INTERNATIONAL STANDARD

ISO 20404

First edition
2023-04

Biotechnology — Bioprocessing — General requirements for the design of packaging to contain cells for therapeutic use

Biotechnologie — Bioprocédés — Exigences générales pour la conception d'emballages destinés à contenir des cellules à usage thérapeutique

Reference number
ISO 20404:2023(E)

© ISO 2023



COPYRIGHT PROTECTED DOCUMENT

© ISO 2023

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

© ISO 2023 – All rights reserved

Contents

Page

Foreword ... **iv**
Introduction ... **v**
1 Scope ... **1**
2 Normative references ... **1**
3 Terms and definitions ... **1**
4 General strategy for packaging design ... **3**
4.1 General ... 3
4.2 Configuration of cells for therapeutic use ... 4
4.2.1 General ... 4
4.2.2 Suspension of cells ... 4
4.2.3 Tissue ... 4
4.3 Process of containing cells for therapeutic use in packaging ... 5
4.4 Disturbances in storage and transportation including contamination ... 5
4.5 Impact on external environment when cells for therapeutic use leak from packaging ... 5
4.6 Interaction between cells for therapeutic use and packaging ... 5
4.7 Usability of packaging in clinical facilities ... 5
4.8 Environmental impact ... 5
5 Design for packaging ... **5**
5.1 General ... 5
5.2 Enclosing process ... 5
5.2.1 Explanation of the enclosing process ... 5
5.2.2 Packaging for the enclosing process ... 6
5.3 Processes from enclosing to usage ... 6
5.3.1 Disturbances that affect cells for therapeutic use ... 6
5.3.2 Leakage ... 7
5.3.3 Interactions between cells for therapeutic use and packaging ... 7
5.4 Usage ... 9
6 Implementing packaging design ... **10**
6.1 General ... 10
6.2 Shape ... 10
6.3 Layers ... 11
6.4 Ports ... 11
6.5 Packaging materials ... 11
6.6 Communication between packaging supplier and packaging user ... 11
7 Quality management ... **12**
8 Examples of test methods ... **12**
8.1 General ... 12
8.2 Test methods related to disturbance ... 12
8.3 Test methods related to leakage ... 12
8.4 Test methods related to interaction between cells for therapeutic use and packaging ... 12
8.5 Other test methods ... 13
Annex A (informative) **Illustrated examples of packaging, packages and shipping containers** ... **15**
Bibliography ... **18**

© ISO 2023 – All rights reserved

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 276, *Biotechnology*.

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.

© ISO 2023 – All rights reserved

Introduction

Medicinal products containing cells as active substances, which are employed in cell therapy or gene therapy, are expected to deliver novel therapeutic value to patients who are currently untreated or under-treated. These products have potential capabilities to repair, replace or regenerate tissues affected by disease or injury. Development of such products is at the forefront of scientific innovation. Therefore, manufacturers of cells for therapeutic use are expected to maintain product quality throughout the product life cycle by continuously improving their ability to process cells with advanced technology.

Cells for therapeutic use are complex products, as compared with conventional pharmaceuticals. They are produced in a variety of culture systems, such as a system in which cells are suspended in a medium, or a system in which tissue formed by cells is immersed in a medium. At the point of their administration, various methods such as surgery or infusion are applied. In addition, special attention is taken in their storage and transportation, which is not always considered in conventional pharmaceuticals. This includes the need to store products in a precisely controlled, closed environment to prevent contamination by foreign substances (viruses, bacteria, mycoplasmas, etc.) at a certain temperature, such as culture environment or at a cryogenic temperature. Even with these complexities, it is indispensable to maintain the quality of cells for therapeutic use from manufacturing to usage.

Packaging is important for cells for therapeutic use to keep their quality. Therefore, a standard for packaging to contain cells for therapeutic use is necessary. Existing standards, such as ISO 3826-1, however, do not provide information for handling cells for therapeutic use.

This document provides general requirements to design packaging intended to contain cells for therapeutic use. It provides useful information for packaging suppliers to manufacture packaging with consideration given to the specific configurations needed for cells for therapeutic use. It is also useful for packaging users when they need to consult with packaging suppliers for custom-made packaging.

This document is intended to help packaging suppliers to design and manufacture packaging in consideration of enclosing, storage, transportation, and utilization processes of cells for therapeutic use. This document is also intended to help packaging users to design and employ packaging in consideration of the above-mentioned processes.

© ISO 2023 – All rights reserved

Biotechnology — Bioprocessing — General requirements for the design of packaging to contain cells for therapeutic use

1 Scope

This document specifies general requirements and considerations for the design of packaging used to contain cells for therapeutic use.

This document is applicable to packaging intended to contain the final products of cells for therapeutic use, as well as their starting and intermediate materials.

