INTERNATIONAL STANDARD

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Aseptic processing of health care products —

Part 2: Sterilizing filtration

Traitement aseptique des produits de santé —

Partie 2: Filtration stérilisante

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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.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 198, *Sterilization of health care products*.

This second edition cancels and replaces the first edition (ISO 13408-2:2003), which has been technically revised.

A list of all parts in the ISO 13408 series can be found on the ISO website.

Introduction

ISO 13408-1 covers general aspects of aseptic processing. Several processes including sterilizing filtration, lyophilization, clean and sterilization in place, isolator systems, and alternative processes for medical devices and combination products were found to be in need of supplementary information, which was too extensive to be included in the corresponding annexes to ISO 13408-1. This information is presented in ISO 13408-2 to ISO 13408-7.

Sterilizing filtration is a critical step in an aseptic manufacturing process. Validation of sterilizing filtration processes can be complex and is generally conducted in both a process and product specific manner. This document describes requirements that, if met, will provide a sterilizing filtration process that consistently removes microorganisms from a fluid (liquid or gas) without negatively affecting the quality of the filtrate. Furthermore, conformity with the requirements ensures that a sterilizing filtration process is both reliable and reproducible so that a determination can be made, with reasonable confidence, that the sterilizing grade filter/s will provide a sterile filtrate under specified operational conditions. This (the reliability and reproducibility of the filtration process) is essential, as unlike a micro-biocidal sterilization process where process variables can be monitored continuously, microbial retention and physical integrity of a sterilising grade filter cannot be monitored on a continuous basis throughout a filtration process.

Where validation establishes a reproducible relationship between the product-specific bacterial retention capability of a sterilizing grade filter and the physical integrity of that filter, then suitable non-destructive pre-use and post-use filter integrity tests are used to determine whether a full-scale sterilizing filtration process has been conducted successfully. During terminal sterilization the kinetics of inactivation follows a mathematical order and allow calculation of a sterility assurance level (SAL). Removal of organisms from a fluid by filtration does not follow such mathematical order and so the use of the term “sterility assurance level” is not appropriate for product sterilized by filtration.

There has been a significant increase in the development and availability of biopharmaceuticals, biologic-based medical devices and cell-based health care products since publication of the initial 2003 edition of this document. This second edition emphasizes the importance of a thorough understanding of the nature of the indigenous bioburden of a fluid that is to be sterilized by filtration, including its relationship to the test microorganism used to determine microbial retention capability of the sterilizing grade filter. For example, Mycoplasma can cause serious contamination problems during the manufacturing of biopharmaceutical, biotechnological and cell-based health care products. A thorough understanding of the indigenous bioburden enables suitable safeguards to be implemented during development, validation and control of a sterilizing filtration process to ensure the safety and quality of the filtered fluid.

While the activities required by this document have been grouped together and are presented in a particular order, this document does not require that the activities be performed in the order that they are presented. The activities required are not necessarily sequential, as the programme of development and validation may be iterative. It is possible that performing these different activities will involve a number of separate individuals and/or organizations, each of whom undertake one or more of these activities. This document does not specify the particular individuals or organizations to carry out the activities.

Guidance on the application of this document is given in Annex A.