EN/ISO 11737-2 “Sterilization of health care products – Microbiological methods – Part 2: Tests of Sterility performed in the definition, validation and maintenance of a sterilisation process’’

Note on differences between 2009 and 2019 versions

Introduction

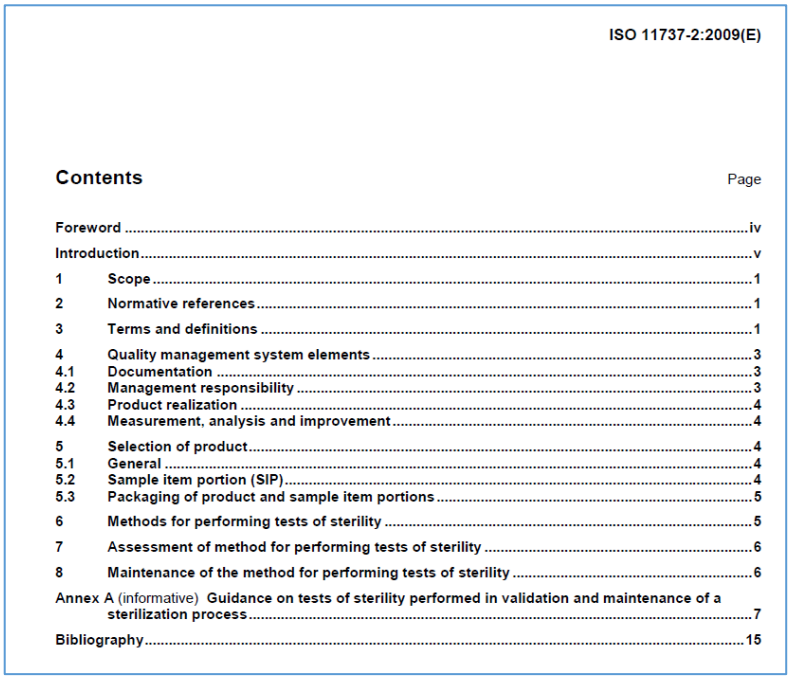
An updated version of document EN/ISO 11737-2 “Sterilization of health care products – Microbiological methods – Part 2: Tests of Sterility performed in the definition, validation and maintenance of a sterilisation process’” was published in 2019, replacing the version that had been published in 2009.

Although the Scope and overall outline of the two documents are similar, there have been some changes in terms of terminology, more detailed guidance in appendices and a new Annex B.

The purpose of this document is to highlight, in general terms, areas of difference between the two versions of the standard.

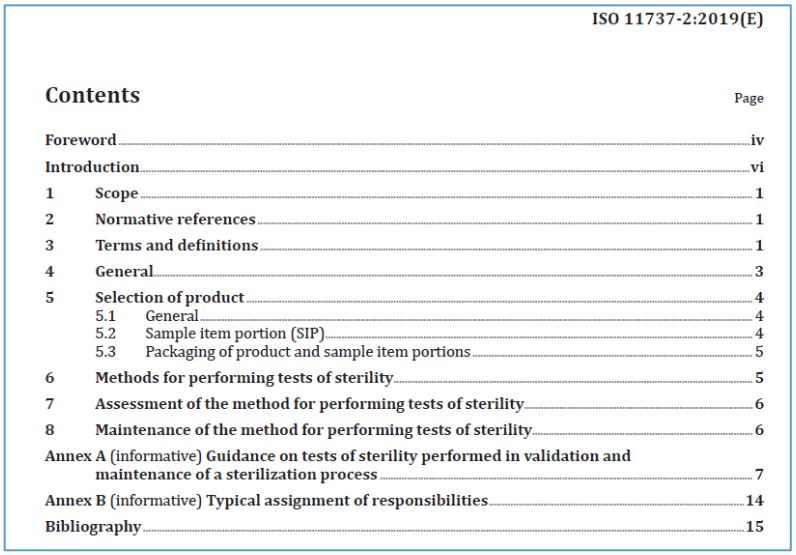
Contents of 11737-2:2019

Figure 1 : Content page of ISO11737-2:2019 and ISO 11737-2 :2009 for comparison



ISO 11737-2:2009(E)

Contents Page



ISO 11737-2:2019(E)

Contents Page

Figure 1 shows the contents of 11737-2:2019 and 2009. The overall structure is very similar to that of 11737-2:2009, but Sections have been renamed and restructured.

One new informative Annex has been added: Annex B Typical alignment of responsibilities.

In the remainder of this document, differences between the two standards will be given, using the numbering and titles of clauses in 11737-2:2019.

