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Manufacture of cell-based health care products — Control of microbial risks during processing

Manufacture de produits de soins de santé fondés sur les cellules — Contrôle des risques microbiaux durant le processus

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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).

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For an explanation on the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the WTO principles in the Technical Barriers to Trade (TBT) see the following URL: Foreword - Supplementary information

The committee responsible for this document is ISO/TC 198, *Sterilization of health care products*.

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Introduction

0.1 General

A cell-based health care product (CBHP) comprises prokaryotic or eukaryotic cells or cell derived biological entities as an essential ingredient. Cell-based or cell derived starting material used in the manufacture of a CBHP can be viable or non-viable and of human, animal, microbial or plant origin. A common feature of CBHPs is that their efficacy is based on their biological properties. They are classified as medicines, medical devices, biologics or combination products depending on the international, national and/or regional regulations that govern supply of these products.

CBHPs might be limited in their ability to withstand sterilization and purification methods. This International Standard focuses on process rather than product. It describes the minimum elements necessary for a risk-based approach to the processing of a CBHP in order to reduce the potential for an increase in intrinsic contamination of product and to avoid extrinsic contamination of product. The design of the processes, equipment, facilities, utilities, the conditions of preparation and addition of buffers and reagents, and training of the operators are key considerations to minimize contamination.

0.2 CBHPs labelled as 'sterile'

A CBHP that is labelled as 'sterile' is sterilized by a terminal sterilization process or is aseptically processed.

Examples of CBHPs that are terminally sterilized include, but are not restricted to, cancellous bone, demineralized bone matrix, catgut sutures, biological heart valves and tissue patches. Sterility assurance for these CBHPs is achieved through suitable design and control of the environment, controls on starting materials and packaging, suitable design and qualification of manufacturing processes including the terminal sterilization process, and the application of appropriate in-process controls and testing. Requirements and guidance for terminal sterilization of CBHPs are contained in ISO 17665-1, ISO/TS 17665-2, ISO 11137-1, ISO 11137-2, ISO 11137-3, ISO 11135, ISO 14160, ISO 20857, ISO 14937 and ISO 25424, as applicable.

Controls for some infectious agents, e.g. viruses and protozoa, might require a multifaceted approach to ensure product quality and safety. Such agents are not specifically considered in the existing standards for terminal sterilization or aseptic processing.

A CBHP that is labelled 'sterile' and which cannot be terminally sterilized is aseptically processed. Sterility assurance for these CBHPs is achieved through suitable design and control of the environment, controls on starting materials and packaging, suitable design and qualification of manufacturing processes, process simulation (in accordance with the requirements of the ISO 13408-series), the application of appropriate in-process controls during manufacture, and testing to demonstrate achievement of aseptic processing conditions. As a prerequisite, starting materials and packaging materials are sterilized by validated processes. In this regard this International Standard does not reiterate requirements for specific processes that are used during processing of a CBHP that is labelled 'sterile'. In cases where a CBHP is aseptically processed and labelled as 'sterile' refer to the ISO 13408-series.

0.3 CBHPs supplied without a label claim for sterility

For a CBHP that is supplied without a label claim for sterility, e.g. corneal tissue or viable skin grafts, processing involves the use of appropriate aseptic techniques at all stages during the process. Components might be subject to bioburden reduction during preparation prior to their assembly or combining to form finished product. This is necessary to minimize the potential for intrinsic contamination of product to increase during processing and to avoid extrinsic contamination of product. The controls and techniques to maintain product quality during processing of these CBHPs might be different from those used for processing of a CBHP that is labelled 'sterile'.

Controls for some infectious agents, e.g. viruses and protozoa, can require a multifaceted approach to ensure product quality and safety.

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Microbiological quality assurance for a CBHP that is supplied without a label claim for sterility is achieved through control of the environment, controls on starting materials and packaging, suitable design and qualification of manufacturing processes, process confirmation and process simulation studies and the application of appropriate in-process controls and testing. Risk assessment underpins selection of suitable microbiological quality criteria for a CBHP that is supplied without a label claim for sterility. These criteria define the acceptability of product based on the absence or presence, or number of microorganisms, per defined quantity of product, to ensure finished product does not pose a microbiological risk to the patient.

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Manufacture of cell-based health care products — Control of microbial risks during processing

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1 Scope

This International Standard specifies the minimum requirements for, and provides guidance on, a risk-based approach for the processing of cell-based health care products (CBHPs) requiring control of viable and non-viable microbial contamination. It is applicable both to CBHPs labelled 'sterile' and to CBHPs not labelled 'sterile'.

This International Standard is not applicable to:

— procurement and transport of cell-based starting material used in processing of a CBHP,

— cell banking,

— control of genetic material,

— control of non-microbial product contamination,

— *in vitro* diagnostics (IVDs), or

— natural medicines.

EXAMPLE Vitamins and minerals, herbal remedies, homoeopathic medicines, traditional medicines such as traditional Chinese medicines, probiotics, other products such as amino acids and essential fatty acids.

This International Standard does not define biosafety containment requirements.

This International Standard does not replace national or regional regulations that apply to the manufacture and quality control of a CBHP.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 11135, *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*

ISO 11137 (all parts), *Sterilization of health-care products — Radiation*

ISO 13022:2012, *Medical products containing viable human cells — Application of risk management and requirements for processing practices*

ISO 13408-1:2008, *Aseptic processing of health care products — Part 1: General requirements*

ISO 13408-1:2008/Amd.1:2013, *Aseptic processing of health care products — Part 1: General requirements / Amendment 1*

ISO 13408-7:2012, *Aseptic processing of health care products — Part 7: Alternative processes for medical devices and combination products*

ISO 14160, *Sterilization of health care products — Liquid chemical sterilizing agents for single-use medical devices utilizing animal tissues and their derivatives — Requirements for characterization, development, validation and routine control of a sterilization process for medical devices*

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