SLOVENSKI STANDARD
SIST EN 552:2000

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Sterilizacija medicinskih pripomoļ kov - Validacija in redni nadzor sterilizacije z obsevanjem

Sterilization of medical devices - Validation and routine control of sterilization by irradiation

Sterilisation von Medizinprodukten - Validierung und Routineüberwachung für die Sterilisation mit Strahlen

Stérilisation de dispositifs médicaux - Validation et contrôle de routine de la stérilisation par irradiation

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Sterilization of medical devices - Validation and routine control of sterilization by irradiation

Stérilisation de dispositifs médicaux - Validation et contrôle de routine de la stérilisation par irradiation

Sterilisation von Medizinprodukten - Validierung und Routineüberwachung für die Sterilisation mit Strahlen

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CEN

European Committee for Standardization
Comité Européen de Normalisation
Europäisches Komitee für Normung

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Annexes

Foreword

This European Standard has been prepared by the Technical Committee CEN/TC 204 "Sterilization of medical devices", the secretariat of which is held by BSI.

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EC Directive(s).

This standard has been considered by CEN/TC 204 as one of a sequence of European standards concerned with three common sterilization processes and their control. These standards are:

EN 550 Sterilization of medical devices - Validation and routine control of ethylene oxide sterilization

EN 552 Sterilization of medical devices - Validation and routine control of sterilization by irradiation

EN 554 Sterilization of medical devices - Validation and routine control of sterilization by moist heat

EN 556 Sterilization of medical devices - Requirements for medical devices to be labelled "STERILE"

In this European Standard the terms defined in clauses 3 are in italic type.

This European Standard shall be given the status of a National Standard, either by publication of an identical text or by endorsement, at the latest by December 1994, and conflicting national standards shall be withdrawn at the latest by December 1994.

According to the CEN/CENELEC Internal Regulations, the following countries are bound to implement this European Standard: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom.

Introduction

A *sterile* product item is one which is free of viable micro-organisms. The European standards for medical devices require, when it is necessary to supply a *sterile* product item, that adventitious microbiological contamination of medical devices from all sources is minimized by all practical means. Even so, product items produced under standard manufacturing conditions in accordance with the requirements for quality systems for *medical devices* (see EN 46001 or EN 46002) may, prior to sterilization, have micro-organisms 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 micro-organisms by the physical and/or chemical agents used to sterilize *medical devices* often approximates to an exponential relationship; inevitably this means that there is always a finite probability that a micro-organism 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 micro-organisms 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 the existence of a non-sterile item in that population. The value taken by this probability is specified elsewhere (see EN 556). However, the principles specified in this standard are applicable irrespective of the stated probability.

Requirements for the quality system for the design/development, production, installation and servicing of *medical devices* are given in EN 46001 and EN 46002 which supplement the EN 29000 series of European standards.

The EN 29000 series of standards designates certain processes used in manufacture as "special" in that 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 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 object of this European standard is standardization in the field of *validation* and routine monitoring of radiation sterilization processes and procedures that are carried out by those who sterilizer *medical devices*. The *validation* of sterilization procedures presupposes that the sterilization equipment complies with appropriate specifications.

This standard contains requirements for the *validation* and routine monitoring of sterilization by irradiation; guidance on the application of this standard is offered in informative annex **A**.

> NOTE: The requirements are the obligatory parts of this standard in that these are to be observed if compliance is to be achieved. The guidance given in annex **A** is not obligatory and it is not provided as a check list for auditors.

This standard describes the requirements for assuring that the activities associated with the process of radiation sterilization are properly performed. These activities comprise documented work programmes designed to demonstrate that the radiation sterilization process, operating within specified limits, will consistently yield products treated with predetermined minimum and maximum doses.

Radiation sterilization is a physical process, involving the exposure of a product to high energy radiation. The product packaged in sealed units is exposed, in specially designed equipment, to gamma rays from cobalt 60 or caesium 137 radionuclides, or to a beam from an electron generator.

Properly applied, radiation sterilization is a safe and reliable industrial sterilization process.

1 Scope

1.1 This European Standard specifies requirements for the *validation*, process control and monitoring of the radiation sterilization of *medical devices*. It is applicable to continuous and batch type gamma *irradiators* using the radionuclides ^{60}Co or ^{137}Cs and to *irradiators* using electrons, at or below an energy level of 10 MeV, generated from machine sources.

1.2 This European Standard specifies the requirements which ensure that a predetermined dose is consistently absorbed by product presented to the sterilization process.

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

NOTE : Attention is drawn to the standards for quality systems (see EN 46001 or EN 46002) which control all stages of manufacture including the sterilization process. It is not a requirement of this standard to have a complete quality system during manufacture but certain elements of such a system are required and these are normatively referenced at appropriate places in the text.

