STANDARDS DEVELOPMENT FOR
REGENERATIVE MEDICINE THERAPIES

The Regenerative Medicine Standards Landscape

Fall 2020

STANDARDS COORDINATING BODY
REGENERATIVE MEDICINE

NEXIGHT GROUP

DISCLAIMER

This report was prepared for the U.S. Food and Drug Administration (FDA), Center for Biologics Evaluation and Research by Nexight Group and The Standards Coordinating Body for Gene, Cell, and Regenerative Medicines and Cell-Based Drug Discovery (SCB) under Order 75F40120F80487. The information and perspectives contained in this report are those of the authors and should not be attributed to the FDA. The mention of trade names, commercial products, or organizations does not imply endorsement of same by the U.S. Government.

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ABOUT THIS REPORT

The *21st Century Cures Act*—signed into law on December 2016—directs the U.S. Food and Drug Administration (FDA), in consultation with the National Institute of Standards and Technology (NIST) and industry stakeholders, to "coordinate and prioritize the development of standards and consensus definition of terms... [that] support, through regulatory predictability, the development, evaluation, and review of regenerative medicine therapies and regenerative advanced therapies."[1] Regenerative medicine therapies present complex challenges related to product testing, scientific protocols, product quality and specifications, performance characteristics, and compliance criteria. Thus, advancing the development and use of standards has the potential to:

- Facilitate innovation and product development by replacing costly, time-intensive trial-and-error processes with proven best practices
- Increase safety and reliability of therapies by defining testing and processing parameters throughout the product life cycle, from raw materials sourcing to clinical administration
- Accelerate review processes by eliminating the need for regulatory bodies to re-validate common operational steps for each new product
- Decrease costs of therapies by increasing testing and process efficiency

DEFINING REGENERATIVE MEDICINE THERAPIES

Section 3033 of the *21st Century Cures Act* defines Regenerative Medicine Therapy as drugs in the form of cell therapies, therapeutic tissue engineering products, human cell and tissue products, or combination products using such therapies or products, except those regulated solely under section 361 of the *Public Health Service Act* and part 1271 of Title 21,

Due to the potential benefits of standards, there is widespread agreement throughout the regenerative medicine community that standards are essential for accelerating innovation and advancing this relatively new field.

Report Objectives

This report provides a snapshot of the current landscape of regenerative medicine standards. It outlines existing and in-development standards, providing a reference that individual organizations can use to identify available standards to improve their operations.

[1] Public Law 114-255, 114th Congress. *21st Century Cures Act*, 2016. Available at: https://www.congress.gov/bill/114th-congress/house-bill/34/text/pl?overview=closed

The existing standards relate to a number of functional areas, including:

- Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

The report also serves to create a baseline for **identifying areas in which new or updated standards could help promote technical and scientific innovation or product development in regenerative medicine therapies.** This information may aid in assessing the maturity of the regenerative medicine therapies space and inform gaps and needs for science and technology development or policy discussions.

Development and Methodology

- **Publishing currency and frequency:** The first iteration of this report was developed in an accelerated 3-month timeframe and published in December 2017, with updates in February 2018, Spring 2019, Fall 2019, and this Fall 2020 edition. Given the constantly evolving nature of the field of regenerative medicine, SCB will continue to engage stakeholders to build on and refine this document in support of its mission.
- **Broad stakeholder input:** To date, nearly 50 experts representing more than 40 universities and research entities, funding organizations, government agencies, industry organizations, manufacturers, professional and scientific associations, and standards developing organizations (SDOs) provided their input to the report via an online poll, one-on-one interviews, and sharing of publications.
- **Research and analysis:** To date, more than 120 publicly available publications, organization websites, white papers, presentations, blog posts, and programmatic descriptions have been analyzed and continue to be reassessed for updates or modifications.

To ensure each edition of this report remains comprehensive, SCB **encourages the regenerative community to share any relevant updates and/or resources**. Submissions may be made through the SCB website.

More detail on Nexight Group and SCB can be found in **Appendix B. About Nexight Group and The Standards Coordinating Body**.

EXECUTIVE SUMMARY

Regenerative medicine therapies—including advanced cell, gene, and tissue-engineered therapies—could help manage and potentially cure many conditions and diseases that are intractable, chronic, and even terminal. However, compared with more mature medical fields with a greater number of marketed products and more robust infrastructure (e.g., traditional pharmaceutical drugs, medical devices), **the regenerative medicine field currently has few finalized standards, preventing many novel therapies from becoming commercially viable.** In fact, while many standards in this report have useful applications for regenerative medicine, the majority were designed for other related fields, with only a portion targeted toward the unique needs of regenerative medicine products, demonstrating **a critical need for more regenerative medicine standards.** A report that outlines the regenerative medicine community's priorities for needed standards, *Community Perspectives: Needed Standards in Regenerative Medicine*, is available on the SCB website and updated regularly.

While developing and publishing standards is important, **the industry must be aware of existing standards** and understand how to comply with them to truly advance the field of regenerative medicine. This report brings current regenerative medicine standards together in one place, providing lists of standards by sector and functional area that can be used as a comprehensive reference for **determining what and how current standards apply to regenerative medicine** and finding standards relevant to an organization's needs. To ensure it provides the most comprehensive list of existing regenerative medicine standards, this report will be updated regularly.

Knowledge of existing standards can also help to identify where additional standards are needed. Coordinated standards development—including refining and expanding existing standards as well as developing new ones—can **target common industry needs, improve product quality and safety, and ultimately reduce the timeline for moving therapies from the laboratory to widespread use in patient care.** Therefore, this review of the existing standards landscape will not only inform but also streamline future standards development efforts.

Existing Regenerative Medicine Standards

This report identifies more than 250 existing standards relevant to regenerative medicine, including more than 40 supportive standards applicable to one or more of the cell therapy, gene therapy, or tissue engineering sectors. Summary information on existing regenerative medicine standards included in this report can be found in **Table 1**.

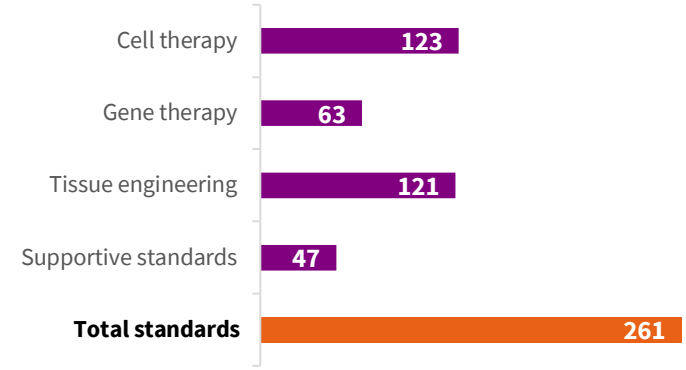
TABLE 1. EXISTING STANDARDS ROLLUP TABLE

STANDARDS AREAS

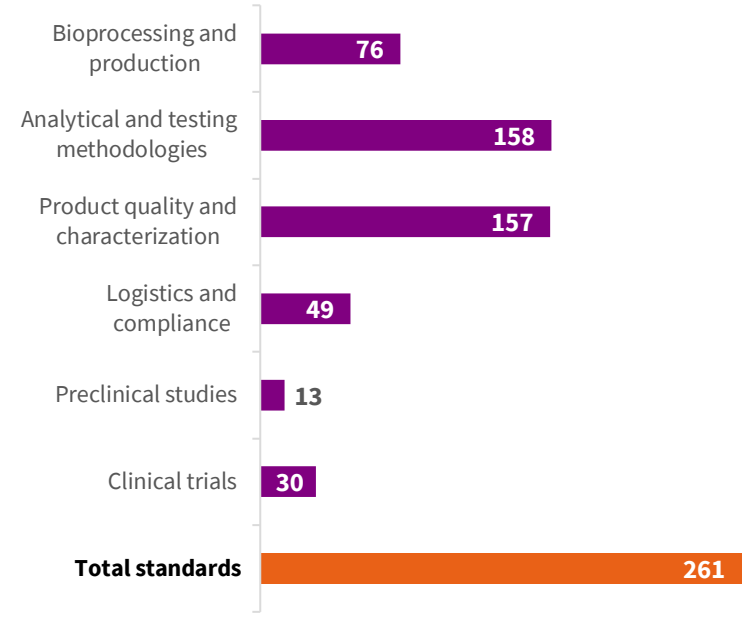
Existing standards address:

