TECHNICAL SPECIFICATION

ISO/TS 22859

First edition
2022-07

Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from umbilical cord tissue

Biotechnologie — Banques biologiques — Exigences relatives aux cellules stromales mésenchymateuses humaines issues des tissus du cordon ombilical

This document is a preview generated by EVS

Reference number
ISO/TS 22859:2022(E)

© ISO 2022

This document is a preview generated by EVS

COPYRIGHT PROTECTED DOCUMENT

© ISO 2022

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 2022 – All rights reserved

Contents

Page

Foreword ... **v**
Introduction ... **vi**
1 Scope ... **1**
2 Normative references ... **1**
3 Terms and definitions ... **1**
4 Abbreviated terms and symbols ... **5**
5 General requirements ... **10**
5.1 General ... 10
5.2 Personnel, facilities and equipment ... 10
5.3 Reagents, consumables and other supplies ... 11
5.4 Management of information and data ... 11
6 Collection of umbilical cord and associated data ... **11**
6.1 Information about the umbilical cord donor ... 11
6.2 Collection procedure ... 12
7 Transport of umbilical cord or hUC-MSCs and associated data to the biobank ... **13**
8 Reception and traceability of umbilical cord tissue or hUC-MSCs and associated data ... **13**
9 Isolation and expansion of hUC-MSCs ... **13**
9.1 Processes ... 13
9.2 Unique identification ... 13
9.3 Testing for infectious agents ... 14
9.4 Isolation of hUC-MSCs and primary culture ... 14
9.5 Subculture and limited expansion ... 14
10 Characterization of hUC-MSCs ... **14**
10.1 General ... 14
10.2 Viability ... 15
10.3 Morphology ... 15
10.4 Population doubling time and subculture/passage ... 16
10.4.1 PDT ... 16
10.4.2 Subculture/passage ... 16
10.5 Cell population purity ... 16
10.6 *In vitro* self-renewal assessment ... 17
10.7 Proliferation ... 17
10.8 Differentiation capability — *In vitro* multilineage differentiation ... 17
10.8.1 General ... 17
10.8.2 *In vitro* adipogenic differentiation ... 17
10.8.3 *In vitro* chondrogenic differentiation ... 18
10.8.4 *In vitro* osteogenic differentiation ... 18
10.9 Immunophenotyping by flow cytometry ... 18
10.10 Paracrine secretion/expression (protein-based assay of secretome) ... 20
10.11 Immunoregulation (modulation of immune cells) ... 20
10.12 Microbial contamination ... 21
11 Quality control ... **21**
12 Storage ... **22**
13 Thawing ... **23**
14 Disposal ... **24**
15 Distribution of hUC-MSCs — Information for users ... **24**
16 Transport of hUC-MSCs ... **24**

This document is a preview generated by EVS

© ISO 2022 – All rights reserved

16.1 General 24
16.2 hUC-MSCs frozen in ampoules or cryovials 25
16.3 Living hUC-MSC cultures 25

Annex A (informative) **Exemplary quality control test procedure for biobanking of hUC-MSCs** **27**

Annex B (informative) **Examples for suitable methods for the isolation and primary culture of hUC-MSCs** **28**

Annex C (informative) **Exemplary methods for characterization of hUC-MSCs** **30**

Bibliography **32**

This document is a preview generated by EVS

© ISO 2022 – 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.

This document is a preview generated by EVS

© ISO 2022 – All rights reserved

Introduction

Mesenchymal stromal cells are a heterogeneous cell population that is characterized by multiple functional properties including the ability to secrete paracrine factors,[8] regulate immune effector cells,[9][10] maintain primitive phenotypes of other cell populations[11][12] and support tissue regeneration.[13][14] Mesenchymal stromal cells can contain a sub-population of stem or progenitor cells that demonstrate *in vitro* self-renewal and differentiation, as has been rigorously demonstrated for umbilical cord-derived progenitor cells.[15]

Mesenchymal stromal cells and mesenchymal stem cells are both abbreviated as "MSCs".[16] For the purpose of this document, the abbreviated term "MSCs" refers to mesenchymal stromal cells.

The functional definition of MSCs has evolved over time as the biology of these cells is better understood. Despite these advances, substantial ambiguities persist regarding the nomenclature, nature, identity, function, mode of isolation and experimental handling of these cells. MSCs are not fully defined by the initial minimal criteria[17] proposed by the International Society of Cell and Gene Therapy (ISCT), and as such require careful characterization by a matrix of functional assays.[16]

MSCs have been isolated from umbilical cord[15], bone marrow[18][19] and other tissue sources, and are widely used for non-clinical research. MSCs from different tissue sources have different properties. Different institutions use different practices for isolating, processing and biobanking these MSCs, making it difficult to compare data and results across institutions. Thus, there is a need for standardized approaches to isolate, process, expand and cryopreserve these MSCs from specific tissue sources.

This document provides requirements for biobanking of human mesenchymal stromal cells derived from umbilical cord tissue (Wharton's jelly) (hUC-MSCs) for research purposes. This document is applicable for academic centres, public and private institutions performing a biobanking service of hUC-MSCs for research and development (R&D) and preclinical studies, not for clinical use.

Importantly, this document is focused on MSCs that have been isolated, manipulated and/or propagated from umbilical cord tissue (also called "Wharton's jelly") in culture for research purposes. These cells are different from unmanipulated cells found in human umbilical cord tissue (Wharton's jelly).

ISBT 128[20] provides terminology and abbreviations for all medicinal products including cell therapy, and abbreviates these as "MSC(WJ)" to denote mesenchymal stromal cells from Wharton's jelly. This document recognizes this abbreviation, but uses the more commonly-used convention in research to denote human mesenchymal stromal cells derived from umbilical cord tissue (Warton's jelly) (hUC-MSCs).[21]

This document is a preview generated by EVS

© ISO 2022 – All rights reserved

Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from umbilical cord tissue

This document is a preview generated by EVS

1 Scope

This document specifies requirements for the biobanking of human mesenchymal stromal cells derived from umbilical cord tissue (i.e. Wharton's jelly), further referred to as hUC-MSCs, including the collection of umbilical cord tissue and associated data, isolation, culture characterization, quality control, cryopreservation, storage, thawing, disposal, distribution and transport.

This document is applicable to all organizations performing biobanking of hUC-MSCs used for research and development.

This document does not apply to hUC-MSCs for the purpose of *in vivo* application in humans, clinical applications or therapeutic use.

NOTE International, national or regional regulations or requirements, or multiple of them, can 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 8601-1, *Date and time — Representations for information interchange — Part 1: Basic rules*

ISO 20387:2018, *Biotechnology — Biobanking — General requirements for biobanking*

ISO 21709:2020, *Biotechnology — Biobanking — Process and quality requirements for establishment, maintenance and characterization of mammalian cell lines*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 20387:2018, ISO 21709:2020 and the following 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
authenticity
quality of being genuine or true

3.2
biobank
legal entity or part of a legal entity that performs *biobanking* (3.3)

[SOURCE: ISO 20387:2018, 3.5]

© ISO 2022 – All rights reserved