This document does not apply to:

a) receptacles used for processing cells in manufacturing processes, e.g. cell culture flask or bag;

b) shipping containers containing packages for transportation;

c) services that utilize packages, e.g. storage services.

NOTE 1 Examples of packaging, packages and shipping containers are illustrated in Annex A.

NOTE 2 The design of packaging includes processes to ensure that the designed packaging is manufactured to a required specification through trial manufacturing, testing and implementation of quality management.

NOTE 3 International, national or regional regulations or requirements can also apply to specific topics covered in this document.

2 Normative references

There are no normative references in this document.

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminology databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at https://www.electropedia.org/

3.1
cells for therapeutic use
product containing cells as the active substance

EXAMPLE Cell therapy medicinal product, tissue engineered product.

Note 1 to entry: The term “cells” refers to cells and *tissues* (3.12) for autologous, allogeneic and xenogeneic use.

Note 2 to entry: This term includes cells as starting materials and those cultured as intermediate materials of the product.

Note 3 to entry: The term “therapeutic use” includes clinical research, hospital exemption and testing use.

© ISO 2023 – All rights reserved

Note 4 to entry: Cells for therapeutic use are often used with additional components. Furthermore, they are sometimes shipped with a pre-treatment drug, concomitant drug or coping drug.

[SOURCE: ISO 21973:2020, 3.1, modified — Notes 2 and 3 to entry modified. Note 4 to entry added.]

3.2
package
packaging (3.3) with its contents

Note 1 to entry: The term "contents" includes the following:

a) cells or a *suspension of cells* (3.11), or both;

b) buffer or medium where a) is immersed;

c) additional components, e.g. cryopreserving agent, pre-treatment drug, concomitant drug, coping drug.

Note 2 to entry: Examples of packages are illustrated in Annex A.

[SOURCE: ISO 11683:1997, 3.3, modified — Notes 1 and 2 to entry added.]

3.3
packaging
form of receptacle intended to contain *cells for therapeutic use* (3.1)

Note 1 to entry: In the field of transportation, packaging can be considered as the primary receptacle.

Note 2 to entry: Examples of packaging are illustrated in Annex A.

3.4
packaging material
material used in *primary packaging* (3.7) and *secondary packaging* (3.8)

3.5
packaging supplier
entity who either manufactures or supplies, or both, *packaging* (3.3) for the *packaging user* (3.6)

3.6
packaging user
entity who makes use of *packaging* (3.3) for *cells for therapeutic use* (3.1)

Note 1 to entry: The packaging user includes the manufacturer of cells for therapeutic use and the provider of starting material, e.g. a cell bank, blood bank, clinical site.

Note 2 to entry: The term "packaging user" excludes clinical facilities and clinical workers.

3.7
primary packaging
packaging (3.3) that comes into direct contact with *cells for therapeutic use* (3.1)

Note 1 to entry: This term can be used in the singular form or the plural form.

Note 2 to entry: Primary packaging is designed to come into direct contact with additives, substrates or preservation solutions.

Note 3 to entry: The content of cells for therapeutic use can have various compositions, which can also be in close contact with the packaging.

3.8
secondary packaging
packaging (3.3) that contains one or more *primary packaging* (3.7)

Note 1 to entry: This term can be used in the singular form or the plural form.

© ISO 2023 – All rights reserved

Note 2 to entry: Secondary packaging can have single or multiple layer(s).

3.9
shipping container
type of container intended to contain and protect *packages* (3.2) during transportation

Note 1 to entry: Examples of shipping containers are illustrated in Annex A.

Note 2 to entry: A shipping container can have functionalities such as repeated use, temperature-regulation, gas composition-regulation and traceability.

3.10
storage container
part of container intended to protect *packages* (3.2) during storage

3.11
suspension of cells
individual cells or aggregates of cells dispersed in a liquid matrix

Note 1 to entry: The liquid matrix can include viscous or gel-like matrices.

[SOURCE: ISO 20391-2:2019, 3.1.6, modified — Term changed from “cell suspension”. “individual cells” replaced “single cells” in the definition. Note 1 to entry added.]

3.12
tissue
organization of cells, cells and extra-cellular constituents, or extra-cellular constituents

[SOURCE: ISO 11139:2018, 3.303]

4 General strategy for packaging design

4.1 General

Cells for therapeutic use are stored and transported within packaging from the cell-supplying site to the manufacturing site, or from the manufacturing site to another manufacturing site, storage or clinical site. The cells are in direct contact with the packaging. Table 1 summarizes the general strategy for the design of packaging for cells for therapeutic use. Table 1 shows the factors that are important when using or manufacturing packaging for cells for therapeutic use. Table 1 also provides cross-references to the requirements for packaging, packaging design and applicable test methods given in this document for each factor.

© ISO 2023 – All rights reserved