- Ancillary materials present during cell therapy production
- Assessment of tissue-engineered medical products (TEMPs) intended for bone repair and formation
- Best practices for manufacturing, testing, and administration of gene therapy products
- Cell counting and measurement methods
- Cell therapy product quality and safety/risk assessment
- Characterization and testing of starting materials for TEMPs
- DNA diagnostic sequencing and molecular diagnostic testing
- DNA extraction methodology
- Gene therapy reference materials (e.g., genomic DNA, reference panels and reagents) and virology standards
- General requirements for cell culturing equipment
- Methods for assessing TEMPs for infectious agents
- Tissue engineering scaffold construction and porousness testing

EXISTING STANDARDS BY REGENERATIVE MEDICINE SECTOR*

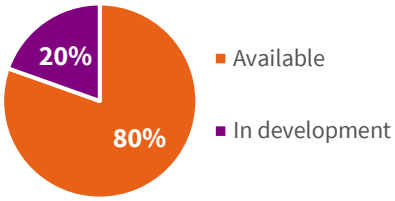


EXISTING STANDARDS BY FUNCTIONAL AREA*

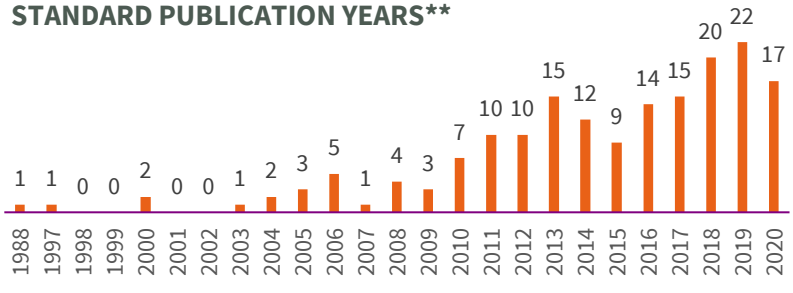


**Standards may apply to multiple sectors and/or functional areas; the bar representing "Total standards" is not a sum of all standards across all sectors or functional areas.*

STANDARD STATUS



STANDARD PUBLICATION YEARS**



EXISTING STANDARDS BY DEVELOPING ORGANIZATION	
5	AABB
1	American Association of Tissue Banks (AATB)
1	American Society of Histocompatibility & Immunogenetics (ASHI)
8	American Type Culture Collection (ATCC)
1	Association of German Engineers (VDI)
78	ASTM International
3	British Standards Institution (BSI)
7	Clinical & Laboratory Standards Institute (CLSI)
1	EuroFlow Consortium
9	European Directorate for the Quality of Medicines and Healthcare (EDQM)
1	European Federation for Immunogenetics (EFI)
8	Foundation for the Accreditation of Cellular Therapy (FACT)
1	Human Cell Differentiation Molecules
6	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)
1	International Council for Commonality in Blood Banking Automation (ICCBBA)
60	International Organization for Standardization (ISO)
6	International Society for Advancement of Cytometry (ISAC)
1	International Society for Biological and Environmental Repositories (ISBER)
3	International Society for Cellular Therapy (ISCT)
1	International Society for Stem Cell Research (ISSCR)
1	International Society of Automation (ISA)
22	National Institute for Biological Standards and Control (NIBSC)
1	ONE Study Consortium
10	Parenteral Drug Association (PDA)
6	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
19	United States Pharmacopeia (USP)

***Publication years could not be found for 44 standards.*

Report Structure

The body of this report contains:

- **Overview of the Current Regenerative Medicine Standards Landscape** — Provides a general introduction to the different types of standards included in the report
- **Standards Summary Sections** — Each standards summary section provides an overview of existing regenerative medicine standards in the sector and includes rollup tables that group standards by functional area for quick reference
- **Appendix A. Glossary of Existing Regenerative Medicine Standards** — Contains tables of more than 250 existing regenerative medicine standards and supportive standards organized by developing organization, with descriptions of each standard, publication information, and functional areas
- **Appendix B. About Nexight and the Standards Coordinating Body** — Describes the background of each organization and the contract with FDA
- **Appendix C. Acronyms and Abbreviations** — Defines the acronyms used in the report

OVERVIEW OF THE CURRENT REGENERATIVE MEDICINE STANDARDS LANDSCAPE

Current standards may exist as legislation, approved materials used for testing, and/or guides on best practices and accepted terminology, among other forms. These standards can be used as resources to improve the safety and efficiency of specific regenerative medicine processes. Existing standards can also be refined and expanded to address evolving technology or used as references or templates for the creation of new standards. For more information on **types of standards, how standards are created, and who develops standards,** refer to the Standards 101 section of the SCB website.

Compared with medical fields with a greater number of marketed products and a more mature infrastructure—such as traditional pharmaceutical drugs, medical devices, and, to a lesser extent, specific biotechnology products—the field of regenerative medicine has few finalized standards. The following sections outline **regenerative medicine standards that are published or in development in the areas of cell therapy, gene therapy, and tissue engineering.** This report also includes **supportive standards that can be used directly in each sector or leveraged when developing sector-specific standards** because they cover many of the same functional areas. Although regulations and guidance documents are defined as government standards in the National Technology Transfer and Advancement Act (NTTAA), government regulations and rules are not listed in the tables that follow.

Please note: a number of existing standards are high-level best practices or guidelines relevant to one or more sectors of cell therapy, gene therapy, and tissue engineering or applicable to multiple standard functional areas (i.e., bioprocessing and production; analytical and testing methodologies; product quality and characterization; logistics and compliance criteria; preclinical studies; and clinical trials). Such standards are captured in each relevant specific therapy sector and standards functional area section. **Appendix A. Glossary of Existing Regenerative Medicine Standards** contains additional information on each standard.

SUMMARY OF CELL THERAPY STANDARDS

Despite exponential growth in cell therapy treatment techniques, there are few commonly accepted laboratory practices for cell therapy and no harmonized standards for cell therapy components, processes, or products. There is **a crucial need for reference guidelines and characterization analytics** so researchers have a consistent, reproducible method to measure cells' functional response to their environments and produce standard data for use in applications and review processes.

More detailed information for each standard is included in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

NAVIGATING THIS SECTION

The following section addresses existing standards in the cell therapy sector. These standards are summarized in **Table 2**, an infographic rollup table containing information on the following:

- Applicable areas (i.e., what the standards address)
- Functional areas (i.e., to what areas of regenerative medicine therapies the standards apply)
- Publication information (i.e., the number of published standards versus the number of standards in development)
- Developing organizations

This rollup table is followed by detailed tables of standards based on functional areas, with standard names/ID numbers, developing organizations, current status, and information on whether the standard was updated since the last version of this report (e.g., if the standard is new to this version of the report, if it has been published as a final standard, or if it has been updated to a new version).

