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**NATIONAL STANDARD OF THE
PEOPLE'S REPUBLIC OF CHINA**

GB/T 45351-2025

**Manufacture of cell-based medical devices - Control of
microbial risks during processing**

基于细胞的医疗器械生产 加工过程中微生物风险控制

(English Translation)

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Foreword

This document is in accordance with the provisions of GB/T 1.1-2020 "Guidelines for standardization work Part 1: Structure and drafting rules for standardization documents" Drafting.

This document is modified to adopt ISO 18362:2016 "Microbiological risk control in the production and processing of cell-based medicinal products".

This document has the following structural adjustments compared to ISO 18362:2016.

- Appendix A corresponds to Appendix F in ISO 18362:2016;
- Appendix B corresponds to Appendix A in ISO 18362:2016;
- Appendix C corresponds to Appendix B in ISO 18362:2016;
- Appendix D corresponds to Appendix C in ISO 18362:2016;
- Appendix E corresponds to Appendix D in ISO 18362:2016;
- Appendix F corresponds to Appendix E in ISO 18362:2016.

The technical differences between this document and ISO 18362:2016 and their reasons are as follows.

- The product scope of this document has been changed to limit it to cell-based medical devices (see Chapter 1) to adapt to my country's technology condition;
- Added "Other cell-based medical products refer to this document for use" (see Chapter 1) to clarify that this document is used in other cell-based the reference for microbial risk control in the processing of medical products containing cells;
- ISO 17665-1 (see 5.1.3) is replaced by the normative reference GB 18278.1 to adapt to my country's technical conditions;
- ISO 11135 (see 5.1.3) is replaced by the normative reference GB 18279 to adapt to my country's technical conditions;
- Replaced ISO 11137 (all parts) (see 5.1.3) with the normative reference GB (T) 18280 (all parts) to adapt to Our country's technical conditions;
- ISO 14937 (see 5.1.3) was replaced by the normative reference GB/T 19974 to adapt to my country's technical conditions;
- ISO 14160 (see 5.1.3) was replaced by the normative reference YY0970 to adapt to my country's technical conditions;
- ISO 20857 (see 5.1.3) was replaced by the normative reference YY/T 1276 to adapt to my country's technical conditions;
- ISO 25424 (see 5.1.3) was replaced by the normative reference YY/T 1464 to adapt to my country's technical conditions;
- Replaced ISO 13408-1 with the normative reference YY/T 0567.1 [see Chapter 3, 5.1.4, 5.2.3c) and Appendix C] to apply According to my country's technical conditions;
- Replaced ISO 13408-7 with the normative reference YY/T 0567.7 [see 5.1.4, 5.2.3c) and Appendix C] to adapt to the technical requirements of my country.

Technical conditions;

--- Added normative reference document GB/T 42061 [see 9.2.1a)] to adapt to my country's technical conditions;

--- ISO 14971 [see 5.2.1a)] was replaced by the normative reference GB/T 42062 to adapt to my country's technical conditions;

--- ISO 14644-4 [see 6.4c)] was replaced by the normative reference GB/T 25915.4 to adapt to my country's technical conditions;

--- Replaced ISO 22442 (all parts) [5.2.2b), 9.2.1a)] with the normative reference YY/T 0771 (all parts), Adapt to my country's technical conditions;

--- European GMP Part II [see 9.2.1a)] has been deleted to meet the feasibility requirements of this document;

--- Deleted ICHQ7 [see 9.2.1a)] and ICHQ9 [see 5.2.1a)] to meet the feasibility requirements of this document.

The following editorial changes were made to this document.

--- Change the name of the standard to "Microbial Risk Control in the Production and Processing of Cell-based Medical Devices";

--- Incorporated the amendments to ISO 18362:2016/Amd.1:2022, the outer margins of the clauses involved are marked with vertical double line (||) is marked;

--- Replace ISO 13485 with the informative reference GB/T 42061 (see Note 4.1);

--- Changed the description of H14 to avoid misunderstanding [see 6.6d)];

--- Deleted the European Pharmacopoeia Certificate of Suitability (CEP) (see 9.2.1) to adapt to my country's national conditions.

--- Replaced ISO 22443-3 with informative reference YY/T 0771.3 (see 9.5);

--- Replaced ISO 11737-1 with the informative reference GB/T 19973.1 (see 12.2.3);

--- Deleted the risk examples of biological products in Table B.1 (see Appendix B) to be consistent with the scope of application of the standard;

--- Changed the ISO cleanliness control level and converted it into the corresponding cleanliness level specified in my country (see Appendix D) to avoid Understanding bias;

--- Replaced ISO 14971 with the informative reference GB/T 42062 (see E.1);

--- Replaced ISO 22442 (all parts) with informative reference YY/T 0771 (all parts) (see E.1);

--- European GMP Part II (see E.1) was deleted.

0.1 Overview

The main components of cell-based medical devices include prokaryotic/eukaryotic cells or biological entities derived from cells.

Cell-based or cell-derived starting materials used in the manufacture of biopharmaceuticals can be in a living or inactivated state and can come from human, animal, microbial, Organisms or plants. A common feature of these medical devices is that their effectiveness comes from their biological properties.

Cell-based medical devices may have certain limitations in their ability to withstand sterilization and purification processes.

This document specifies the factors that need to be considered when applying a risk-based approach to the processing of such medical devices.

factors to reduce the possibility of increasing endogenous contamination of the product and prevent the introduction of exogenous contamination into the product.

The following key factors should be considered, including process design, equipment, facilities, common media, preparation conditions, addition of buffers and reagents, and operator Training.

0.2 Cell-based medical devices labeled "sterile"

Cell-based medical devices labeled "sterile" are generally sterilized through a terminal sterilization process or processed in an aseptic manner.

Examples of cell-based medical devices that are sterilized by terminal sterilization include, but are not limited to. cancellous bone, demineralized bone matrix, catgut, Sterility assurance for these medical devices is achieved through reasonable environmental design and control, of starting materials and packaging.

This can be achieved through appropriate manufacturing process design and validation (including terminal sterilization processes and the application of reasonable on-line controls and testing).

The requirements and guidelines for the terminal sterilization process of cell-based medical devices can be found in GB 18278.1, ISO/T S17665-2, GB 18280.1, GB 18280.2, GB/T 18280.3, GB 18279, YY0970, YY/T 1276, for reference, please refer to GB/T 19974 and YY/T 1464.

Some infectious agents (such as viruses and protozoa) may require a multifaceted approach to ensure product quality and safety.

Current terminal sterilization or aseptic processing standards do not specifically address these pathogens.