BS EN ISO 11137-2:2015

BSI Standards Publication

Sterilization of health care products — Radiation

Part 2: Establishing the sterilization dose

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National foreword

This British Standard is the UK implementation of EN ISO 11137-2:2015. It is identical to ISO 11137-2:2013. It supersedes BS EN ISO 11137-2:2013 which is withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/198, Sterilization and Associated Equipment and Processes.

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

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EUROPEAN STANDARD

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English Version

Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose (ISO 11137-2:2013)

Stérilisation des produits de santé - Irradiation - Partie 2: Établissement de la dose stérilisante (ISO 11137-2:2013)

Sterilisation von Produkten für die Gesundheitsfürsorge - Strahlen - Teil 2: Festlegung der Sterilisationsdosis (ISO 11137-2:2013)

This European Standard was approved by CEN on 20 May 2015.

CEN members are bound to comply with the CEN/CENELEC Internal Regulations which stipulate the conditions for giving this European Standard the status of a national standard without any alteration. Up-to-date lists and bibliographical references concerning such national standards may be obtained on application to the CEN-CENELEC Management Centre or to any CEN member.

This European Standard exists in three official versions (English, French, German). A version in any other language made by translation under the responsibility of a CEN member into its own language and notified to the CEN-CENELEC Management Centre has the same status as the official versions.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
EUROPÄISCHES KOMITEE FÜR NORMUNG

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Ref. No. EN ISO 11137-2:2015 E

Foreword

The text of ISO 11137-2:2013 has been prepared by Technical Committee ISO/TC 198 “Sterilization of health care products” of the International Organization for Standardization (ISO) and has been taken over as EN ISO 11137-2:2015 by Technical Committee CEN/TC 204 “Sterilization of medical devices” the secretariat of which is held by BSI.

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 2015, and conflicting national standards shall be withdrawn at the latest by December 2015.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document supersedes EN ISO 11137-2:2013.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directives.

For relationship with EU Directives, see informative Annexes ZA, ZB and ZC, which are integral parts of this document.

The following referenced documents are indispensable for the application of this document. For undated references, the edition of the referenced document (including any amendments) listed below applies. For dated references, only the edition cited applies. However, for any use of this standard within the meaning of Annex ZA, ZB or ZC, the user should always check that any referenced document has not been superseded and that its relevant contents can still be considered the generally acknowledged state-of-art.

When an IEC or ISO standard is referred to in the ISO standard text, this should be understood as a normative reference to the corresponding EN standard, if available, and otherwise to the dated version of the ISO or IEC standard as listed below.

NOTE The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

Table — Correlation between normative references and dated EN and ISO standards

Normative references as listed in Clause 2 of the ISO standard	Equivalent dated standard	
	EN	ISO
ISO 11137	EN ISO 11137-1:2006/A1:2013	ISO 11137-1:2006/A1:2013
ISO 11737-1	EN ISO 11737-1:2006 + AC:2009	ISO 11737-1:2006 + Cor 1:2007
ISO 11737-2	EN ISO 11737-2:2009	ISO 11737-2:2009

According to the CEN-CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, Former Yugoslav Republic of Macedonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey and the United Kingdom.

Endorsement notice

The text of ISO 11137-2:2013 has been approved by CEN as EN ISO 11137-2:2015 without any modification.

Annex ZA
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 90/385/EEC on active implantable medical devices

This European Standard has been prepared under a mandate given to CEN/CENELEC by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 90/385/EEC on active implantable medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the normative clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with 90/385/EEC, as amended by 2007/47/EC. This means that risks have to be reduced ‘as far as possible’, ‘to a minimum’, ‘to the lowest possible level’, ‘minimized’ or ‘removed’, according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer’s policy for determining **acceptable risk** must be in compliance with essential requirements 1, 4, 5, 8, 9 and 10 of the Directive.

NOTE 3 This Annex ZA is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

Table ZA.1 — Correspondence between this European Standard and Directive 90/385/EEC

Clauses of this European Standard	Essential Requirements (ERs) of EU Directive 90/385/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	7	Only a sterilization process using ionizing radiation is considered by this standard. This relevant Essential Requirement is only partly addressed in this European Standard. Design and packaging for maintenance of sterility during transportation and storage are not covered. Aspects of manufacture other than those related to sterilization are not covered.