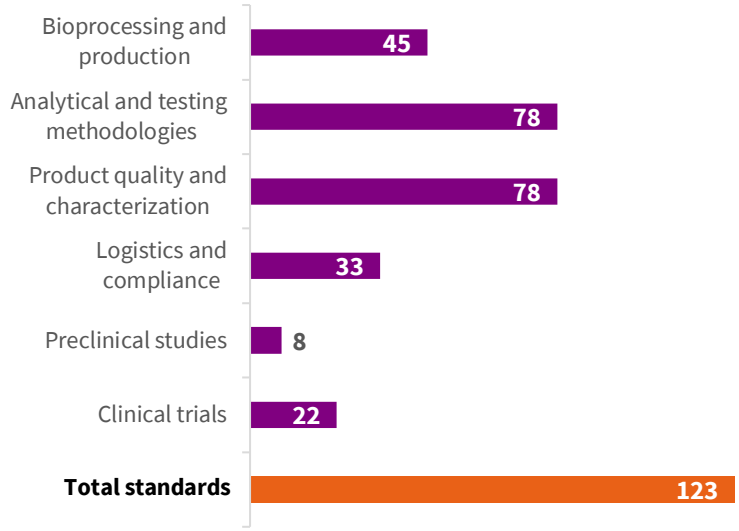
TABLE 2. CELL THERAPY STANDARDS ROLLUP

STANDARDS AREAS

Cell Therapy standards address:

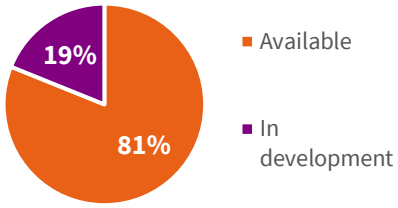
- Ancillary materials present during cell therapy production
- Assessment of adhesive characteristics of cells
- Cell counting and measurement methods
- Clinical translation of stem cell research
- General requirements for cell culturing equipment
- Potency assay development for cell therapy products
- Product quality and safety/risk assessment

EXISTING STANDARDS BY FUNCTIONAL AREA*

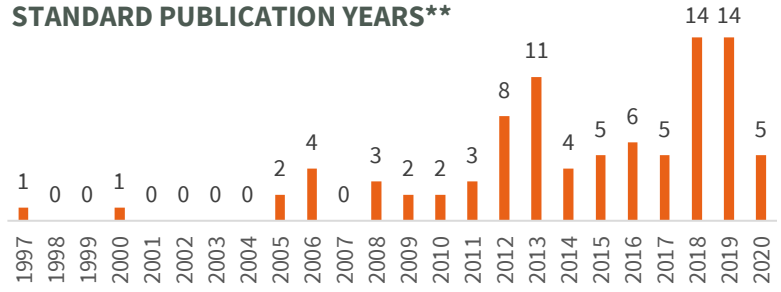


**Standards may apply to multiple functional areas; the bar representing "Total standards" is not a sum of all standards across all functional areas.*

STANDARD STATUS



STANDARD PUBLICATION YEARS**



EXISTING CELL THERAPY STANDARDS BY DEVELOPING ORGANIZATION

4	AABB
28	ASTM International
3	British Standards Institution (BSI)
1	EuroFlow Consortium
6	European Directorate for the Quality of Medicines and Healthcare (EDQM)
8	Foundation for the Accreditation of Cellular Therapy (FACT)
6	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)
1	International Council for Commonality in Blood Banking Automation (ICCBBA)
25	International Organization for Standardization (ISO)
6	International Society for Advancement of Cytometry (ISAC)
1	International Society for Biological and Environmental Repositories (ISBER)
3	International Society for Cellular Therapy (ISCT)
1	International Society for Stem Cell Research (ISSCR)
1	ONE Study Consortium
8	Parenteral Drug Association (PDA)
3	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
18	United States Pharmacopeia (USP)

*** Publication years could not be found for 13 standards.*

Cell Therapy Bioprocessing and Production Standards

Bioprocessing—another way to describe biomanufacturing—involves the design and development of processes, materials, and equipment for manufacturing products from raw/ancillary biological materials (e.g., the characterization of starting materials such as cells, gene therapy vectors, and biomaterials). **Table 3** lists cell therapy standards related to bioprocessing and production. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 3. CELL THERAPY SUMMARY: ROLLUP OF BIOPROCESSING AND PRODUCTION STANDARDS

45 standards	10 organizations	36 available	9 in development

CELL THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	AABB	Standards for Cellular Therapy Services (9th Edition)	Published 2019	
ASTM E2097-00*	ASTM International	Standard Guide for Determining the Impact of Extractables from Non-Metallic Materials on the Safety of Biotechnology Products	Published 2014	New
ASTM F3163-16*	ASTM International	Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds	Published 2016	
ASTM F3294-18*	ASTM International	Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy	Published 2018	Updated **Expanded Description**
ASTM WK66032*	ASTM International	Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment	In development; initiated November 2018	Updated **Expanded Description**
PAS 83:2012*	British Standards Institution (BSI)	Developing human cells for clinical applications in the European Union and the United States of America	Published 2012	

CELL THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
EP 5.2.12*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Raw materials of biological origin for the production of cell-based and gene therapy medicinal products	Published 2017	
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Common Standards for Cellular Therapies (Second Edition)	Published 2019	Updated **Expanded Description**
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A	FACT	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, & Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
N/A*	FACT	NetCord-FACT International Standards for Cord Blood Collection, Banking, & Release for Administration (Seventh Edition)	Published 2019	Updated **Seventh Edition**
N/A*	FACT	NetCord-FACT Cord Blood Accreditation Manual (Seventh Edition)	Published 2019	Updated **Seventh Edition**
ICH Q7*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ICH Q9*	ICH	Quality risk management	Published 2005	
ICH Q10*	ICH	Pharmaceutical quality system	Published 2008	

CELL THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ICCBBA ST-002 ISBT 128 global standard*	International Council for Commonality in Blood Banking Automation (ICCBBA)	Standard terminology for medical products of human origin	Published 2017; revised 2020	Updated
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO/CD 20399*	ISO	Biotechnology — Ancillary materials present during the production of cellular therapeutic products	In development; initiated November 2019	New
ISO/TS 20399-1:2018*	ISO	Biotechnology - Ancillary materials present during the production of cellular therapeutic products — Part 1: General requirements	Published 2018	Updated
ISO/TS 20399-2:2018*	ISO	Biotechnology – Ancillary materials present during the production of cellular therapeutic products – Part 2: Best practice guidance for ancillary material suppliers	Published 2018	
ISO/WD TS 20399-3:2018*	ISO	Biotechnology – Ancillary materials present during the production of cellular therapeutic products – Part 3: Best practice guidance for ancillary material users	Published 2018	
ISO/WD TS 22859-1	ISO	Biotechnology – Requirements for human mesenchymal stromal cells derived from umbilical cord	In development; initiated July 2018	Updated **Expanded Description**

CELL THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/WD TS 23565*	ISO	Biotechnology – Bioprocessing – General requirements and considerations for equipment systems used in manufacturing of cellular therapeutic products	In development; initiated September 2018	Updated
ISO/CD 24088-1*	ISO	Biotechnology — Biobanking — Requirements for the collection, processing, storage and transportation of microorganisms — Part 1: Bacteria and archaea	In development; initiated October 2019	New
ISO/CD 24603*	ISO	Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells	In development; initiated October 2019	New
ISO/CD 24651*	ISO	Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from bone marrow	In development; initiated October 2019	New
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
N/A	United States Pharmacopeia (USP)	Scaffold Human Amniotic Membrane Allograft	Published; Currently Official USP41-NF36 2S; 2019	
N/A*	USP	Trypsin Recombinant Porcine	Published	

CELL THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
Catalog #1148089*	USP	Collagenase I (2 x 0.5ml) reference material	Released	
Catalog #1148090*	USP	Collagenase II (2 x 0.5ml) reference material	Released	
Catalog #1270548*	USP	Fetal Bovine Serum (10ml) reference material	Released	
Catalog #1311714*	USP	rHuman IL-4 (51mcg) reference material	Released	
USP <89>*	USP	Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing	Published; Currently Official USP41-NF36; 2015	
USP <89.1>*	USP	Collagenase I	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <89.2>*	USP	Collagenase II	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <90>*	USP	Fetal Bovine Serum Quality Attributes & Functionality Tests	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <92>*	USP	Growth Factors and Cytokines Used in Cell Therapy Manufacturing	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1024>*	USP	Bovine Serum	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**

