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Aseptic processing of health care products —

Part 2: Filtration

Traitement aseptique des produits de santé —

Partie 2: Filtration

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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 13408-2 was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

ISO 13408 consists of the following parts, under the general title *Aseptic processing of health care products*:

— *Part 1: General requirements*

— *Part 2: Filtration*

The following parts are under preparation:

— *Part 3: Freeze-drying*

— *Part 4: Sterilization in place*

— *Part 5: Cleaning in place*

— *Part 6: Isolator/barrier technology*

Introduction

During the process of preparing ISO 13408-1:1998, which addresses general requirements, several items, e.g. filtration, freeze-drying and steam-in-place, were found to be in need of supplementary information which was too large to be given in corresponding Annexes. This part of ISO 13408 includes requirements and guidance that are to be observed when aseptically manufacturing health care products by filtration.

ISO 13408-1:1998 will be revised soon after the publication of this part of ISO 13408, as clause 20 of ISO 13408-1:1998 is replaced by this part of ISO 13408.

Aseptic processing of health care products —

Part 2: Filtration

1 Scope

This part of ISO 13408 specifies requirements for sterilizing filtration as part of aseptic processing of health care products. It also offers guidance to filter users concerning general requirements for set-up, validation and routine operation of a sterilizing filtration process, to be used for aseptic processing of health care products.

This part of ISO 13408 is not applicable to removal of viruses. Sterilizing filtration is not applicable to fluids containing particles as effective ingredient larger than the pore size of a filter (e.g. bacterial whole-cell vaccines).

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 13408-1:1998, *Aseptic processing of health care products — Part 1: General requirements*

ISO/TS 11139:2001, *Sterilization of health care products — Vocabulary*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 13408-1, ISO/TS 11139 and the following apply.

3.1
bacterial challenge test
test to evaluate the capability of a filter to retain organisms from a bacterial suspension under defined conditions

3.2
bioburden
population of viable microorganisms in a fluid prior to sterilizing filtration

NOTE For the purposes of this part of ISO 13408, the definition of bioburden is narrower than that in ISO/TS 11139.

3.3
chemical compatibility
ability of the process fluids not to adversely affect the properties of filter materials and/or filter assembly components and vice versa

3.4
fibre
particle having an aspect (length-to-width) ratio of 10 or more

[ISO 14644-1:1999, 2.2.7]

3.5
fibre-releasing filter
filter which, even after any appropriate treatment such as washing or flushing, will release fibres into the filtrate

3.6
filter
porous material through which a liquid or a gas is passed to remove viable and non-viable particles

3.7
filter assembly
filter cartridge(s) or filter material installed into a housing or holder

NOTE This can be done by the filter user or by the filter manufacturer, e.g. in the form of pre-assembled filter units.

3.8
filter cartridge
filter material assembled into a unit

3.9
filter equipment
gauge, valve and other items attached to filter assembly

3.10
filtration
process to remove viable and/or non-viable particles from liquids and/or gases by passage through a porous material

3.11
filtration system
filter assembly equipped with filter equipment

cf. **filter equipment** (3.9)

3.12
fluid
liquid or a gas

NOTE The fluid subjected to the filtration process may be the formulation to be produced, or a part of the formulation, or a process fluid.

3.13
fluid-sterilizing filter
filter that is capable of removing a defined challenge of microorganisms from a fluid under defined filtration process conditions

NOTE Typically, such a filter has a nominal pore size rating of less than or equal to 0,22 µm.

3.14
integrity test
non-destructive physical test which can be correlated to the bacterial retention capability of a filter/filter assembly

3.15
microorganism
entity, encompassing bacteria, fungi, protozoa and viruses

NOTE For the purposes of this part of ISO 13408, viruses are not addressed.

3.16
nominal pore size rating
pore size of a filter as claimed and stated by the filter manufacturer

3.17
worst case
most challenging pre-determined condition(s) and specification(s) applied in a process to be validated

4 General requirements

The requirements of ISO 13408-1:1998 shall apply.

5 Selection of filters and filter assemblies based on filter manufacturer's data

5.1 Selection shall document the choice of the most suitable type(s) of filter, taking into account the chemical and physical characteristics of the filters as established by the filter manufacturers.

NOTE For further information see A.1.

5.2 The filters selected shall have a quality certificate.

NOTE For further information see A.2.

5.3 Filters shall not contain asbestos and shall not be fibre-releasing. Where the use of fibre-releasing filters is dictated by product need, it shall be demonstrated that the fibres are removed downstream of filtration.

6 Fluid-specific selection criteria based on filter user's data

6.1 The filter user shall evaluate filter characteristics following a documented filter evaluation programme that takes into account the fluid to be filtered and the process used for filtration. Filter characteristics shall not be adversely affected by the fluid to be filtered; conversely, the product shall not be adversely affected by the filter. Adsorption of fluid components and extraction of filter components shall be evaluated.

6.2 For filter characterization, the following shall be taken into account:

a) compatibility between filter and fluid;

   1) effects of the formulation and process conditions on the chemical and physical attributes and performance of the filter;

   2) effects of the filter on the relevant biological, chemical and physical attributes of the product;

b) process characteristics;

   1) effective filter surface area required;

   2) pre-filtration requirements for reduction of particulate matter and reduction of bioburden.

Compatibility and process criteria, as applicable, should also be applied to pre-filters in view of their intended use.