INTERNATIONAL STANDARD

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Aseptic processing of health care products —

Part 4: Clean-in-place technologies

Traitement aseptique des produits de santé —

Partie 4: Technologies de nettoyage sur place

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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

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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 13408-4 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*

— *Part 3: Lyophilization*

— *Part 4: Clean-in-place technologies*

— *Part 5: Sterilization in place*

— *Part 6: Isolator systems*

Introduction

During the process of preparing ISO 13408-1 several items, e.g. filtration, lyophilization drying and sterilization-in-place technologies, were found to be in need of supplementary information that was too voluminous to be given in corresponding annexes.

This part of ISO 13408 includes requirements and guidance that are to be observed during clean-in-place processes. The purpose of this part of ISO 13408 is to achieve standardization in the field of validation and routine control of clean-in-place processes used in the manufacture of health care products.

Clean-in-place processes allow parts of the equipment or an entire process system to be cleaned without being dismantled, reducing the need for disassembling and connections under clean conditions. For example, tanks, vessels, freeze-dryers, piping and other processing equipment used for manufacture may be cleaned in place.

The clean-in-place process is in most instances followed by sterilization-in-place process (described in ISO 13408-5). While clean-in-place and sterilization-in-place methods differ considerably in technology, the concept of *in situ* treatment is similar.

Design considerations of all systems are critical to ensure that clean-in-place technologies can be successfully applied to clean manufacturing equipment to the desired level of cleanliness.

Aseptic processing of health care products —

Part 4:
Clean-in-place technologies

1 Scope

This part of ISO 13408 specifies the general requirements for clean-in-place (CIP) processes applied to product contact surfaces of equipment used in the manufacture of sterile health care products by aseptic processing and offers guidance on qualification, validation, operation and control.

This part of ISO 13408 is applicable to processes where cleaning agents are delivered to the internal surfaces of equipment designed to be compatible with CIP, which may come in contact with the product.

This part of ISO 13408 is not applicable to processes where equipment is dismantled and cleaned in a washer.

This part of ISO 13408 does not supersede or replace national regulatory requirements, such as Good Manufacturing Practices (GMPs) and/or compendial requirements that pertain to particular national or regional jurisdictions.

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

ISO/IEC 90003, *Software engineering — Guidelines for the application of ISO 9001:2000 to computer software*

3 Terms and definitions

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

3.1
cleaning agent
organic or inorganic chemical including water, detergent or mixture thereof, used as an aid in the cleaning process for cleaning equipment

3.2
clean-in-place
CIP
method of cleaning of the internal surfaces of parts of the equipment or an entire process system without or with minimal disassembly

NOTE CIP also includes the removal of remaining residual cleaning agent to an acceptable level which is defined based on the nature of the product and the process tolerance.