CELL THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Cell Therapy Analytical and Testing Methodologies Standards

Analytical methods and testing methodologies are used to detect, measure, and/or monitor certain attributes of a material and the state in which it is located (e.g., flow cytometry and microscopy for cell characterization). **Table 4** lists cell therapy standards related to analytical and testing methodologies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 4. CELL THERAPY SUMMARY: ROLLUP OF ANALYTICAL AND TESTING METHODOLOGIES STANDARDS

78 standards	**13** organizations	**68** available	**10** in development

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	AABB	Standards for Cellular Therapy Services (9th Edition)	Published 2019	
N/A*	AABB	Standards for Molecular Testing for Red Cell Platelet and Neutrophil Antigens (4th Edition)	Published 2018	
ASTM E3231-19*	ASTM International	Standard Guide for Cell Culture Growth Assessment of Single-Use Material	Published 2019	New
ASTM F2131-02*	ASTM International	Standard Test Method for In Vitro Biological Activity of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) Using the W-20 Mouse Stromal Cell Line	Published 2012	
ASTM F2149-16*	ASTM International	Standard Test Method for Automated Analyses of Cells—the Electrical Sensing Zone Method of Enumerating and Sizing Single Cell Suspensions	Published 2016	
ASTM F2259-10*	ASTM International	e1 Standard Test Method for Determining the Chemical Composition and Sequence in Alginate by Proton Nuclear Magnetic Resonance (1H NMR) Spectroscopy	Published 2012	
ASTM F2664-19e1*	ASTM International	Standard Guide for Assessing the Attachment of Cells to Biomaterial Surfaces by Physical Methods	Published 2011; updated 2019	Updated

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2944-20*	ASTM International	Standard Practice for Automated Colony Forming Unit (CFU) Assays—Image Acquisition and Analysis Method for Enumerating and Characterizing Cells and Colonies in Culture	Published 2012; updated 2020	Updated
ASTM F2997-13*	ASTM International	Standard Practice for Quantification of Calcium Deposits in Osteogenic Culture of Progenitor Cells Using Fluorescent Image Analysis	Published 2013	
ASTM F2998-14*	ASTM International	Guide for Using Fluorescence Microscopy to Quantify the Spread Area of Fixed Cells	Published 2014	
ASTM F3163-16*	ASTM International	Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds	Published 2016	
ASTM F3294-18*	ASTM International	Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy	Published 2018	Updated **Expanded Description**
ASTM F3354-19*	ASTM International	Standard Guide for Evaluating Extracellular Matrix Decellularization Processes	Published 2019	New
ASTM F3368-19*	ASTM International	Standard Guide for Cell Potency Assays for Cell Therapy and Tissue Engineered Products	Published 2019	Published
ASTM WK17329*	ASTM International	New Terminology for Terminology for Cell Signaling Related to Medical and Surgical Devices	In development; initiated November 2007	Updated **Expanded Description**
ASTM WK55364*	ASTM International	Quantifying Cell Proliferation in 3D-Scaffolds by a Non-Destructive Method	In development; initiated July 2016	
ASTM WK63854	ASTM International	New Practice for Material Biocompatibility	In development; initiated June 2018	
PAS 83:2012*	British Standards Institution (BSI)	Developing human cells for clinical applications in the European Union and the United States of America	Published 2012	
PAS 84:2012	BSI	Cell therapy and regenerative medicine: Glossary	Published 2012	

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
PAS 93:2011*	BSI	Characterization of human cells for clinical applications: Guide	Published 2011	
N/A	EuroFlow Consortium	EuroFlow standardization of flow cytometer instrument settings and immunophenotyping protocols	Published 2012	
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated **4th Edition**
EP 2.6.27*	EDQM	Microbiological examination of cell-based preparations	Published 2017	
EP 2.7.23*	EDQM	Numeration of CD34/CD45+ cells in haematopoietic products	Published	Updated **Expanded Description**
EP 2.7.28*	EDQM	Colony-forming cell assay for human haematopoietic progenitor cells	Published	Updated **Expanded Description**
EP 2.7.29*	EDQM	Nucleated cell count and viability	Published	Updated **Expanded Description**
EP 5.2.12*	EDQM	Raw materials of biological origin for the production of cell-based and gene therapy medicinal products	Published 2017	
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Common Standards for Cellular Therapies (Second Edition)	Published 2019	Updated **Expanded Description**
N/A*	FACT	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Quality Handbook (Second Edition)	Published 2015	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
N/A*	FACT	NetCord-FACT International Standards for Cord Blood Collection, Banking, & Release for Administration (Seventh Edition)	Published 2019	Updated **Seventh Edition**
N/A*	FACT	NetCord-FACT Cord Blood Accreditation Manual (Seventh Edition)	Published 2019	Updated **Seventh Edition**
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO 20391-1:2018	ISO	Biotechnology - Cell Counting - Part 1: General guidance on cell counting methods	Published 2018	
ISO 20391-2:2019*	ISO	Biotechnology - Cell Counting - Part 2: Experimental design and statistical analysis to quantify counting performance	Published 2019	
ISO/TR 20396-1*	ISO	Biotechnology - Data publication - Part 1: Preliminary considerations and concepts	In development	
ISO 21899:2020*	ISO	Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks	Published 2020	Published

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/DIS 23033*	ISO	Biotechnology — Analytical methods — General guidelines for the characterization and testing of cellular therapeutic products	In development; initiated November 2017	Updated **Expanded Description**
ISO/NP 23511*	ISO	Biotechnology - General guidance on detection methods of cell cross-contamination	In development	
ISO/WD 24190*	ISO	Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses	In development; initiated 2019	Updated **Expanded Description**
ISO/CD 24603*	ISO	Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells	In development; initiated October 2019	New
FCS 3.1	International Society for Advancement of Cytometry (ISAC)	Flow Cytometry Standard (FCS) Implementation Guidance	Published 2012	
N/A	ISAC	Classification Results File Format (CLR)	Published 2015	
N/A	ISAC	Gating-ML 2.0 data exchange standard for gating description	Published 2015	
N/A	ISAC	Image Cytometry Experiment Format	Published 2011	
N/A	ISAC	Mean Equivalent Soluble Fluorophores (MESF) and Equivalent Reference Fluorophore (ERF)	Published 2008	
N/A	ISAC	Minimum Information about a Flow Cytometry Experiment	Published 2008	
N/A	International Society for Cellular Therapy (ISCT)	Potency assay development for cellular therapy products	Published 2011	
N/A	ONE Study Consortium	Standardization of whole blood immune phenotype monitoring by flow cytometry for clinical trials: panels and methods from the ONE study	Published 2013	
TR 33*	Parenteral Drug Association (PDA)	Evaluation, Validation, and Implementation of Alternative and Rapid Microbiological Methods	Published 2013	

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
TR 47*	PDA	Preparation of Virus Spikes Used for Virus Clearance Studies	Published 2010	
TR 50*	PDA	Alternative Methods for Mycoplasma Testing	Published 2010	
TR 57*	PDA	Analytical Method Validation and Transfer for Biotechnology Products	Published 2012	
TR 57-2*	PDA	Analytical Method Development and Qualification for Biotechnology Products	Published 2015	
TR 75*	PDA	Consensus Method for Rating 0.1µm Mycoplasma Reduction Filters	Published 2016	
TR 81*	PDA	Cell-Based Therapy Control Strategy	Published 2019	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
Catalog #1084292	United States Pharmacopeia (USP)	CD34+ Cell Enumeration System Suitability (1.24 x 104 cells) reference material	Released	
Catalog #1148089*	USP	Collagenase I (2 x 0.5ml) reference material	Released	
Catalog #1148090*	USP	Collagenase II (2 x 0.5ml) reference material	Released	
Catalog #1270548*	USP	Fetal Bovine Serum (10ml) reference material	Released	
Catalog #1311714*	USP	rHuman IL-4 (51mcg) reference material	Released	