1.4 This European Standard covers the determination of the maximum dose but does not cover specifically the assessment of the suitability of a product for its intended use after radiation sterilization.

1.5 This European Standard does not cover radiation protection requirements associated with operating irradiation plants.

NOTE : Attention is drawn to the existence in some countries of national regulations laying down safety requirements when operating irradiation plants.

2 Normative references

This European Standard incorporates by dated or undated reference, provisions from other publications. These normative references are cited at the appropriate places in the text and the publications are listed hereafter. For dated references, subsequent amendments to or revisions of any of these publications apply to this European Standard only when incorporated in it by amendment or revision. For undated references the latest edition of the publication referred to applies.

EN 556[1)]	Sterilization of medical devices - Requirements for medical devices to be labelled 'STERILE'.
EN 1174-1[1)]	Sterilization of medical devices - Estimation of the population of micro-organisms on product - Part 1: Requirements
EN 29001 : 1987	Quality systems - Model for quality assurance in design/development, production, installation and servicing.
EN 29002 : 1987	Quality systems - Model for quality assurance in production and installation
EN 46001 : 1993	Particular requirements for the application of EN 29001 for medical devices.
EN 46002 : 1993	Particular requirements for the application of EN 29002 for medical devices.

1) In preparation

3 Definitions

For the purposes of this Standard the following definitions apply.

3.1 absorbed dose: Quantity of radiation energy imparted per unit mass of matter.

NOTE: The unit of absorbed dose is the gray (Gy) where 1 gray is equivalent to the absorption of 1 joule per kilogram (= 100 rad).

3.2 accumulated dose: Sum of the *absorbed doses* regardless of whether the exposure to radiation is continuous or discontinuous.

3.3 average beam current: Time-averaged current produced by an electron beam generator.

3.4 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.

NOTE: Each *batch* is identified by a unique number or code.

3.5 batch (type) irradiator: *Irradiator* which cannot be loaded or unloaded with product whilst the *irradiator* is operating.

3.6 bioburden: Population of viable micro-organisms on a product and/or a package.

NOTE: In the context of irradiation sterilization, *bioburden* is determined immediately prior to sterilization.

3.7 bulk density: Mass of the product and all associated packaging in the *irradiation container* divided by the volume determined by the dimensions of the outermost packaging.

3.8 calibration: Comparison of a measurement system or device of unknown accuracy to a measurement system or device of a known accuracy to detect, correlate, report or eliminate by adjustment, any variation from the required performance limits of the unverified measurement system or device.

3.9 commissioning: See **installation qualification**.

3.10 continuous (type) irradiator: *Irradiator* which can be loaded and unloaded with product whilst the *irradiator* is operating.

3.11 dose: See **absorbed dose**.

3.12 dose distribution: Spacial variation in *absorbed dose* throughout a defined region and material.

3.13 dose mapping: Exercise conducted to determine the distribution of radiation dose throughout a load of product or simulated product of specified density, arranged in an *irradiation container* in a defined configuration.

3.14 dosimeter: Material or device having a reproducible measurable response to radiation, which can be used to measure the absorbed dose at a given location.

3.15 dosimetric system: System comprising the *dosimeters* and the measuring devices to be used for dose measurement.

3.16 dosimetry: Measurement of *absorbed dose* by the use of *dosimeters*.

3.17 electron beam: Continuous or pulsed stream of high energy electrons.

3.18 electron energy: Average kinetic energy of the electrons.

3.19 installation qualification; commissioning: Obtaining and documenting evidence that equipment has been provided and installed in accordance with its specifications and that it functions within pre-determined limits when operated in accordance with the operational instructions.

3.20 irradiation container: Outermost container in which the product is irradiated.

3.21 irradiator: Assembly that includes the source of radiation, conveyor and source mechanisms, safety devices, shield, and which permits safe and reliable sterilization processing.

3.22 irradiator operator: Company or body responsible for delivery of a specified dose to *medical devices* (product).

3.23 medical device: (The definition given in EN 46001 applies.)

3.24 national standard: Standard recognized by an official national decision as the basis for fixing the value(s), in a country, of all other standards of the quantity concerned.

NOTE: The *national standard* in a country is often a *primary standard* (3.28).

3.25 parametric release: Declaring product as "sterile", based on physical process data rather than on the basis of sample testing or biological indicator results.

3.26 performance qualification: Obtaining and documenting evidence that the equipment as commissioned will produce acceptable product when operated according to the process specification.

3.27 **primary manufacturer**: Company or body responsible for the fabrication, performance and safety of a *medical device*.

3.28 **primary standard**: Standard that is designated or widely acknowledged as having the highest metrological qualities and whose values are accepted without reference to other standards.

