TECHNICAL SPECIFICATION

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First edition

General requirements of tissue engineered medical products

Exigences générales relatives aux TEMP

PROOF/ÉPREUVE

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Foreword

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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 150, *Implants for Surgery*, Subcommittee SC 7, *Tissue-engineered medical products*.

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

Advances in the field of biological sciences have made possible the generation of a new type of medical product that when administered to the human body, may repair, replace, regenerate or enhance the function of impaired tissues or organs.

Extensive experience acquired through the administration of living human cells has yielded solid knowledge about the quality requirements and the risks associated with their use.

However, the development of tissue engineered medical products (TEMPs) that are not simply obtained from a human donor or by separating living tissues, but rather are grown from various cell sources and are manipulated during manufacture to meet the medical needs of the patient, introduces new challenges with regard to quality requirements and risk management for the benefit of patients.

TEMPs utilizing human material are quite diverse, but share a set of common quality requirements for their safe use. These kinds of products require special attention for contamination control, such as infectious agents transmitting disease (e.g. Hepatitis, HIV, TSE) and harmful chemicals, unintended decomposition or degradation induced by inappropriate handling at any stage of the manufacturing process, tumorigenic potential, induction of an immunogenic reaction in the recipient, traceability of cells, critical materials, and the final product are key to product quality and its safe use.

This document has been developed with the objective of assisting interested parties, such as manufacturers and regulators, establish suitable quality parameters and specifications for the final TEMPs as well as cells, critical materials, processing steps and appropriate controls ensuring the safety of TEMPs.

General requirements of tissue engineered medical products

1 Scope

This document specifies general requirements for tissue engineered medical products (TEMPs), which are used in regenerative medicine. With regard to safety, this document outlines requirements for materials, manufacture, quality control, and unintentional biological effects elicited by TEMPs. This document does not address requirements for clinical trials and efficacy.

This document is not applicable to tissue engineered products used for diagnosis, *ex-vivo* testing or extracorporeal treatments of patients (e.g. dialysis with TEMP components). TEMPs containing viable xenogenic cells, genetically modified cells, or cells derived from abnormal cells or tissues (e.g. cancerous tissues) are also excluded from the scope. The combination of TEMPs with medical devices, with the exception of scaffolds comprised of synthetic and/or naturally-derived (e.g. animal sourced) materials, is also excluded from the scope.

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

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 13022, *Medical products containing viable human cells — Application of risk management and requirements for processing practices*

ISO/TS 20399-1, *Biotechnology — Ancillary materials present during the production of cellular therapeutic products — Part 1: General requirements*

ISO/TS 20399-2, *Biotechnology — Ancillary materials present during the production of cellular therapeutic products — Part 2: Best practice guidance for ancillary material suppliers*

ISO/TS 20399-3, *Biotechnology — Ancillary materials present during the production of cellular therapeutic products — Part 3: Best practice guidance for ancillary material users*

ISO 22442-1, *Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management*

ISO 22442-2, *Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling*

ISO 22442-3, *Medical devices utilizing animal tissues and their derivatives — Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents*

ISO/TR 22442-4, *Medical devices utilizing animal tissues and their derivatives — Part 4: Principles for elimination and/or inactivation of transmissible spongiform encephalopathy (TSE) agents and validation assays for those processes*

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
active substance
substance comprised of manipulated cells, engineered tissues and/or other materials in the finished TEMP which have biological activity for its intended use

3.2
allogenic
cells, tissues, and organs in which the donor and recipient are genetically separate individuals of the same species

[SOURCE: ASTM F2312-11:2020, Clause 4, modified — alternative terms have been removed.]

3.3
autologous
cells, tissues, and organs in which the donor and recipient is the same individual

[SOURCE: ASTM F2312-11:2020, Clause 4, modified — alternative terms have been removed.]

3.4
bioactive agent
agent (e.g. peptide or protein) produced by (and purified from) naturally occurring or recombinant organisms, tissues or cell lines or synthetic analogs of such molecules

3.5
cellular therapeutic product
administration of cells to repair, modify or regenerate the recipient's cells, tissues, and organs or their structure and function, or both

[SOURCE: ASTM F2312-11:2010, Clause 4, modified — term has been modified from "cell therapy".]

3.5.1
cell line
progeny of a primary culture after the first subculture

Note 1 to entry: A cell line may be finite or continuous.

3.6
excipient
material that is present in the *TEMP* (3.18) administered to a patient(s), other than the active substance(s)

EXAMPLE Cryopreservation components.

3.7
finished TEMP
final formulated TEMP in its immediate container closure

3.8
genetically modified
having an altered or modified genetic material

[SOURCE: ASTM F2312-11:2020, Clause 4]

3.9
lifespan
period during which something exists

[SOURCE: ISO 19108:2002, 4.1.21]

3.10
medical device
instrument, apparatus, implement, machine, appliance, implant, reagent for *in vitro* use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

— diagnosis, prevention, monitoring, treatment or alleviation of disease;

— diagnosis, monitoring, treatment, alleviation of or compensation for an injury;

— investigation, replacement, modification, or support of the anatomy or of a physiological process;

— supporting or sustaining life;

— control of conception;

— disinfection of medical devices;

— providing information by means of *in vitro* examination of specimens derived from the human body; and

— does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which can be assisted in its intended function by such means

[SOURCE: ISO/IEC Guide 63:2019, 3.7]

3.11
medical product
medicinal product (drug), biological product, medical device or a combination of these

[SOURCE: ISO 13022:2012, 3.4]

3.12
ancillary material
AM
material that comes into contact with the TEMP during manufacturing, 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 plasticware that comes into contact with the TEMP or its components, but include consumables which 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.

[SOURCE: ISO/TS 20399-1:2018, 3.1]

3.13
regenerative medicine
process of repairing, replacing, or regenerating human cells, tissues or organs to restore or establish normal function

[SOURCE: PAS 84:2012, 2.266]