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Biotechnology — General requirements for transportation of cells for therapeutic use

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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 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.

Introduction

Cells for therapeutic use provide potential cures for the most challenging disease conditions. However, in contrast to the unprecedented clinical benefits, managing the production and logistics of cells for therapeutic use proves to be challenging. Not only the cost is exceedingly high to produce and transport these products, the concerns over product safety and efficacy due to potential manufacturing or transportation deficiencies have started mounting as more products are being developed and tested.

The cell therapy workflow begins with collection of cells (including tissues). With autologous cells for therapeutic use, cells are collected from patients in the clinical setting before shipping to manufacturing sites for processing and production. After manufacturing and testing for release, cells for therapeutic use are transported to clinical sites for administration into patients.

Issues related to cell transportation have been identified in the product workflow. Some of these issues include monitoring and controlling transportation conditions, managing traceability and maintaining chain of custody, and establishing clear expectations and communications between cell product manufacturer and transportation service provider. These issues all have significant impact on cells for therapeutic use quality that can ultimately affect product safety and effectiveness. Therefore, there is a need for standards to ensure cell transportation is appropriately and adequately planned, executed, traced and documented.

This document intends to provide general requirements and points to consider for transportation service providers, clients and senders to ensure cell quality, safety and efficacy during the transportation process.

Application of this document presupposes awareness of applicable legal requirements.

ISO 13022:2012, Annex G contains guidance for transport of human cells.

Biotechnology — General requirements for transportation of cells for therapeutic use

1 Scope

This document specifies general requirements and reviews the points to consider for the transportation of cells for therapeutic use, including storage during transportation.

Transportation starts from the transfer of the packaged cells by the sender to the transportation service provider and ends when the package is delivered to the receiver at its destination.

This document does not apply to transportation of cells within one facility.

This document includes the development of a transportation plan including verification and validation, communication between the client and the transportation service provider, and associated documentation.

This document does not specify particular conditions for transportation such as specification for shipping container, ambient temperature control, etc.

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 terminological databases for use in standardization at the following addresses:

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

— IEC Electropedia: available at http://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: For the purpose of this document, “cells” mean human cells and tissues of autologous as well as allogeneic.

Note 2 to entry: For the purpose of this document, this term includes cells collected as starting materials and cultured as intermediate materials.

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

3.2
chain of custody
responsibility for or control of materials as they move through each step of a process

Note 1 to entry: For the purpose of this document, “chain of custody” is the proven path starting from the transfer of the packaged cells from the *sender* (3.11) to the *transportation service provider* (3.13) and ends when the package is received at its destination.

3.3
client
entity requesting cell transportation by contract with *transportation service provider* (3.13)

3.4
document
information and the medium on which it is contained

EXAMPLE Record, specification, procedure document, drawing, report, standard.

Note 1 to entry: The medium can be paper, magnetic, electronic or optical computer disc, photograph or master sample, or combination thereof.

Note 2 to entry: A set of documents, for example specifications and records, is frequently called "documentation".

Note 3 to entry: Some requirements (e.g. the requirement to be readable) relate to all types of documents. However there can be different requirements for specifications (e.g. the requirement to be revision controlled) and for records (e.g. the requirement to be retrievable).

[SOURCE: ISO 9000:2015, 3.8.5]

3.5
documented information
information required to be controlled and maintained by an organization and the medium on which it is contained

Note 1 to entry: Documented information can be in any format and media and from any source.

Note 2 to entry: Documented information can refer to:

— the management system, including related processes;

— information created in order for the organization to operate (documentation);

— evidence of results achieved [*records* (3.8)].

Note 3 to entry: This constitutes one of the common terms and core definitions for ISO management system standards given in Annex SL of the Consolidated ISO Supplement to the ISO/IEC Directives, Part 1.

[SOURCE: ISO 9000:2015, 3.8.6]

3.6
inspection
determination of conformity to specified requirements

[SOURCE: ISO 9000:2015, 3.11.7, modified — Notes to entry have been deleted.]

3.7
receiver
entity that gets *cells for therapeutic use* (3.1) from the *transportation service provider* (3.13)

3.8
record
document (3.4) stating results achieved or providing evidence of activities performed

Note 1 to entry: Records can be used, for example, to formalize *traceability* (3.12) and to provide evidence of *verification* (3.15), preventive action and corrective action.