The Foreword lists the following summary of changes :

The main changes compared to the previous edition are as follows:

— addition of a requirement concerning the test samples and the interval of time between the manufacture of product and the exposure to the sterilizing agent being as short as possible;

— addition of a requirement about the samples staying immersed in the culture media and providing a rationale where this is not possible;

— provision of additional guidance regarding performing tests of sterility on packaging, clarifying that package testing is not typically done except when it is an integral part of the product;

— provision of additional guidance regarding what is meant by "controlled environment" for performing tests of sterility;

— provision of additional guidance to discuss circumstances where the method suitability test does not give acceptable results, stating that after multiple attempts to eliminate inhibitory substances, it is appropriate to accept a reduction of inhibitory substances, with an accompanying rationale and risk assessment;

— provision of guidance regarding identification of microbial growth in a test of sterility, saying generally for positive growth the microorganism(s) should be identified;

— provision of guidance regarding method suitability, saying that consideration should be given to periodically demonstrating ongoing method suitability in order to ensure that an accumulation of minor changes over time has not occurred;

— addition of a table to clarify where typical responsibilities reside for the manufacturer or the laboratory.

Introduction

More clarity has been included here on the use of fractional exposure/verification doses and their intent. Item c has been added and the final paragraph express that performing a test of sterility on a product that has been exposed to the complete sterilisation process provides no scientifically usable data and is not recommended.

Extract :

International Standards specifying procedures for the development, validation and routine control of the processes used for sterilization of medical devices have been prepared [see ISO 11135, ISO 11137 (all parts), ISO 14937, ISO 14160, ISO 17665-1 and ISO 20857]. An element of validation might consist of exposing medical devices to the sterilizing agent with the extent of treatment being reduced relative to that which will be used in routine sterilization processing, in order to provide a knowledge of the resistance to the agent of the microbial contamination as it occurs naturally on medical devices. The reduced exposures applied in these instances are often called fractional exposures or verification doses. Subsequent to this reduced exposure, medical devices are subjected individually to tests of sterility as described in this document. Examples of the use of such tests are in:

a) establishing a dose for sterilization by radiation,

b) demonstrating the continued validity of an established sterilization dose, and

c) establishing a cycle for sterilization by evaluating the product's naturally occurring bioburden.

Product that has been exposed to a terminal sterilization process in its final packaged form has a very low probability of the presence of a viable microorganism; such as one in one million or 10^{-6}. As such, performing a test of sterility on product that has been exposed to the complete sterilization process provides no scientifically usable data and is not recommended.

Scope (Clause 1)

The Scope introduces the term ‘healthcare product’ to replace the term ‘medical device’ – this continues throughout the document.

Clarity added on what this document is NOT applicable to.

Additional references added ISO 20867, ISO 11737-2 itself.

Addition of ‘… not applicable to…c) test of sterility or test for sterility for demonstration of product shelf life, stability and/or package integrity..’

Normative References (Clause 2)

All removed as compared from the 2009 version.

Terms and Definitions (Clause 3)

This Clause introduces some new terms: namely aseptic technique / health care product / method suitability and removes aerobic organism, anaerobic organism, growth promotion test.

General (Clause 4)

Title changed from 'quality management system elements'

Section condensed from 2009 but no change to intent.

Selection of products (Clause 5)

Section has additional wording but no change to intent. Reference added to ‘product family’.
Added 5.1.3 : ‘The rationale for the number of product items that are selected and the number of batches from which this selection is made shall be documented.’

Added note in 5.2.2.1 : ‘When selecting the portion that contains the most severe microbial challenge, the relationship of the bioburden of the SIP tested to the entire product bioburden should be established.’
Added note about calculation of SIP. Table of SIP calculation moved to Annex A.

Methods for performing tests of sterility (Clause 6)

Added a third method to the list of options ; direct immersion, removal of organisms, filtration of liquid products.

Added wording in 6.1a) ‘The product shall be immersed in the culture media for the duration of the incubation time where possible. A rationale shall be provided if this is not possible, such as with buoyant materials.’

Added 6.4 b) ‘Establishment of a recovery efficiency followed by a risk assessment to determine the appropriateness of the removal process’.

Added wording to 6.6 and introduction of the wording ‘method suitability’; ‘The test system shall be evaluated in a method suitability test (also called bacteriostasis / fungistasis) to ensure that the ability to sustain microbiological growth is not affected.’

Assessment of the method for performing tests of sterility (Clause 7)

No significant changes.

Maintenance of the method for performing tests of sterility (Clause 8)

Added wording to 8.2, ' Modifications to the parameters of a test of sterility'… shall be assessed..

Annex A

In general more detail added in the guidance sections.