3.29 **product category**: 1) For sterilization by exposure to gamma radiation, products of similar bulk density exhibiting a similar pattern of dose distribution.
2) For sterilization by exposure to electron radiation, products of similar *maximum surface weight* exhibiting a similar pattern of dose distribution.

3.30 **product path**: Route followed by the product in an irradiator during processing, with reference to the radiation source position.

3.31 **secondary standard**: Standard whose value(s) is (are) assigned by comparison with a *primary standard*.

3.32 **source activity**: Quantity of the radionuclide cobalt 60 or caesium 137, expressed in becquerels, present in the radiation source.

NOTE: In some instances, *source activity* may be expressed in curies. 1 ci = $3{,}7 \times 10^{10}$ Bq.

3.33 **sterile**: Condition of a *medical device* that is free from viable micro-organisms. (See EN 556).

3.34 **sterilizing dose**: The *absorbed dose*, expressed in grays, required to achieve compliance with EN 556.

3.35 **sterilizing dose auditing**: Action taken to detect whether or not a change in the *sterilizing dose* is required.

3.36 **surface weight**: Weight of a columnar section of unit surface area, either:

a) through the product within its outermost package; or

b) through the irradiation container,

in the direction of the electron beam.

NOTE: The units for *surface weight* are grams per square centimetre.

3.37 **maximum surface weight**: *Surface weight* of the columnar section at the position of maximum value.

3.38 timer setting: Pre-selected periods on the timer which control the duration of irradiation exposure.

3.39 transfer standard: Standard used as an intermediary to compare other standards, material measures or measuring instruments.

3.40 validation: Documented procedure for obtaining, recording and interpreting data required to show that a process will consistently comply with predetermined specifications.

NOTE: For irradiation sterilization, *validation* covers three activities: *installation qualification*, establishment of process specification and *performance qualification*.

4 General

NOTE: The manufacturer of the product has responsibility for the quality of the product including the selection of the appropriate *sterilizing dose*. The operator of the radiation sterilization facility (*irradiator operator*) has responsibility for delivering the stipulated *absorbed dose*.

Medical devices to be sterilized shall be manufactured under conditions that ensure that their *bioburden* is consistently low (see EN 556). Employing a quality system complying with EN 46001 or EN 46002 meets this requirement.

The documented procedures and instructions required by this standard shall be implemented effectively. Documentation and records shall be reviewed and approved by designated personnel (see 4.1).

4.1 Personnel

Responsibility for the maintenance of *irradiators*, for the *validation* and routine control of sterilization by irradiation and for the release of product shall be assigned to qualified personnel as specified in 4.1.2.2 and 4.18 of EN 29001 : 1987 or in 4.1.2.2 and 4.17 of EN 29002 : 1987.

4.2 Choice of sterilizing dose

One of two possible approaches, as described in 4.2.1 and 4.2.2, shall be taken in establishing the *sterilizing dose*.

4.2.1 A knowledge of the number and resistance to radiation of the innate microbial population present on or in the *medical device* shall be obtained and used to determine the *sterilizing dose*.

The *sterilizing dose* chosen shall be capable of achieving compliance with EN 556.

Basic technical requirements to generate the required knowledge and to confirm consistency with time shall include the following.

a) Access to competent microbiological laboratory services.

b) Access to either:

1) a ^{60}Co or ^{137}Cs radiation source capable of delivering accurate and precise doses ranging from 1 kGy upwards; or

2) the electron irradiator, which is to be used in processing, to deliver a dose or a series of doses less than the *sterilizing dose*.

The tolerances within which the delivered doses may fall can vary according to the magnitude of the target dose; the rationale for the choice of these tolerances shall be documented and their values shall be specified.

c) For the estimation of *bioburden* in accordance with EN 1174-1, use of samples of *medical devices* taken randomly from at least three representative batches of manufactured product.

d) For the determination of radiation resistance of the natural microbial population, use of samples of *medical devices* taken randomly from one or more representative batches of manufactured product.

e) Performance of a *sterilizing dose auditing* procedure at a frequency to be determined by the *primary manufacturer*.

If compliance with a), b), c), d) and e) cannot be achieved, this approach in choosing a *sterilizing dose* shall not be followed.

4.2.2 Product is treated with a minimum dose of 25 kGy.

NOTE: Historically, 25 kGy has been found to be an effective *sterilizing dose*.

In following this approach, the *primary manufacturer* shall have evidence to show compliance with EN 556. To obtain evidence of compliance, the *primary manufacturer* shall have access to competent microbiological laboratory services.

4.3 Dosimetry

NOTE 1: For *installation qualification* of the *irradiator* and the *performance qualification* of the process, *dose mapping* is performed (see 5.1.1.3 and 5.2.1.3, respectively) in which measurements of *absorbed dose* are made in multiple locations within the *irradiation container*.