
**Aseptic processing of health care
products —**

**Part 6:
Isolator systems**

Traitement aseptique des produits de santé —

Partie 6: Systèmes isolateurs



This document is a preview generated by EKO



COPYRIGHT PROTECTED DOCUMENT

© ISO 2021

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Email: copyright@iso.org
Website: www.iso.org

Published in Switzerland

Contents

Page

Foreword	v
Introduction	vi
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 Quality system elements	3
5 Basic principle of isolator systems	3
5.1 General	3
5.2 Negative pressure isolators	4
6 Isolator system specification	4
6.1 General	4
6.2 Risk management	4
6.2.1 General	4
6.2.2 Negative pressure isolator systems	5
6.3 User requirement specification	5
7 Design of isolator systems	5
7.1 General	5
7.2 Materials of construction	6
7.3 Air-handling system	6
7.3.1 General	6
7.3.2 Air change rate	6
7.3.3 Airflow pattern	6
7.3.4 Temperature/humidity	7
7.3.5 Particulate air specifications	7
7.3.6 Recirculation of air	7
7.3.7 Pressure differentials	7
7.4 Operator interface	7
7.4.1 Isolator gloves/sleeves	7
7.4.2 Suits/half-suits	8
7.4.3 Access to the isolator/transfer systems	8
7.4.4 Devices acting as transfer ports	8
7.5 Ancillary isolator equipment	9
7.5.1 Portable and mobile equipment	9
7.6 Surrounding room classification	9
7.7 Process utilities	9
8 Validation	9
8.1 General	9
8.2 Design qualification	10
8.2.1 General	10
8.2.2 Product/process application	10
8.2.3 Ergonomics	10
8.2.4 Cleaning	10
8.2.5 Bio-decontamination	11
8.2.6 Selection of bio-decontamination agent	11
8.2.7 Development and validation of bio-decontamination processes	12
8.2.8 Bio-decontamination agent generation and testing	12
8.2.9 Bio-decontamination parameters	13
8.2.10 Aeration and residue limits	13
8.2.11 Log reduction	13
8.2.12 Surface bio-decontamination of items	14
8.2.13 Development and validation of sterilization processes	14

8.3	Installation qualification	14
8.3.1	General	14
8.3.2	Installation	14
8.4	Operational qualification	15
8.5	Performance qualification	16
8.5.1	General	16
8.5.2	Cleaning	16
8.5.3	Bio-decontamination	16
8.5.4	Process simulation tests	16
8.6	Review and approval of validation	16
8.7	Requalification	17
9	Routine monitoring and control	17
9.1	Procedures	17
9.2	System integrity	17
9.3	Bio-decontamination process monitoring	17
9.4	Environmental monitoring	18
9.5	Change control	18
9.6	Maintenance and calibration	18
10	Personnel training	19
Annex A (informative) Devices acting as transfer ports for portable and mobile equipment		20
Annex B (informative) Isolator system — Explanation of terms used and flow of air and material		23
Annex C (informative) Isolator system — Direct/indirect product contact surfaces		24
Bibliography		25

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 of 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 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 13408-6:2005), which has been technically revised. It also incorporates the Amendment ISO 13408-6:2005/Amd.1:2013. The main changes compared to the previous edition are as follows:

- changes to the Introduction;
- changes to the Scope;
- addition of the new Clause 5 "Basic principle of Isolator system";
- addition of risk management approach in Clause 6 "Isolator system specification";
- addition of new informative [Annex A](#) "Devices acting as transfer ports for portable and mobile equipment";
- addition of new informative [Annex B](#) "Isolator system – Explanation of terms used and flow of air and material";
- addition of new informative [Annex C](#) "Isolator system – Direct/indirect product contact surfaces "

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

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

A health care product that is labelled “sterile” is manufactured using suitably designed, validated and controlled processes. Wherever possible, it is terminally sterilized in its final, sealed container. When this is not possible, the product is aseptically processed.

Aseptic processing is an exacting and demanding discipline designed to maintain sterility through all stages of preparation, manufacturing, filling and sealing in final containers. It relies on a number of independent factors for prevention of recontamination of previously sterilized components during the assembly or filling of product into a final container.

An effective risk management system addressing aseptic processing design (including the use of barrier separation technology), validation and control, and which identifies, assesses, eliminates (where applicable) and controls contamination risks is a prerequisite to provide assurance of sterility for aseptically processed product.

Various separation systems exist to protect the critical processing zone of an aseptic processing area from non-viable particulate and microbiological contamination and to separate process operators from the critical processing zone.

These systems range from controlled airflow devices based on aerodynamic protection through to separation barriers that combine physical and aerodynamic protection to separate the external cleanroom environment from the critical processing zone, minimizing exposure of this zone to process operators and thereby reducing the opportunities for contamination during processing.

Isolator systems provide physical separation whilst facilitating operator intervention into the controlled processing environment under barrier conditions typically via sealed glove-sleeve systems that are physically connected with glove-ports to the isolator barrier screen(s). To establish a controlled environment, reduction of viable and non-viable particulates within isolators is achieved by validated and reproducible cleaning and bio-decontamination processes, principally achieved through the use of automated methods.

In addition to control of bio-contamination and non-viable particulates, isolator systems can include control features, which together with operating practices provide product containment to control cross contamination between process contaminants and product batches, and to manage risk to operators.

Aseptic processing of health care products —

Part 6: Isolator systems

1 Scope

This document specifies the requirements for and provides guidance on the specification, selection, qualification, bio-decontamination, validation, operation and control of isolator systems related to aseptic processing of health care products and processing of cell-based health care products.

This document does not specify requirements for restricted access barrier systems (RABS).

This document does not supersede or replace national regulatory requirements such as Good Manufacturing Practices (GMPs) and/or compendia requirements that pertain in particular to national or regional jurisdictions.

This document does not specify requirements for isolators used for sterility testing; however, some of the principles and information in this document could be applicable to this application.

This document does not define biosafety containment requirements.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 13408-1:2008, *Aseptic processing of health care products — Part 1: General requirements*

ISO 13408-4, *Aseptic processing of health care products — Part 4: Clean-in-place technologies*

ISO 13408-7, *Aseptic processing of health care products — Part 7: Alternative processes for medical devices and combination products*

ISO 14644-1:2015, *Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness by particle concentration*

ISO 14644-7, *Cleanrooms and associated controlled environments — Part 7: Separative devices (clean air hoods, gloveboxes, isolators and mini-environments)*

ISO 18362, *Manufacture of cell-based health care products — Control of microbial risks during processing*

ISO/IEC 90003, *Software engineering — Guidelines for the application of ISO 9001:2015 to computer software*

ISO 11139, *Sterilization of health care products — Vocabulary of terms used in sterilization and related equipment and process standards*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 11139 and the following apply.