CELL THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <89>*	USP	Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing	Published; Currently Official USP41-NF36; 2015	
USP <89.1>*	USP	Collagenase I	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <89.2>*	USP	Collagenase II	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <90>*	USP	Fetal Bovine Serum Quality Attributes & Functionality Tests	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <92>*	USP	Growth Factors and Cytokines Used in Cell Therapy Manufacturing	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <127>	USP	Flow Cytometric Enumeration of CD34+ Cells	Published	
USP <130>*	USP	Protein A Quality Attributes	Published; Currently Official USP41-NF36; 2013	
USP <1027>	USP	Flow Cytometry	Published; Currently Official USP41-NF36; 2013	
USP <1043>*	USP	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Cell Therapy Product Quality and Characterization Standards

Product quality and characterization standards focus on defining quality attributes (e.g., identity, quantity, purity, sterility, biological activity/potency) of materials used in regenerative medicine therapies and provide a clear understanding of their intended use. These standards provide guidance on topics such as establishing a quality management system or designing measurements with sufficient selectivity, sensitivity, resolution, and robustness to enable subsequent decision making. **Table 5** lists cell therapy standards related to product quality and characterization. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 5. CELL THERAPY SUMMARY: ROLLUP OF PRODUCT QUALITY AND CHARACTERIZATION STANDARDS

78 standards	13 organizations	65 available	13 in development

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A	AABB	Hematopoietic Stem Cell Transplantation: A Handbook for Clinicians (2nd Edition)	Published 2014	
N/A*	AABB	Standards for Cellular Therapy Services (9th Edition)	Published 2019	
N/A*	AABB	Standards for Molecular Testing for Red Cell Platelet and Neutrophil Antigens (4th Edition)	Published 2018	
ASTM E1531-00(2006)*	ASTM International	Standard Practice for Detection of Mycoplasma Contamination of Cell Cultures by Growth on Agarose Medium	Published 2006; withdrawn 2014	New
ASTM E1532-00(2006)*	ASTM International	Standard Practice for Detection of Mycoplasma Contamination of Cell Cultures by Use of Bisbenzamide DNA-Binding Fluorochrome	Published 2006; withdrawn 2014	New
ASTM E1533-00(2006)*	ASTM International	Standard Practice for Indirect Detection of Mycoplasma in Cell Culture by 4`-6-Diamidino-2-2 Phenylindole (DAPI) Staining	Published 2006; withdrawn 2014	New

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM E1536-00(2006)*	ASTM International	Standard Practice for Detection of Mycoplasma Contamination of Bovine Serum by Large Volume Method	Published 2006; withdrawn 2014	New
ASTM E2097-00*	ASTM International	Standard Guide for Determining the Impact of Extractables from Non-Metallic Materials on the Safety of Biotechnology Products	Published 2014	New
ASTM F2131-02*	ASTM International	Standard Test Method for In Vitro Biological Activity of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) Using the W-20 Mouse Stromal Cell Line	Published 2012	
ASTM F2149-16*	ASTM International	Standard Test Method for Automated Analyses of Cells—the Electrical Sensing Zone Method of Enumerating and Sizing Single Cell Suspensions	Published 2016	
ASTM F2315-18*	ASTM International	Standard Guide for Immobilization or Encapsulation of Living Cells or Tissue in Alginate Gels	Published 2011; updated 2018	
ASTM F2944-20*	ASTM International	Standard Practice for Automated Colony Forming Unit (CFU) Assays—Image Acquisition and Analysis Method for Enumerating and Characterizing Cells and Colonies in Culture	Published 2012; updated 2020	Updated
ASTM F2997-13*	ASTM International	Standard Practice for Quantification of Calcium Deposits in Osteogenic Culture of Progenitor Cells Using Fluorescent Image Analysis	Published 2013	
ASTM F2998-14*	ASTM International	Guide for Using Fluorescence Microscopy to Quantify the Spread Area of Fixed Cells	Published 2014	
ASTM F3106-14*	ASTM International	Standard Guide for in vitro Osteoblast Differentiation Assays	Published 2014	
ASTM F3163-16*	ASTM International	Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds	Published 2016	
ASTM F3206-17*	ASTM International	Standard Guide for Assessing Medical Device Cytocompatibility with Delivered Cellular Therapies	Published 2017	

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F3209-16*	ASTM International	Standard Guide for Autologous Platelet-Rich Plasma for Use in Tissue Engineering and Cell Therapy	Published 2016	
ASTM F3294-18*	ASTM International	Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy	Published 2018	Updated **Expanded Description**
ASTM F3354-19*	ASTM International	Standard Guide for Evaluating Extracellular Matrix Decellularization Processes	Published 2019	New
ASTM F3368-19*	ASTM International	Standard Guide for Cell Potency Assays for Cell Therapy and Tissue Engineered Products	Published 2019	Published
ASTM F3369-19e1*	ASTM International	Standard Guide for Assessing the Skeletal Myoblast Phenotype	Published 2019	
ASTM WK17329*	ASTM International	New Terminology for Terminology for Cell Signaling Related to Medical and Surgical Devices	In development; initiated November 2007	Updated **Expanded Description**
ASTM WK66032*	ASTM International	Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment	In development; initiated November 2018	Updated **Expanded Description**
PAS 83:2012*	British Standards Institution (BSI)	Developing human cells for clinical applications in the European Union and the United States of America	Published 2012	
PAS 93:2011*	BSI	Characterization of human cells for clinical applications: Guide	Published 2011	
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated **4th Edition**
EP 2.7.23*	EDQM	Numeration of CD34/CD45+ cells in haematopoietic products	Published	Updated **Expanded Description**

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
EP 2.7.28*	EDQM	Colony-forming cell assay for human haematopoietic progenitor cells	Published	Updated **Expanded Description**
EP 2.7.29*	EDQM	Nucleated cell count and viability	Published	Updated **Expanded Description**
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Common Standards for Cellular Therapies (Second Edition)	Published 2019	Updated **Expanded Description**
N/A*	FACT	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Quality Handbook (Second Edition)	Published 2015	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, & Administration (Seventh Edition)	Published 2018	
N/A*	FACT	NetCord-FACT International Standards for Cord Blood Collection, Banking, & Release for Administration (Seventh Edition)	Published 2019	Updated **Seventh Edition**
N/A*	FACT	NetCord-FACT Cord Blood Accreditation Manual (Seventh Edition)	Published 2019	Updated **Seventh Edition**

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ICH Q5A (R1)*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Guideline for viral safety evaluation of biotechnology products derived from cell lines of human or animal origin quality of biotechnological products	Published 1997	
ICH Q5E*	ICH	Comparability of biotechnological/biological products subject to changes in their manufacturing process	Published 2005	
ICH Q7*	ICH	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ICH Q8 (R2)*	ICH	Pharmaceutical development	Published 2009	
ICH Q10*	ICH	Pharmaceutical quality system	Published 2008	
ICCBBA ST-002 ISBT 128 global standard*	International Council for Commonality in Blood Banking Automation (ICCBBA)	Standard terminology for medical products of human origin	Published 2017; revised 2020	Updated
ISO 13022:2012*	International Organization for Standardization (ISO)	Medical products containing viable human cells - Application of risk management & requirements for processing practices	Published 2012	
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO 20391-2:2019*	ISO	Biotechnology - Cell Counting - Part 2: Experimental design and statistical analysis to quantify counting performance	Published 2019	
ISO/CD 20399*	ISO	Biotechnology — Ancillary materials present during the production of cellular therapeutic products	In development; initiated November 2019	New