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

Annex ZB
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC on medical devices

This European Standard has been prepared under a mandate given to CEN/CENELC by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the normative clauses of this standard given in Table ZB.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with 93/42/EEC, as amended by 2007/47/EC. This means that risks have to be reduced 'as far as possible', 'to a minimum', 'to the lowest possible level', 'minimized' or 'removed', according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with essential requirements 1, 2, 5, 6, 7, 8, 9, 11 and 12 of the Directive.

NOTE 3 This Annex ZA is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

Table ZB.1 — Correspondence between this European Standard and EU Directive 93/42/EEC

Clauses of this European Standard	Essential Requirements (ERs) of EU Directive 93/42/EEC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	8.3	Only a sterilization process using inoizing radiation is considered by this standard. This relevant ER is only partly addressed in this International Standard and only in conjunction with ISO 11137-1. Design and packaging for maintenance of sterility during transportation and storage are not covered. Aspects of manufacture other than those related to sterilization are not covered.
4, 5, 6, 7, 8, 9, 10	8.4	This relevant ER is only partly addressed in this International Standard and only in conjunction with ISO 11137-1. Aspects of manufacture other than those related to sterilization are not covered.

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

Annex ZC
(informative)

Relationship between this European Standard and the Essential Requirements of EU Directive 98/79/EC on *in vitro* diagnostic medical devices

This European Standard has been prepared under a mandate given to CEN/CENELEC by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 98/79/EC on in vitro diagnostic medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the normative clauses of this standard given in Table ZC.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

NOTE 1 Where a reference from a clause of this standard to the risk management process is made, the risk management process needs to be in compliance with 98/79/EC. This means that risks have to be reduced 'as far as possible', 'to a minimum', 'to the lowest possible level', 'minimized' or 'removed', according to the wording of the corresponding essential requirement.

NOTE 2 The manufacturer's policy for determining **acceptable risk** must be in compliance with essential requirements Part A: 1, 2 and 5; Part B: 1.2, 2, 3, 5, 6, and 7 of the Directive.

NOTE 3 This Annex ZA is based on normative references according to the table of references in the European foreword, replacing the references in the core text.

NOTE 4 When an Essential Requirement does not appear in Table ZA.1, it means that it is not addressed by this European Standard.

Table ZC.1 — Correspondence between this European Standard and Directive 98/79/EC

Clauses of this European Standard	Essential Requirements (ERs) of EU Directive 98/79/EC	Qualifying remarks/Notes
4, 5, 6, 7, 8, 9, 10	B.2.3	Only a sterilization process using inoizing radiation is considered by this standard. This relevant ER is only partly addressed in this International Standard and only in conjunction with ISO 11137-1. Design and packaging for maintenance of sterility during transportation and storage are not covered. Aspects of manufacture other than those related to sterilization are not covered.

4, 5, 6, 7, 8, 9, 10	B.2.4	This relevant Essential requirement is addressed in this International Standard in conjunction with ISO 11137-1 and only with regard to: - sterilization, not covering other special microbiological state - devices for which sterilization by radiation is appropriate .

WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this standard.

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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 11137-2 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This third edition cancels and replaces the second edition (ISO 11137-2:2012), of which it constitutes a minor revision with the following changes:

— addition of the word “and” in 9.1, second paragraph, third sentence;

— addition of the word “not” in 10.3.4.1, third paragraph;

— correction of the language used to describe requirements for interpretation of results during a verification dose experiment in the second paragraph in 7.2.6.2, 7.3.7.2, 9.2.6.3, 9.3.7.3, 9.4.6.3, and 9.5.7.3.

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

This part of ISO 11137 describes methods that can be used to establish the sterilization dose in accordance with one of the two approaches specified in 8.2 of ISO 11137-1:2006. The methods used in these approaches are:

— dose setting to obtain a product-specific dose;

— dose substantiation to verify a preselected dose of 25 kGy or 15 kGy.

The basis of the dose setting methods described in this part of ISO 11137 (Methods 1 and 2) owe much to the ideas first propounded by Tallentire**[19][20][21]**. Subsequently, standardized protocols were developed**[10][11]**, which formed the basis of the dose setting methods detailed in the AAMI Recommended Practice for Sterilization by Gamma Radiation**[6][8]**.

