

**Tervishoiutoodete aseptiline töötlemine. Osa 3:  
Lüofiliseerimine (ISO 13408-3:2006)**

Aseptic processing of health care products - Part 3:  
Lyophilization (ISO 13408-3:2006)

## EESTI STANDARDI EESSÕNA

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<p>Käesolev Eesti standard EVS-EN ISO 13408-3:2011 sisaldab Euroopa standardi EN ISO 13408-3:2011 ingliskeelset teksti.</p> <p>Standard on kinnitatud Eesti Standardikeskuse 29.07.2011 käskkirjaga ja jõustub sellekohase teate avaldamisel EVS Teatajas.</p> <p>Euroopa standardimisorganisatsioonide poolt rahvuslikele liikmetele Euroopa standardi teksti kättesaadavaks tegemise kuupäev on 29.06.2011.</p> <p>Standard on kättesaadav Eesti standardiorganisatsioonist.</p>	<p>This Estonian standard EVS-EN ISO 13408-3:2011 consists of the English text of the European standard EN ISO 13408-3:2011.</p> <p>This standard is ratified with the order of Estonian Centre for Standardisation dated 29.07.2011 and is endorsed with the notification published in the official bulletin of the Estonian national standardisation organisation.</p> <p>Date of Availability of the European standard text 29.06.2011.</p> <p>The standard is available from Estonian standardisation organisation.</p>
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English Version

**Aseptic processing of health care products - Part 3:  
Lyophilization (ISO 13408-3:2006)**Traitement aseptique des produits de santé - Partie 3:  
Lyophilisation (ISO 13408-3:2006)Aseptische Herstellung von Produkten für die  
Gesundheitsfürsorge - Teil 3: Gefriertrocknung (ISO 13408-  
3:2006)

This European Standard was approved by CEN on 10 June 2011.

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EUROPÄISCHES KOMITEE FÜR NORMUNG**Management Centre: Avenue Marnix 17, B-1000 Brussels**

## Foreword

The text of ISO 13408-3:2006 has been prepared by Technical Committee ISO/TC 198 "Sterilization of health care products" of the International Organization for Standardization (ISO) and has been taken over as EN ISO 13408-3:2011 by Technical Committee CEN/TC 204 "Sterilization of medical devices" the secretariat of which is held by BSI.

This European Standard shall be given the status of a national standard, either by publication of an identical text or by endorsement, at the latest by December 2011, and conflicting national standards shall be withdrawn at the latest by December 2011.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. CEN [and/or CENELEC] shall not be held responsible for identifying any or all such patent rights.

This document supersedes EN 13824:2004.

This document has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association, and supports essential requirements of EU Directives.

For relationship with EU Directives, see informative Annexes ZA, ZB, or ZC, which are integral parts of this document.

According to the CEN/CENELEC Internal Regulations, the national standards organizations of the following countries are bound to implement this European Standard: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, Switzerland and the United Kingdom.

### Endorsement notice

The text of ISO 13408-3:2006 has been approved by CEN as a EN ISO 13408-3:2011 without any modification.

## Annex ZA (informative)

### Relationship between this European Standard and the Essential Requirements of EU Directive 90/385/EEC on Active Implantable Medical Devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 90/385/EEC on active implantable medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in Table ZA.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

**Table ZA.1 — Correspondence between this European Standard and Directive 90/385/EEC**

Clauses of this EN	Essential Requirements (ERs) of Directive 90/385/EEC	Qualifying remarks/Notes
4,5,6,7,8,9	7	This relevant Essential Requirement is only partly addressed in this European Standard and only in conjunction with EN ISO 13408-1

**WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this Standard.**

## Annex ZB (informative)

### Relationship between this European Standard and the Essential Requirements of EU Directive 93/42/EEC on Medical Devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 93/42/EEC on medical devices.

Once this standard is cited in the Official Journal of the European Union under that Directive and has been implemented as a national standard in at least one Member State, compliance with the clauses of this standard given in Table ZB.1 confers, within the limits of the scope of this standard, a presumption of conformity with the corresponding Essential Requirements of that Directive and associated EFTA regulations.

**Table ZB.1 — Correspondence between this European Standard and Directive 93/42/EEC**

Clauses of this EN	Essential Requirements (ERs) of Directive 93/42/EEC	Qualifying remarks/Notes
4,5,6,7,8,9	8.3	This relevant Essential Requirement is only partly addressed in this European Standard and only in conjunction with EN ISO 13408-1
4,5,6,7,8,9	8.4	This relevant Essential Requirement is addressed in this European standard only in conjunction with EN ISO 13408-1

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## Annex ZC (informative)

### Relationship between this European Standard and the Essential Requirements of EU Directive 98/79/EC on *in vitro* diagnostic medical devices

This European Standard has been prepared under a mandate given to CEN by the European Commission and the European Free Trade Association to provide a means of conforming to Essential Requirements of the New Approach Directive 98/79/EC on *in vitro* diagnostic medical devices.

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**Table ZC.1 — Correspondence between this European Standard and Directive 98/79/EC**

Clauses of this EN	Essential Requirements (ERs) of Directive 98/79/EC	Qualifying remarks/Notes
4,5,6,7,8,9	B.2.3	This relevant Essential Requirement is only partly addressed in this European Standard and only in conjunction with EN ISO 13408-1
4,5,6,7,8,9	B.2.4	This relevant Essential Requirement is addressed in this European standard only in conjunction with EN ISO 13408-1

**WARNING — Other requirements and other EU Directives may be applicable to the product(s) falling within the scope of this Standard.**

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## Introduction

This part of ISO 13408 deals with lyophilization, which is a physical-chemical drying process designed to remove solvents from both aqueous and non-aqueous systems, primarily to achieve product or material stability. Lyophilization is synonymous to the term freeze-drying. Lyophilization involves freezing an aqueous system and removing the solvent, first by sublimation (primary drying) and then by desorption (secondary drying), to a level that no longer supports chemical reactions or biological growth. The result is a stable, well-formed product meant to rapidly disperse or solubilize while retaining biological or other activity. Because it is often the final step in an aseptic process with direct impact on the safety, quality, identity, potency and purity of a product, lyophilization is a critical processing step.

Where the finished lyophilized product is intended to be sterile, the product to be dried is an aqueous system that has already been sterilized. Therefore, all activities that can affect the sterility of the product or material need to be regarded as extensions of the aseptic processing of that sterilized product or material. In general, the predominant challenge in ensuring product or material sterility during lyophilization is to prevent microbiological and particulate contamination between the filling operation and completion of the lyophilization process. Of special, equipment-related concern is the protection of the product or material from microbiological contamination within the chamber.

# Aseptic processing of health care products —

## Part 3: Lyophilization

### 1 Scope

This part of ISO 13408 specifies requirements for, and offers guidance on, equipment, processes, programmes and procedures for the control and validation of lyophilization as an aseptic process. It does not address the physical/chemical objectives of a lyophilization process.

### 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 9001, *Quality management systems — Requirements*

ISO 13408-1, *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 13408-5, *Aseptic processing of health care products — Part 5: Sterilization in place*

### 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

##### **lyophilization**

physical-chemical drying process designed to remove solvents from both aqueous and non-aqueous systems, by sublimation and desorption

#### 3.2

##### **leak test**

physical test for the capability to provide a quantifiable leakage rate under repeatable test conditions

### 4 Quality system elements

#### 4.1 General

4.1.1 The requirements of ISO 13408-1 shall apply.

4.1.2 Documented procedures for each phase of the development, validation, routine monitoring, control and maintenance of the lyophilizer shall be prepared and implemented.