BS ISO 20399:2022

BSI Standards Publication

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

bsi.

National foreword

This British Standard is the UK implementation of ISO 20399:2022. It supersedes PD ISO/TS 20399-2:2018, PD ISO/TS 20399-1:2018 and PD ISO/TS 20399-3:2018, which are withdrawn.

The UK participation in its preparation was entrusted to Technical Committee BTI/1, Biotechnologies.

A list of organizations represented on this committee can be obtained on request to its committee manager.

Contractual and legal considerations

This publication has been prepared in good faith, however no representation, warranty, assurance or undertaking (express or implied) is or will be made, and no responsibility or liability is or will be accepted by BSI in relation to the adequacy, accuracy, completeness or reasonableness of this publication. All and any such responsibility and liability is expressly disclaimed to the full extent permitted by the law.

This publication is provided as is, and is to be used at the recipient's own risk.

The recipient is advised to consider seeking professional guidance with respect to its use of this publication.

This publication is not intended to constitute a contract. Users are responsible for its correct application.

Published by BSI Standards Limited 2023

ISBN 978 0 539 14623 3

ICS 07.080

Compliance with a British Standard cannot confer immunity from legal obligations.

This British Standard was published under the authority of the Standards Policy and Strategy Committee on 31 January 2023.

Amendments/corrigenda issued since publication

Date	Text affected

BS ISO 20399:2022

INTERNATIONAL STANDARD

ISO 20399

First edition
2022-12-01

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

Biotechnologie — Matériaux auxiliaires présents lors de la production de produits thérapeutiques cellulaires et de produits de thérapie génique

Reference number
ISO 20399:2022(E)

COPYRIGHT PROTECTED DOCUMENT

ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

Contents

Page

Foreword ..... **v**
Introduction ..... **vi**
1 Scope **1**
2 Normative references **1**
3 Terms and definitions **1**
4 Abbreviated terms **4**
5 Strategy **5**
5.1 Key concepts on AM 5
5.2 AM-related responsibilities 5
5.3 Qualification considerations of AM 6
5.4 Animal-derived components of AM 7
5.4.1 General 7
5.4.2 Key considerations in the use of animal-derived components 7
5.4.3 Viral inactivation 8
6 Evaluation criteria and risk mitigation for AM containing biological material **8**
6.1 Evaluation criteria for AM selection 8
6.2 Mitigation of risk 10
6.2.1 Scientific approach 10
6.2.2 Supplier audit and questionnaires 11
6.2.3 Risk assessment 12
7 AM characteristics and quality attributes **12**
7.1 AM components, identity and purity 12
7.1.1 General 12
7.1.2 Identity and quantity of component(s) 13
7.1.3 Purity and impurity 13
7.1.4 Lot-to-lot consistency for AMs containing proprietary components 13
7.2 AM storage and stability 14
7.2.1 General 14
7.2.2 Stability and storage conditions 14
8 AM manufacturing and biosafety **15**
8.1 Quality management system 15
8.2 Manufacturing process 16
8.3 Container and closure systems 16
8.4 Animal and human-derived components 16
8.5 Safety to cells and humans 17
9 AM performance **17**
9.1 General 17
9.2 Quality and testing 18
9.3 Qualification activity 18
9.4 Performance assay 19
9.5 Performance assay results 19
10 AM documentation **19**
10.1 General 19
10.2 Reporting requirements 20
10.3 Certificate of analysis 21
10.4 Additional certificates 22
10.4.1 Certificate of origin 22
10.4.2 Certificate of compliance 22
10.4.3 Certificate of irradiation 22
11 Managing changes to components **22**

11.1 Impact of changes to components 22
11.2 Measures for managing changes to components 22

Annex A (informative) **Decision chart of AMs** **24**

Annex B (informative) **Example workflow from AM supplier to AM user** **26**

Annex C (informative) **Information on AM and materials used to produce AMs** **27**

Annex D (informative) **Considerations for the characterization of AMs** **29**

Annex E (informative) **Quality declarations for manufactured biological materials used in the manufacture of a cell-based therapeutic product** **30**

Bibliography **31**

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*.

This first edition cancels and replaces ISO/TS 20399-1:2018, ISO/TS 20399-2:2018 and ISO/TS 20399-3:2018, which have been technically revised.

The main changes are as follows:

— merging of the three parts of the ISO 20399 series;

— change in definitions of key terms including “ancillary material” and “cellular therapeutic product”;

— addition of Clause 5 “Strategy”, including key concepts, animal-derived components, mutual responsibilities and qualification;

— revision and rearrangement of requirements and recommendations with emphasis on clarifying responsibility of involved parties and emphasis of a risk-based approach.

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) refer to materials that come into contact with the cellular therapeutic product during cell processing but are not intended to be part of the final product formulation. See Annex A for a list of AM examples.

AM can be a complex mixture of many components. AMs include, for example, salts, buffers, culture media, supplements such as growth factors, enzymes and antibodies for immuno-purification. Where a material is composed of multiple materials such as culture media, all components are AMs. Variation in their lot-to-lot composition can hamper the ability to produce consistent cell and gene therapy products with specified quality attributes.

As such, AMs can have implications with regard to the safety and effectiveness of cell and gene therapy products. Appropriate control of AMs is determined by a risk-based approach.

This document specifies definitions for AMs.

This document provides recommendations and requirements to the AM suppliers and the AM users to ensure consistent manufacture and performance of AMs. This document also describes the information that can be obtained and provided to the AM users to demonstrate lot-to-lot consistency of the AM with respect to identity, purity, storage and stability, traceability, biosafety, and performance. Furthermore, this document provides recommendations and requirements to ensure that the quality of AMs enables the production of safe and effective final products.

Presently, a number of standards and guidance documents define the proper processing of cell and gene therapy products to ensure safety and efficacy. However, these standards only indirectly relate to AMs. This document is separate from the standards governing cell processing requirements. This document addresses issues with AMs and makes the expectations of the AM suppliers and the AM users clear.

INTERNATIONAL STANDARD **ISO 20399:2022**

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

1 Scope

This document specifies requirements and gives guidance to suppliers and users of ancillary materials (AMs) to improve the consistency and quality of AMs of biological (human and animal) and chemical origin used in the production of cellular therapeutic products and gene therapy products for human use.

This document is applicable to materials that are used for cell processing and that come into contact with the active substance and that do not intentionally form part of the final cell and gene therapy product.

EXAMPLE 1 Reagents, anticoagulants, cytokines, growth factors, enzymes, antibodies, serum (human or bovine), buffered solutions, culture media, dishes (coated with biological material), beads (coated with biological material), cryoprotectants (agents for cryopreservation), activation agents/reagents, non-mammalian cell (e.g. insect cell, bacterial cell), plasmid, viral vector.

This document does not apply to materials that are not used for cell processing, materials that do not come into contact with the active substance, or materials that intentionally form part of the final cell and gene therapy product.

EXAMPLE 2 Cells that are either starting materials, intermediates or final form of a cellular therapeutic product, feeder cells, additives used post bioprocessing, scaffolds, non-biological consumables (e.g. beads, dishes, tissue culture flasks, bags, tubing, pipettes, needles), other plasticware that come into contact with the cell or tissue, apparatus, instruments.

A decision flowchart is given in Annex A.

NOTE International, regional or national regulations or requirements 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*

3 Terms and definitions

For the purposes of this document, the following terms and definitions 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
active substance
substance that has biological activity in a *cellular therapeutic product* (3.9) for its intended use