Methods 1 and 2 and the associated sterilization dose audit procedures use data derived from the inactivation of the microbial population in its natural state on product. The methods are based on a probability model for the inactivation of microbial populations. The probability model, as applied to bioburden made up of a mixture of various microbial species, assumes that each such species has its own unique D_{10} value. In the model, the probability that an item will possess a surviving microorganism after exposure to a given dose of radiation is defined in terms of the initial number of microorganisms on the item prior to irradiation and the D_{10} values of the microorganisms. The methods involve performance of tests of sterility on product items that have received doses of radiation lower than the sterilization dose. The outcome of these tests is used to predict the dose needed to achieve a predetermined sterility assurance level (SAL).

Methods 1 and 2 can also be used to substantiate 25 kGy if, on performing a dose setting exercise, the derived sterilization dose for an SAL of 10^{-6} is less than or equal to 25 kGy. The basis of the method devised specifically for substantiation of 25 kGy, Method VD_{max}, was put forward by Kowalski and Tallentire**[16]**. Subsequent evaluations involving computational techniques demonstrated that the underlying principles were soundly based**[15]** and field trials confirmed that Method VD_{max} is effective in substantiating 25 kGy for a wide variety of medical devices manufactured and assembled in different ways**[18]**.

A standardized procedure for the use of VD_{max} for substantiation of a sterilization dose of 25 kGy has been published in the AAMI Technical Information Report *Sterilization of health care products — Radiation sterilization — Substantiation of 25 kGy as a sterilization dose — Method* VD_{max}**[7]**, a text on which the method described herein is largely based. Method VD_{max} is founded on dose setting Method 1 and, as such, it possesses the high level of conservativeness characteristic of Method 1. In a similar manner to the dose setting methods, it involves performance of tests of sterility on product items that have received a dose of radiation lower than the sterilization dose. The outcomes of these tests are used to substantiate that 25 kGy achieves an SAL of 10^{-6}.

To link the use of VD_{max} for the substantiation of a particular preselected sterilization dose, the numerical value of the latter, expressed in kilograys, is included as a superscript to the VD_{max} symbol. Thus, for substantiation of a sterilization dose of 25 kGy, the method is designated Method VD_{max}^{25}.

Method VD_{max}^{15} is based on the same principles as Method VD_{max}^{25}. The test procedure is similar to that of Method VD_{max}^{25}, but Method VD_{max}^{15} is limited to product with an average bioburden less than or equal to 1,5. The outcomes of the associated tests of sterility are used to substantiate that 15 kGy achieves a sterility assurance level of 10^{-6}.

This part of ISO 11137 also describes methods that can be used to carry out sterilization dose audits in accordance with ISO 11137-1:2006, Clause 12. Following establishment of the sterilization dose, sterilization dose audits are performed routinely to confirm that the sterilization dose continues to achieve the desired SAL.

INTERNATIONAL STANDARD **ISO 11137-2:2013(E)**

Sterilization of health care products — Radiation —

Part 2: Establishing the sterilization dose

1 Scope

This part of ISO 11137 specifies methods for determining the minimum dose needed to achieve a specified requirement for sterility and methods to substantiate the use of 25 kGy or 15 kGy as the sterilization dose to achieve a sterility assurance level, SAL, of 10^{-6}. This part of ISO 11137 also specifies methods of sterilization dose audit used to demonstrate the continued effectiveness of the sterilization dose.

This part of ISO 11137 defines product families for sterilization dose establishment and sterilization dose audit.

2 Normative references

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

ISO 11137-1:2006, *Sterilization of health care products — Radiation — Part 1: Requirements for the development, validation and routine control of a sterilization process for medical devices*

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 definition, validation and maintenance of a sterilization process*

3 Terms, definitions, and abbreviated terms

For the purposes of this document, the terms and definitions given in ISO 11137-1 and the following apply.

3.1 Terms and definitions

3.1.1
batch
defined quantity of product, intended or purported to be uniform in character and quality, which has been produced during a defined cycle of manufacture

[ISO/TS 11139:2006, definition 2.1]

3.1.2
bioburden
population of viable microorganisms on or in product and/or sterile barrier system

[ISO/TS 11139:2006, definition 2.2]