Note 2 to entry: Generally records need not be under revision control.

[SOURCE: ISO 9000:2015, 3.8.10]

3.9
risk assessment
overall process comprising a risk analysis and a risk evaluation

[SOURCE: ISO/IEC Guide 51:2014, 3.11]

3.10
risk control
process in which decisions are made and measures implemented by which risks are reduced to, or maintained within, specified levels

[SOURCE: ISO/IEC Guide 63:2019, 3.12]

3.11
sender
entity that hands over *cells for therapeutic use* (3.1) to *transportation service provider* (3.13)

3.12
traceability
ability to trace the history, application or location of an object

Note 1 to entry: When considering a product or a service, traceability can relate to:

— the origin of materials and parts;

— the processing history;

— the distribution and location of the product or service after delivery.

Note 2 to entry: In the field of metrology, the definition in ISO/IEC Guide 99 is the accepted definition.

[SOURCE: ISO 9000:2015, 3.6.13]

3.13
transportation service provider
entity that provides international and domestic transportation service of *cells for therapeutic use* (3.1)

Note 1 to entry: Transportation service provider can outsource the whole or part of cell transportation to external service providers. In that case, some requirements described in this document [e.g. the requirement regarding documented information (3.5)] can be met by the activities of external service providers. The activities of external service providers vary according to the agreement between the transportation service provider and external service provider, but its activities are managed by transportation service provider.

3.14
validation
confirmation, through the provision of objective evidence, that the requirements for a specific intended use or application have been fulfilled

Note 1 to entry: The objective evidence needed for a validation is the result of a test or other form of determination such as performing alternative calculations or reviewing *documents* (3.4).

Note 2 to entry: The word “validated” is used to designate the corresponding status.

Note 3 to entry: The use conditions for validation can be real or simulated.

[SOURCE: ISO 9000:2015, 3.8.13]

3.15
verification
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

Note 1 to entry: The objective evidence needed for a verification can be the result of an *inspection* (3.6) or of other forms of determination such as performing alternative calculations or reviewing *documents* (3.4).

Note 2 to entry: The activities carried out for verification are sometimes called a qualification process.

Note 3 to entry: The word “verified” is used to designate the corresponding status.

[SOURCE: ISO 9000:2015, 3.8.12]

4 General concepts

Consistent quality in transportation of cells for therapeutic use is enabled by establishing:

a) cell transportation specification based on appropriate sharing information between transportation service provider and client, including:

   1) information provided by the client regarding biosafety of cells for therapeutic use during transportation;

   2) information provided by the client regarding storage/handling conditions to preserve cell quality and ensure the therapeutic cell functions.

      NOTE Cell quality can be ensured by demonstrating that the physical, chemical, biological, or microbiological properties are within an appropriate limit, range, or distribution.

b) operational procedure for cell transportation supported by risk management, verification and/or validation;

c) organizational requirements for transportation of cells for therapeutic use; including the establishment of an appropriate quality management system, training for personnel assigned to a specific cell transportation process, tracking systems, scheduling systems to ensure appropriate protocols are followed;

d) container and facilities requirements including the secure and access control of the facility, ensuring that cells for therapeutic use are not contaminated or tampered;

e) documentation for all stages of cell transportation that demonstrates chain of custody throughout the transportation cycle, including but not limited to equipment performance, cleaning and equipment-use history;

   NOTE Documentation can be a part of quality management system.

f) system to record each process of cell transportation.

   NOTE The following are examples of the records associated with cell transportation:

   1) objective measurements (e.g. temperature);

   2) transportation logs (e.g. time, name, commodity and signature);

   3) records of data logger;

   4) visual inspection;

   5) shipping containers;

      — unit type (e.g. dry shipper);

      — qualification (in the case of dry shipper, weight, nitrogen evaporation rate and liquid nitrogen capacity);

      — cleaning and disinfection records.

Items of requirements for transportation of cells for therapeutic use agreed between transportation service provider and client should be documented and confirmed in writing by each party that they accept the agreed conditions.

