance, implant, *in vitro* reagent or calibrator, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purpose(s) of:

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

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

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

— supporting or sustaining life;

— control of conception;

— disinfection of medical devices;

— providing information for medical purposes by means of in vitro examination of specimens derived from the human body;

and which does not achieve its primary 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

[ISO 13485:2003]

NOTE This definition from ISO 13485:2003 has been developed by the Global Harmonization Task Force (GHTF 2002).

3.21
microorganism

entity of microscopic size, encompassing bacteria, fungi, protozoa and viruses

NOTE A specific standard might not require demonstration of the effectiveness of the sterilization process in inactivating all types of microorganisms, identified in the definition above, for validation and/or routine control of the sterilization process.

[ISO/TS 11139:2006]

3.22
operational qualification
OQ
process of obtaining and documenting evidence that installed equipment operates within predetermined limits when used in accordance with its operational procedures

[ISO/TS 11139:2006]

3.23
performance qualification
PQ
process of 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 product meeting its specification

[ISO/TS 11139:2006]

3.24
preventive action
action to eliminate the cause of a potential nonconformity or other undesirable potential situation

NOTE 1 There can be more than one cause for a potential nonconformity.

NOTE 2 Preventive action is taken to prevent occurrence whereas “corrective action” (3.7) is taken to prevent recurrence.

[ISO 9000:2005]

3.25
primary manufacturer
body responsible for the design and manufacture of a medical device, together with the safety and performance of that medical device when placed on the market

3.26
process interruption
intentional or unintentional stoppage of the irradiation process

3.27
process parameter
specified value for a process variable

NOTE The specification for a sterilization process includes the process parameters and their tolerances.

[ISO/TS 11139:2006]

3.28
process variable
condition within a sterilization process, changes in which alter microbicidal effectiveness

EXAMPLES Time, temperature, pressure, concentration, humidity, wavelength.

3.29
processing category
group of different product that can be sterilized together

NOTE Processing categories can be based on, for instance, composition, density or dose requirements.

3.30
product
result of a process

[ISO 9000:2005]

NOTE For the purposes of sterilization standards, product is tangible and can be raw material(s), intermediate(s), sub-assembly(ies) or health care product(s).

3.31
product family
group of different product that can be given the same sterilization dose

3.32
requalification
repetition of part of validation for the purpose of confirming the continued acceptability of a specified process

[ISO/TS 11139:2006]

3.33
services
supplies from an external source, needed for the function of equipment

EXAMPLES Electricity, water, compressed air, drainage.

3.34
specification
approved document stipulating requirements

3.35
specify
stipulate in detail within an approved document

[ISO/TS 11139:2006]

3.36
sterile
free from viable microorganisms

[ISO/TS 11139:2006]

3.37
sterility
state of being free from viable microorganisms

NOTE In practice, no such absolute statement regarding the absence of microorganisms can be proven (see **sterilization**) 3.39.

[ISO/TS 11139:2006]

3.38
sterility assurance level
SAL
probability of a single viable microorganism occurring on an item after sterilization

NOTE The term SAL takes a quantitative value, generally 10^{-6} or 10^{-3}. When applying this quantitative value to assurance of sterility, an SAL of 10^{-6} has a lower value but provides greater assurance of sterility than an SAL of 10^{-3}.

[ISO/TS 11139:2006]

3.39
sterilization
validated process used to render product free from viable microorganisms

NOTE In a sterilization process, the nature of microbial inactivation is exponential and thus the survival of a microorganism on an individual item can be expressed in terms of probability. While this probability can be reduced to a very low number it can never be reduced to zero [see **"sterility assurance level"** (3.38)].

[ISO/TS 11139:2006]

3.40
sterilization dose
minimum dose to achieve the specified requirements for sterility

3.41
sterilization process
series of actions or operations needed to achieve the specified requirements for sterility