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 21709*	ISO	Biotechnology – Biobanking – Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines	In development; initiated August 2017	Updated
ISO/NP 23511*	ISO	Biotechnology - General guidance on detection methods of cell cross-contamination	In development	
ISO/WD TS 23565*	ISO	Biotechnology – Bioprocessing – General requirements and considerations for equipment systems used in manufacturing of cellular therapeutic products	In development; initiated September 2018	Updated
ISO/WD 24190*	ISO	Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses	In development; initiated 2019	Updated **Expanded Description**
ISO/WD 24421*	ISO	Biotechnology — Minimum requirements for optical signal measurements in photometric methods for biological samples	In development; initiated June 2020	New
ISO/CD 24603*	ISO	Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells	In development; initiated October 2019	New
ISO/CD 24651*	ISO	Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from bone marrow	In development; initiated October 2019	New
N/A*	International Society for Biological and Environmental Repositories (ISBER)	ISBER Best Practices for Repositories (Fourth Edition)	Published 2018	
N/A	International Society for Cellular Therapy (ISCT)	Minimal criteria for defining multipotent mesenchymal stromal cells	Published 2009	
N/A	ISCT	Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal/stem cells – IFATS/ISCT statement	Published 2013	

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A*	Parenteral Drug Association (PDA)	Cryopreservation of Cells	In development	
TR 47*	PDA	Preparation of Virus Spikes Used for Virus Clearance Studies	Published 2010	
TR 81*	PDA	Cell-Based Therapy Control Strategy	Published 2019	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
Catalog #1148089*	United States Pharmacopeia (USP)	Collagenase I (2 x 0.5ml) reference material	Released	
Catalog #1148090*	USP	Collagenase II (2 x 0.5ml) reference material	Released	
Catalog #1270548*	USP	Fetal Bovine Serum (10ml) reference material	Released	
Catalog #1311714*	USP	rHuman IL-4 (51mcg) reference material	Released	
USP <89>*	USP	Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing	Published; Currently Official USP41-NF36; 2015	
USP <89.1>*	USP	Collagenase I	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <89.2>*	USP	Collagenase II	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**

CELL THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <90>*	USP	Fetal Bovine Serum Quality Attributes & Functionality Tests	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <92>*	USP	Growth Factors and Cytokines Used in Cell Therapy Manufacturing	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <130>*	USP	Protein A Quality Attributes	Published; Currently Official USP41-NF36; 2013	
USP <1024>*	USP	Bovine Serum	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1043>*	USP	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Cell Therapy Logistics and Compliance Criteria Standards

Logistics and compliance involve the coordinated collection, manufacturing, and administration of cells and other therapy products across therapy manufacturers, providers, and receivers. Standards can help to ensure consistent and appropriate handling techniques, environmental and storage controls, and data and product traceability. **Table 6** lists cell therapy standards related to logistics and compliance criteria. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 6. CELL THERAPY SUMMARY: ROLLUP OF LOGISTICS AND COMPLIANCE CRITERIA STANDARDS

33 standards	10 organizations	25 available	8 in development

CELL THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	AABB	Hematopoietic Stem Cell Transplantation: A Handbook for Clinicians (2nd Edition)	Published 2014	
N/A*	AABB	Standards for Cellular Therapy Services (9th Edition)	Published 2019	
N/A*	AABB	Standards for Molecular Testing for Red Cell Platelet and Neutrophil Antigens (4th Edition)	Published 2018	
ASTM E1565-00*	ASTM International	Standard Guide for Inventory Control and Handling of Biological Material Maintained at Low Temperatures	Published 2019	
ASTM E1566-00*	ASTM International	Standard Guide for Handling Hazardous Biological Materials in Liquid Nitrogen	Published 2000; revised 2019	New
ASTM WK66032*	ASTM International	Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment	In development; initiated November 2018	Updated **Expanded Description**

CELL THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Common Standards for Cellular Therapies (Second Edition)	Published 2019	Updated **Expanded Description**
N/A*	FACT	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Quality Handbook (Second Edition)	Published 2015	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
N/A*	FACT	NetCord-FACT International Standards for Cord Blood Collection, Banking, & Release for Administration (Seventh Edition)	Published 2019	Updated **Seventh Edition**
N/A*	FACT	NetCord-FACT Cord Blood Accreditation Manual (Seventh Edition)	Published 2019	Updated **Seventh Edition**
ICH Q7*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ICH Q10*	ICH	Pharmaceutical quality system	Published 2008	
ISO 20387:2018*	International Organization for Standardization (ISO)	Biotechnology - Biobanking - General requirements for biobanking	Published 2018	

CELL THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO/AWI 20404*	ISO	Biotechnology — Bioprocessing — General requirements for packaging to contain cells for therapeutic use	In development; initiated October 2020	New
ISO 21709*	ISO	Biotechnology – Biobanking – Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines	In development; initiated August 2017	Updated
ISO 21899:2020*	ISO	Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks	Published 2020	Published
ISO/ TR 22758:2020*	ISO	Biotechnology - Biobanking - Implementation guide for ISO 20387	Published 2020	Published
ISO/WD TS 23494-1*	ISO	Biotechnology - Provenance information model for biological material and data — Part 1: Design concepts and general requirements	In development	Updated **Expanded Description**
ISO/CD 24088-1*	ISO	Biotechnology — Biobanking — Requirements for the collection, processing, storage and transportation of microorganisms — Part 1: Bacteria and archaea	In development; initiated October 2019	New

CELL THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A*	International Society for Biological and Environmental Repositories (ISBER)	ISBER Best Practices for Repositories (Fourth Edition)	Published 2018	
ISSCR 2016*	International Society for Stem Cell Research (ISSCR)	Guidelines for STEM cell research and clinical translation	Published 2016	
N/A*	Parenteral Drug Association (PDA)	Cryopreservation of Cells	In development	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
USP <1043>*	United States Pharmacopeia (USP)	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Cell Therapy Preclinical Study Standards

Preclinical studies test a drug, procedure, or other medical treatment in animals and are required to take place before clinical trials in humans can be started. Because the preclinical phase of research is critical to decision making about a possible future therapy, experiments done at this stage should be based on best practice methods (e.g., choosing the most appropriate animal model, ensuring that experiments are comparable and reproducible in different labs). **Table 7** lists cell therapy standards related to preclinical studies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 7. CELL THERAPY SUMMARY: ROLLUP OF PRECLINICAL STUDY STANDARDS

8 standards	4 organizations	8 available	0 in development

CELL THERAPY STANDARDS ADDRESSING PRECLINICAL STUDIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ASTM F3206-17*	ASTM International	Standard Guide for Assessing Medical Device Cytocompatibility with Delivered Cellular Therapies	Published 2017	
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated 4th Edition
ICH Q5A (R1)*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Guideline for viral safety evaluation of biotechnology products derived from cell lines of human or animal origin quality of biotechnological products	Published 1997	
ICH Q8 (R2)*	ICH	Pharmaceutical development	Published 2009	
ICH Q9*	ICH	Quality risk management	Published 2005	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated Expanded Description
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated Expanded Description

CELL THERAPY STANDARDS ADDRESSING PRECLINICAL STUDIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**

Cell Therapy Clinical Trial Standards

Clinical trials are research studies that determine whether a regenerative medicine strategy, treatment, or device is safe and effective for human use. These studies must follow strict scientific research standards (e.g., indication-specific endpoints, data collection, analytics) to ensure patients are protected and results are reliable. **Table 8** lists cell therapy standards related to clinical studies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 8. CELL THERAPY SUMMARY: ROLLUP OF CLINICAL TRIAL STANDARDS

22 standards	8 organizations	21 available	1 in development

CELL THERAPY STANDARDS ADDRESSING CLINICAL TRIALS
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	AABB	Standards for Cellular Therapy Services (9th Edition)	Published 2019	
N/A	AABB	Standards for Patient Blood Management Program (2nd Edition)	Published 2018	
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated **4th Edition**
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Common Standards for Cellular Therapies (Second Edition)	Published 2019	Updated **Expanded Description**
N/A*	FACT	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, & Administration (Seventh Edition)	Published 2018	

