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Biotechnology — Ancillary materials present during the production of cellular therapeutic products —

Part 1: General requirements

Biotechnologie — Matériaux auxiliaires présents lors de la production de produits thérapeutiques cellulaires —
Partie 1: Exigences générales

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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).

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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*.

A list of all parts in the ISO/TS 20399 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

Ancillary materials (AMs) are materials that come into contact with the cellular therapeutic product during the manufacturing process, but are not intended to be in the final product.

AMs include culture media and growth factors, among other biological and non-biological components. They can be a complex mixture of many components, and a variation in their lot-to-lot composition can hamper the ability to produce consistent cellular therapeutic products with specified quality attributes.

As such, AMs can have implications with regard to the safety and effectiveness of a cellular therapeutic product. Appropriate control of ancillary materials is determined by a risk-based approach.

This document specifies definitions and general requirements for AMs and contributes to their control by suppliers and users of such materials.

The ISO/TS 20399 series provides general requirements and guidance regarding ancillary materials to maintain a high level of lot-to-lot consistency, as well as the accompanying documentation, so that consistent ancillary materials products and documentation provided by the suppliers can help AM users.

It is intended to ensure the quality and consistency of AMs used in the manufacturing of cellular therapeutic products. Good manufacturing practice (GMP) is taken into account, when necessary.

Biotechnology — Ancillary materials present during the production of cellular therapeutic products —

Part 1: General requirements

1 Scope

This document specifies definitions and general requirements for ancillary materials (AMs) used in cell processing of cellular therapeutic products.

This document is applicable to cellular therapeutic products, including those gene therapy products whereby cells form part of the final product. It does not apply to products without cells.

This document does not cover the selection, assessment or control of starting materials and excipients.

NOTE International, regional or national 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 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
ancillary material
AM
material that comes into contact with the cell or tissue product during cell-processing, but is not intended to be part of the final product formulation

Note 1 to entry: AMs exclude non-biological consumables (e.g. tissue culture flasks, bags, tubing, pipettes, needles) and other plastic ware that comes into contact with the cell or tissue, but include consumables which can have a biological component (e.g. coated dishes or beads).

Note 2 to entry: AMs exclude cells (e.g. feeder cells).

Note 3 to entry: In some cases AM is described as raw material.

3.2
AM user
entity who makes use of *AM* (3.1) and conducts cell-processing for cellular therapeutic product

3.3
AM supplier
entity who manufactures and/or supplies the *AM* (3.1) for *AM user* (3.2)

3.4
animal-derived component free
ADCF
absence of animal or human origin material(s)

Note 1 to entry: The main purpose of defining ADCF is to provide necessary information for a user's risk assessment of ancillary material.

Note 2 to entry: There are levels of ADCF, which are listed in 5.2.2.

Note 3 to entry: In some cases, animal-derived component free (ADCF) is described as animal origin free.

Note 4 to entry: In cases where there is absence of non-human animal components, the term xeno-free is commonly used.

3.5
cellular therapeutic product
product containing cells as the active substance

EXAMPLE Cell therapy medicinal product, tissue engineered product.

3.6
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 unbroken path of an AM product from the production of AM to the end customer. It covers controls, distribution and logistics to the end-user.

3.7
excipient
material that is present in the *cellular therapeutic product* (3.5) administered to a patient(s), other than the active substance(s)

EXAMPLE Cryopreservation components.

Note 1 to entry: For the purpose of this document, "active substance" corresponds to cellular therapeutic product.

3.8
maximum shelf life
period during which an *AM* (3.1) is expected to comply with the specifications, if stored under defined conditions

3.9
specification
list of tests, references to analytical procedures, and appropriate acceptance criteria that would be expected to be met to demonstrate suitability for its intended use definition

3.10
stability
characteristic of a material, when stored under specified conditions, to maintain a value(s) for stated property(ies) within specified limits for a specified period of time

[SOURCE: ISO Guide 30:2015, 2.1.15, modified — "reference material" has been replaced by "material", "a specified property value" has been replaced by "a value(s) for stated property(ies)", the Note 1 to entry has been deleted.]

3.11
starting material
any substance of cellular origin that constitutes the *cellular therapeutic product* (3.5)

4 Abbreviated terms

ADCF	animal-derived component free
AM	ancillary material
BSE	bovine spongiform encephalopathy
CoA	certificate of analysis
CoO	certificate of origin
SDS	safety data sheet
GHS	globally harmonized system
TSE	transmissible spongiform encephalopathy

5 Considerations

5.1 General considerations

Ancillary materials described in this document are materials introduced during manufacturing of cellular therapeutic products generally used to control or enhance cell expansion. These materials are referred to as AM.

AM can affect quality attributes of cellular therapeutic products.

— Quality and consistency are critical for AMs known to affect cell processing.

— Safety and the chain of custody are critical for AMs, particularly animal-derived AMs, which potentially remain as components of the cellular therapeutic product.

5.2 Animal-derived components of AM

5.2.1 General

Materials of biological origin, particularly of human or animal origin, can present particular risks, including transmission of adventitious agents or introduction of biological impurities.

This does not necessarily limit the use of biologically-derived components for manufacturing AMs or materials used further downstream in the manufacturing of cellular therapeutic products. The use of a risk-based approach for the selection of essential materials is therefore essential.

5.2.2 Levels of ADCF

The main purpose of defining ADCF is to provide necessary information for a user's risk assessment of AM.

An AM is designated ADCF level 1 or 2, when one of the following definitions is fulfilled.

a) Level 1 (product level): the AM does not contain any materials from animal or human source as its ingredients.

NOTE Level 1 is intended to address the level of risk to be considered. It indicates that materials from an animal or human source are not an intended part of the product, but it does not technically ensure that materials from an animal or human source are not carried over into the AM during production.