A.1 Scope

A.1.2	Addition: 'tests for sterility are excluded from this document because they are not performed in the definition, validation and maintenance of a sterilisation process. Tests for sterility are not appropriate for confirmation of a sterilisation process effectiveness, a sterility assurance level, or attributes associated with the sterility of a product such a package integrity or product shelf life.'

A.5 Selection of product

A.5.2.1	Addition: 'this might not be feasible if the product cannot be accommodated in available laboratory testing vessels'. 'If a product cannot be tested in available laboratory containers, it may be divided into two or more containers and these containers scored together as one, if one container yields a positive result, the entire product item is considered positive'.
A.5.2.2	Addition: 'as large a portion of the product as possible should be used for SIP… Consideration should be given to aspects of manufacturing that contribute to the distribution of microorganisms on product.' 'Product such as drapes, lengths of tubing, etc. are types of product that couldbe expected to have an even distribution of bioburden. This might not apply in case of application of manual steps for cutting or folding of drapes as well as for cutting, transportation, and assembly of tubing.'
A.5.2.3	Addition: Examples of an SIP that can be selected from the device with a more severe challenge to the sterilisation process are tubing sets with connections, stopcocks etc. Additional examples have been added to table A.1.
A.5.3	No change

A.6 Methods of performing tests of sterility

A.6.1	a) Addition of statement: ' if this is not possible due to the buoyant nature of the product, a procedure should be implemented to periodically manipulate the container so that contact is facilitated during the incubation period.' b) Addition of : 'as elution of microorganisms form product is often not as effective for a test of sterility compared to direct immersion. Therefore

	direct immersion methods are preferable whenever practicable. If the direct immersion method is not practicable an elution method can be considered. In the elution methods, an understanding of the recovery efficiency coupled with a risk assessment and rationale is critical.
A.6.2	NEW : Guidance on when packaging material is included in the test of sterility and consideration for the contact with culture media.
A.6.3	Addition : 'conducting the test in a laminar flow hood, micro safety cabinet, or other equipment ensuring the same particulate and microbiological level, within a microbiologically controlled room or in barrier isolation in a microbially controlled environment. Ref ISO 14644 / 14698.' Addition : minimising the amount of materials in the hood, Addition : 'taking care not to disrupt the airflow patterns during manipulation'.
A.6.4	Addition: ' …performing an elution of product by directly culturing…'
A.6.5	Addition: '…with the aid of vacuum or pressure..'
A.6.6	Addition: '…is called the method suitability test (also called bacteriostasis / fungistasis test' Addition : 'Microbicidal substances can bind to filter membranes, care should be taken to ensure the use of suitable filter membranes to minimise the potential for binding' Addition : 'Guidance on the procedures, organisms, titers and incubation times for method suitability can be found in current Pharmacopeias. However the incubation temperature and culture media have to be the same as those used in performing the tests of sterility.' Addition : ' Multiple attempts should be made using different culturing conditions to eliminate or reduce inhibitory substances to the point where there is no longer an acceptable risk. After multiple attempts are made, if the inhibitory substance is not eliminated, it is appropriate to accept a reduction of inhibitory substances, with an accompanying rationale and risk assessment.'
A.6.7	Addition: …'e.g the presence of anaerobes or mycobacteria.'
A.6.9	Addition: …' and colour change. Generally, when product items are positive for microbial growth, the microorganism(s) should be identified.

A.7 Assessment of method for performing tests of sterility.

A.7	Addition : 'Factors which might affect the occurrence of false positives include: breach in the sterile barrier, contamination during testing, contamination from handling during incubation' Addition : 'The occurrence of false negatives in tests of sterility can affect the interpretation of data obtained in validation by making a treatment with the sterilising agent more effective.' Addition : … allowing for microorganisms to lose viability'. Addition : 'If the occurrence of positive tests of sterility can be ascribed to incorrect performance of the tests of sterility, a sterilising agent related issue

	or another relevant cause , corrective action can be implemented and a repeat test of sterility can be performed.

A.8 Maintenance of the method for performing tests of sterility.

A.8.1	Addition: 'Because the test of sterility is vital to support definition, validation and maintenance of a sterilisation process for a product or product family, a change to product, the processes used to manufacture product, sterilisation process or to the parameters of the test of sterility, necessitates consideration of the need to demonstrate ongoing method suitability. Consideration should be given to the effects of cumulative changes over time. Changes to the test of sterility should be carried out within a documented change control process'. Addition : 'Even in the absence of planned changes to product , the processes used to manufacture product or to the parameters to the tests of sterility, consideration should be given to periodically reviewing ongoing method suitability to ensure that an accumulation of minor changes over time has not occurred that could adversely affect the continued suitability of the test method.'

Annex B

Annex B	Addition: New Annex regarding assignment of responsibilities