CELL THERAPY STANDARDS ADDRESSING CLINICAL TRIALS ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
N/A*	FACT	NetCord-FACT International Standards for Cord Blood Collection, Banking, & Release for Administration (Seventh Edition)	Published 2019	Updated **Seventh Edition**
N/A*	FACT	NetCord-FACT Cord Blood Accreditation Manual (Seventh Edition)	Published 2019	Updated **Seventh Edition**
ICH Q5A (R1)*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Guideline for viral safety evaluation of biotechnology products derived from cell lines of human or animal origin quality of biotechnological products	Published 1997	
ICH Q5E*	ICH	Comparability of biotechnological/biological products subject to changes in their manufacturing process	Published 2005	
ICH Q7*	ICH	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ICH Q8 (R2)*	ICH	Pharmaceutical development	Published 2009	
ICH Q9*	ICH	Quality risk management	Published 2005	
ICH Q10*	ICH	Pharmaceutical quality system	Published 2008	
ISO/WD 24190*	International Organization for Standardization (ISO)	Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses	In development; initiated 2019	Updated **Expanded Description**
ICCBBA ST-002 ISBT 128 global standard*	International Council for Commonality in Blood Banking Automation (ICCBBA)	Standard terminology for medical products of human origin	Published 2017; revised 2020	Updated
ISSCR 2016*	International Society for Stem Cell Research (ISSCR)	Guidelines for STEM cell research and clinical translation	Published 2016	

CELL THERAPY STANDARDS ADDRESSING CLINICAL TRIALS ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**

SUMMARY OF GENE THERAPY STANDARDS

Currently, further research is needed to assess the effectiveness and safety of gene therapies for commercial use. As a result, most gene therapy products are only available to patients involved in clinical trials. Furthermore, variations in manufacturing, measurement, and analytical techniques across developers of experimental gene therapy products make it difficult to evaluate product quality and safety, or to address the impact of manufacturing changes or innovations intended to improve product safety and efficacy. A common set of standards in gene therapy would **advance development of treatments beyond the realm of clinical trials to approved, safe treatments** for genetic diseases and syndromes.

More detailed information for each standard is included in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

NAVIGATING THIS SECTION

The following section contains existing standards in the gene therapy sector. These standards are summarized in **Table 9**, an infographic rollup table containing information on the following:

- Applicable areas (i.e., what the standards address)
- Functional areas (i.e., to what areas of regenerative medicine therapies the standards apply)
- Publication information (i.e., the number of published standards versus the number of standards in development)
- Developing organizations

This rollup table is followed by detailed tables of standards based on functional areas, with standard names/ID numbers, developing organizations, current status, and information on whether the standard was updated since the last version of this report (e.g., if the standard is new to this version of the report, if it has been published as a final standard, or if it has been updated to a new version).

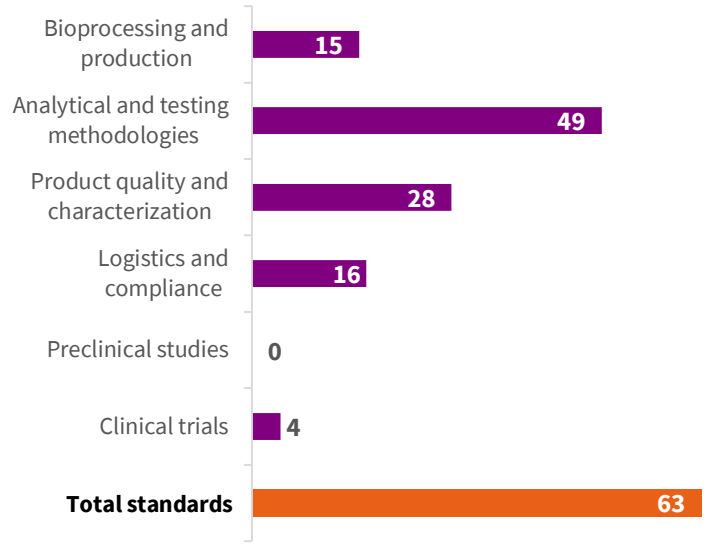
TABLE 9. GENE THERAPY STANDARDS ROLLUP

STANDARDS AREAS

Gene therapy standards address:

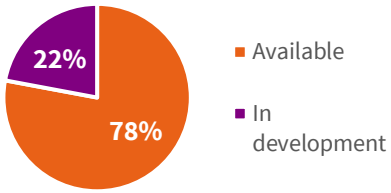
- DNA diagnostic sequencing and molecular diagnostic testing
- DNA extraction methodology
- General best practices for manufacturing, testing, and administration of gene therapy products
- Reference materials (e.g., genomic DNA, vector plasmids, cell lines, reference panels and reagents) and virology standards
- Testing for acceptable levels of residual host-cell proteins in gene therapy products

EXISTING STANDARDS BY FUNCTIONAL AREA*

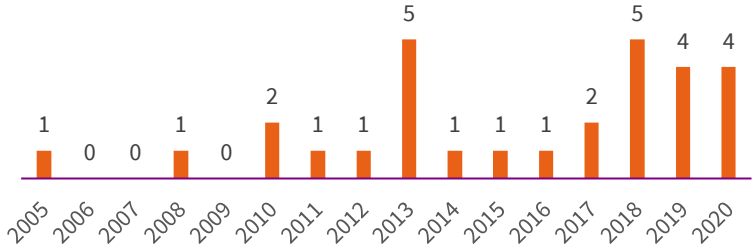


**Standards may apply to multiple functional areas; the bar representing "Total standards" is not a sum of all standards across all functional areas.*

STANDARD STATUS



STANDARD PUBLICATION YEARS**



EXISTING GENE THERAPY STANDARDS BY DEVELOPING ORGANIZATION

8	American Type Culture Collection (ATCC)
2	ASTM International
1	Clinical & Laboratory Standards Institute (CLSI)
5	European Directorate for the Quality of Medicines and Healthcare (EDQM)
4	Foundation for the Accreditation of Cellular Therapy (FACT)
16	International Organization for Standardization (ISO)
16	National Institute for Biological Standards and Control (NIBSC)
7	Parenteral Drug Association (PDA)
4	United States Pharmacopeia (USP)

***Publication years could not be found for 24 standards.*

Gene Therapy Bioprocessing and Production Standards

Bioprocessing—another way to describe biomanufacturing—involves the design and development of processes, materials, and equipment for manufacturing products from raw/ancillary biological materials (e.g., the characterization of starting materials such as cells, gene therapy vectors, and biomaterials). **Table 10** lists gene therapy standards related to bioprocessing and production. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 10. GENE THERAPY SUMMARY: ROLLUP OF BIOPROCESSING AND PRODUCTION STANDARDS

15 standards	**5** organizations	**10** available	**5** in development

GENE THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
EP 5.2.12*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Raw materials of biological origin for the production of cell-based and gene therapy medicinal products	Published 2017	
EP 5.14*	EDQM	Gene transfer medicinal products for human use	Published 2008	Updated **Expanded Description**
N/A	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, & Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	

GENE THERAPY STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/DIS 5058-1*	ISO	Biotechnology — Genome Editing — Part 1: Terminology	In development; initiated May 2020	New
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO/DIS 20688-1*	ISO	Biotechnology – Nucleic acid synthesis – Part 1: Requirements for the production and quality control of synthesized oligonucleotides	Published 2020	Published
ISO/PWI 20688-2*	ISO	Biotechnology - Nucleic acid synthesis - Part 2. General definitions and requirements for the production and quality control of synthesized gene fragments, genes and genomes	In development	
ISO/WD TS 22859-1	ISO	Biotechnology – Requirements for human mesenchymal stromal cells derived from umbilical cord	In development; initiated July 2018	Updated **Expanded Description**
TR 42	Parenteral Drug Association (PDA)	Process Validation of Protein Manufacturing	Published 2005	
USP <1046>*	United States Pharmacopeia (USP)	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	
USP <1047>*	USP	Gene Therapy Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**

