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Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose

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Sterilization of health care products - Radiation - Part 2: Establishing the sterilization dose

Stérilisation des produits de santé - Irradiation - Partie 2: Etablissement de la dose de stérilisation

This draft European Standard is submitted to CEN members for parallel enquiry. It has been drawn up by the Technical Committee CEN/TC 204.

If this draft becomes a European Standard, 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.

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EUROPEAN COMMITTEE FOR STANDARDIZATION
COMITÉ EUROPÉEN DE NORMALISATION
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Foreword

This document (prEN ISO 11137-2:2004) has been prepared by Technical Committee ISO/TC 198 "Sterilization of health care products" in collaboration with Technical Committee CEN/TC 204 "Sterilization of medical devices", the secretariat of which is held by BSI.

This document is currently submitted to the parallel Enquiry.

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 Directive(s).

Endorsement notice

The text of ISO/DIS 11137-2:2004 has been approved by CEN as prEN ISO 11137-2:2004 without any modifications.

DRAFT INTERNATIONAL STANDARD ISO/DIS 11137-2

ISO/TC **198** Secretariat: **ANSI**

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Sterilization of health care products — Radiation —

Part 2: Establishing the sterilization dose

Stérilisation des produits de santé — Irradiation —

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ISO/CEN PARALLEL ENQUIRY

The CEN Secretary-General has advised the ISO Secretary-General that this ISO/DIS covers a subject of interest to European standardization. **In accordance with the ISO-lead mode of collaboration as defined in the Vienna Agreement, consultation on this ISO/DIS has the same effect for CEN members as would a CEN enquiry on a draft European Standard.** Should this draft be accepted, a final draft, established on the basis of comments received, will be submitted to a parallel two-month FDIS vote in ISO and formal vote in CEN.

In accordance with the provisions of Council Resolution 15/1993 this document is circulated in the English language only.

Conformément aux dispositions de la Résolution du Conseil 15/1993, ce document est distribué en version anglaise seulement.

To expedite distribution, this document is circulated as received from the committee secretariat. ISO Central Secretariat work of editing and text composition will be undertaken at publication stage.

Pour accélérer la distribution, le présent document est distribué tel qu'il est parvenu du secrétariat du comité. Le travail de rédaction et de composition de texte sera effectué au Secrétariat central de l'ISO au stade de publication.

Contents

Page

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.

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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*, Subcommittee.

This document, along with ISO 11137-1 and ISO 11137-3, cancels and replaces the first edition of ISO 11137 and has been technically revised.

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

— *Part 1: Requirements for the 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 may be used to establish the sterilization dose in accordance with one of the two approaches specified in 8.2 of ISO 11137-1. The methods employed in these approaches are,

a) dose setting to obtain a product-specific dose, and

b) dose substantiation to verify a preselected dose of 25 kGy.

The basis of the dose setting methods described in this standard (Methods 1 and 2) owe much to the ideas first propounded by Tallentire (Tallentire, 1973; Tallentire, Dwyer and Ley, 1971; Tallentire and Khan, 1978). Subsequently, standardized protocols were developed (Davis *et al,* 1981; Davis, Strawderman and Whitby, 1984) which formed the basis of the dose setting methods detailed in the AAMI *Recommended Practice for Sterilization by Gamma Radiation* (AAMI 1984, 1991).

Methods 1 and 2 and the associated audit procedures use data derived from the inactivation of the microbial population in its natural state. 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 employed to predict the dose needed to achieve a predetermined sterility assurance level (SAL). Following establishment and use of the sterilization dose, audits are routinely performed to confirm that the sterilization dose continues to achieve the desired SAL.

Methods 1 and 2 may also be used to substantiate 25 kGy if, on performing a dose setting exercise, the derived sterilization dose is equal to or less than 25 kGy. The basis of the method devised specifically for substantiation of 25 kGy, Method VD_{max}, was put forward by Kowalski and Tallentire (1999). Subsequent evaluations involving computational techniques demonstrated that the underlying principles were soundly based (Kowalski, Aoshuang, and Tallentire, 2000) 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. A standardized procedure for the method 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}* (AAMI TIR 27, 2001), 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 employed to substantiate that 25 kGy achieves an SAL of 10^{-6}. Following substantiation and use of 25 kGy, audits are performed routinely to confirm the continued appropriateness of 25 kGy as the sterilization dose.

Method VD^{15}_{max} is based on the same principles as Method VD^{25}_{max} described above. The test procedure is the same as Method VD^{25}_{max} but VD^{15}_{max} is limited to product with average bioburden in the range of 0.1 to 1.5 inclusive. The outcomes of these tests are employed to substantiate that 15 kGy achieves a sterility assurance level of 10^{-6}.

Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose

1 Scope

1.1 This International Standard describes methods of 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 International Standard also describes methods of dose auditing to demonstrate the continued effectiveness of the sterilization dose.

1.2 While the dose setting and dose substantiation methods described in this International Standard meet the requirements specified in 8.2 of the International Standard 11137-1, other methods that also meet these requirements may be used. For this reason, International Standard 11137-2 is considered "informative." The use of the terms "shall", "should", etc. should be considered within the context of this Standard only; that is, if the decision is made to use one of the methods, then the method has to be followed in its entirety in adherence with the requirements ("shall") and with due consideration of the recommendations ("should") as set forth in this International Standard.

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. Members of IEC and ISO maintain registers of currently valid International Standards.

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

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

ISO 11737-1 *Sterilization of medical devices – Microbiological methods – Part 1: Estimation of population of microorganisms on products*

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

3 Terms and definitions

For purposes of this International Standard, the terms and definitions in ISO 11137-1 and the following apply:

3.1 Terms

3.1.1
A
dose to adjust downwards the median ffp dose to the FFP dose

3.1.2
CD*
number of positive tests of sterility obtained from tests performed individually on 100 product items irradiated in a Method 2 verification dose experiment

3.1.3
d*
dose derived from an incremental dose experiment performed on product items withdrawn from a given production batch

NOTE See 8.2.3.3.1 or 8.3.3.3.1 for the criteria for selection of d*, depending upon whether Method 2A or 2B is being applied.

3.1.4
D*
initial estimate of the dose to provide an SAL of 10^{-2} for the test items

NOTE Generally, it is the median of the 3 d* values derived for a given product.

3.1.5
D**
final estimate of the dose to provide an SAL of 10^{-2} for the test items that is used in the calculation of the sterilization dose

3.1.6
DD*
dose delivered in a Method 2 verification dose experiment

3.1.7
DS
estimate of D_{10} value of microorganisms present on product after exposure to DD*

3.1.8
D_{10} value
time or radiation dose required to achieve inactivation of 90% of a population of the test microorganism under stated exposure conditions

[ISO TS 11139:2001]

NOTE For the purposes of this International Standard, D_{10} applies to the radiation dose only and not time.

3.1.9
ffp (first fraction positive dose)
lowest dose of an incremental dose series, applied to items withdrawn from a given production batch, at which at least one of the associated 20 tests of sterility is negative

3.1.10
FFP (First Fraction Positive dose)
dose at which 19 positives out of the 20 tests of sterility are expected to occur, calculated by subtracting A from the median of 3 ffp doses

3.1.11
FNP (First No Positive dose)
estimate of the dose to provide an SAL of 10^{-2} for the test items, which is used in the calculation of DS

3.1.12
VD_{max}
maximal verification dose for a given bioburden, consistent with the attainment of an SAL of 10^{-6} at a specified sterilization dose

3.2 Definitions

3.2.1
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

3.2.2
false positive
test result interpreted as growth arising from the sample tested when either the growth resulted from extraneous microbial contamination or turbidity occurred due to an interaction between the sample and the test medium

3.2.3
fraction positive
quotient with the number of positive tests of sterility in the numerator and the number of tests performed in the denominator

3.2.4
incremental dose
dose within a series of doses applied to a number of product, or portions thereof, and used in a dose setting method to obtain or confirm the sterilization dose

3.2.5
negative test of sterility
test result for which there is no detectable microbial growth on product, or portion thereof, subjected to a test of sterility

3.2.6
positive test of sterility
test result for which there is detectable microbial growth on product, or portion thereof, subjected to a test of sterility

3.2.7
sample item portion (SIP)
defined portion of a health care product that is tested

3.2.8
sterilization dose audit
exercise undertaken to confirm the appropriateness of an established sterilization dose

3.2.9
verification dose
dose of radiation predicted to give a predetermined SAL used in establishing the sterilization dose

4 Definition and maintenance of product families for dose setting, dose substantiation and sterilization dose auditing

4.1 General

The establishment of a sterilization dose and the carrying out of sterilization dose audits are activities that are part of process definition (8 of ISO 11137-1) and maintaining process effectiveness (12 of ISO 11137-1). Product may be grouped into families, and product families defined for these activities are based principally on the number and types of microorganisms present on or in product (the bioburden). Process variables such as density and product configuration within its packaging are not considered in the establishment of these product families because they are not factors that influence bioburden. The principles for defining product