Gene Therapy Analytical and Testing Methodologies Standards

Analytical and testing methodologies are used to detect, measure, and/or monitor certain attributes of a material and the state in which it is located (e.g., flow cytometry and microscopy for cell characterization). **Table 11** lists gene therapy standards related to analytical and testing methodologies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 11. GENE THERAPY SUMMARY: ROLLUP OF ANALYTICAL AND TESTING METHODOLOGIES STANDARDS

49 standards	8 organizations	41 available	8 in development

GENE THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ATCC RSM VR-1516*	American Type Culture Collection (ATCC)	Adenovirus Type 5 Reference Material	Released	
ATCC VR-1616*	ATCC	rAAV (Recombinant adeno-associated virus) serotype 2 reference material	Released	
ATCC VR-1816*	ATCC	rAAV (Recombinant adeno-associated virus) serotype 8 reference material	Released	
MM09-A2	Clinical & Laboratory Standards Institute (CLSI)	Nucleic Acid Sequencing Methods in Diagnostic Laboratory Medicine; Approved Guideline—Second Edition	Published 2014	
EP 2.6.34*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Host-cell protein assays	Published 2017	
EP 2.6.35*	EDQM	Quantification and characterisation of residual host-cell DNA	Published 2019	Published

GENE THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
EP 2.7.29*	EDQM	Nucleated cell count and viability	Published	Updated **Expanded Description**
EP 5.2.12*	EDQM	Raw materials of biological origin for the production of cell-based and gene therapy medicinal products	Published 2017	
EP 5.14*	EDQM	Gene transfer medicinal products for human use	Published 2008	Updated **Expanded Description**
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
ISO/DIS 5058-1*	ISO	Biotechnology — Genome Editing — Part 1: Terminology	In development; initiated May 2020	New
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**

GENE THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 20395:2019*	ISO	Biotechnology – Requirements for evaluating the performance of quantification methods for nucleic acid target sequences – Part 1: qPCR and dPCR	Published 2019	
ISO/TR 20396-1*	ISO	Biotechnology - Data publication - Part 1: Preliminary considerations and concepts	In development	
ISO/CD 20397-1*	ISO	Biotechnology - General requirements for massive parallel sequencing - Part 1: Nucleic acid and library preparation	In development	
ISO/FDIS 20397-2	ISO	Biotechnology – Massively parallel sequencing – Part 2: Quality evaluation of sequencing data	In development; initiated July 2017	
ISO/PWI 20688-2*	ISO	Biotechnology - Nucleic acid synthesis - Part 2. General definitions and requirements for the production and quality control of synthesized gene fragments, genes and genomes	In development	
ISO 21899:2020*	ISO	Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks	Published 2020	
ISO/WD TS 24420	ISO	Biotechnology — Massively parallel DNA sequencing — General requirements for data processing of shotgun metagenomics	In development; initiated June 2020	
04/224	National Institute for Biological Standards and Control (NIBSC)	Factor V Leiden, Human gDNA	Released	
05/130	NIBSC	WHO International Genetic Reference Panel for Prothrombin Mutation G20210A, Human gDNA	Released	

GENE THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
07/222	NIBSC	WHO International Reference Reagent: RhD/SRY plasma DNA sensitivity standard	Released 2012	
08/158	NIBSC	WHO International Genetic Reference Panel for Fragile X Syndrome, Human DNA	Released	
08/160	NIBSC	08/160: WHO International Genetic Reference Panel for Hemophilia A Intron 22 inversion	Released	
09/138	NIBSC	WHO International Genetic Reference Panel for the quantitation of BCR-ABL translocation by RQ-PCR	Released	
09/140	NIBSC	WHO International Genetic Reference Panel, Prader Willi and Angelman Syndromes, Human gDNA	Released	
10/136-001	NIBSC	HLA-DRB1 Genotyping Reference panel - CE marked material	Released	
10/232	NIBSC	International Reference Reagent: Genomic DNA for blood group genotyping RBC1(AR1R1)	Released	
10/234	NIBSC	International Reference Reagent: Genomic DNA for blood group genotyping RBC12(ODΨ)	Released	
10/236	NIBSC	International Reference Reagent: Genomic DNA for blood group genotyping RBC4 (AR1R1)	Released	
10/238	NIBSC	International Reference Reagent: Genomic DNA for blood group genotyping RBC5(Brr)	Released	
11/214	NIBSC	International Reference Reagent: Blood Group Genotyping Reference Panel	Released	
11/218	NIBSC	MLH1/MSH2 Exon Copy Number Reference Panel	Released	

GENE THERAPY STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A	NIBSC	Clinical virology standards (nearly 20 clinical virology network reference materials)	Released	
N/A	NIBSC	WHO 1st International Reference Panel for Genomic JAK2 V617F	Released	
TR 33*	Parenteral Drug Association (PDA)	Evaluation, Validation, and Implementation of Alternative and Rapid Microbiological Methods	Published 2013	
TR 47*	PDA	Preparation of Virus Spikes Used for Virus Clearance Studies	Published 2010	
TR 50*	PDA	Alternative Methods for Mycoplasma Testing	Published 2010	
TR 57*	PDA	Analytical Method Validation and Transfer for Biotechnology Products	Published 2012	
TR 57-2*	PDA	Analytical Method Development and Qualification for Biotechnology Products	Published 2015	
TR 75*	PDA	Consensus Method for Rating 0.1µm Mycoplasma Reduction Filters	Published 2016	
USP <130>*	United States Pharmacopeia (USP)	Protein A Quality Attributes	Published; Currently Official USP41-NF36; 2013	
USP <1043>*	USP	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	
USP <1047>*	USP	Gene Therapy Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**

Gene Therapy Product Quality and Characterization

Product quality and characterization standards focus on defining quality attributes (e.g., identity, quantity, purity, sterility, biological activity/potency) of materials used in regenerative medicine therapies and provide a clear understanding of their intended use. These standards provide guidance on topics such as establishing a quality management system or designing measurements with sufficient selectivity, sensitivity, resolution, and robustness to enable subsequent decision making. **Table 12** lists gene therapy standards related to product quality and characterization. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 12. GENE THERAPY SUMMARY: ROLLUP OF PRODUCT QUALITY AND CHARACTERIZATION STANDARDS

28 standards	6 organizations	23 available	5 in development

GENE THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ASN-0002-2011	American Type Culture Collection (ATCC)	Authentication of Human Cell Lines: Standardization of STR Profiling	Published 2011	
ATCC CRL-2972	ATCC	HeLa RC32 cell line	Released	
ATCC MBA-331	ATCC	TR-UF-11 vector plasmid	Released	
ATCC RSM VR-1516*	ATCC	Adenovirus Type 5 Reference Material	Released	
ATCC VR-539D	ATCC	Molecular Standards for Herpes Simplex Virus (HSV-1)	Released	
ATCC VR-540D	ATCC	Molecular Standards for Herpes Simplex Virus (HSV-2)	Released	
ATCC VR-1616	ATCC	Recombinant Adeno-Associated Virus 2 Reference Standard Material (AAV2 RSM)	Released	
ATCC VR-1816	ATCC	Adeno-Associated Virus 8 Reference Standard Material (AAV8 RSM)	Released	

GENE THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
EP 2.6.34*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Host-cell protein assays	Published 2017	
EP 2.6.35*	EDQM	Quantification and characterisation of residual host-cell DNA	Published 2019	
EP 2.7.29*	EDQM	Nucleated cell count and viability	Published	 **Expanded Description**
EP 5.14*	EDQM	Gene transfer medicinal products for human use	Published 2008	 **Expanded Description**
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	
ISO/DIS 5058-1*	ISO	Biotechnology — Genome Editing — Part 1: Terminology	In development; initiated May 2020	
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	 **Expanded Description**

GENE THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO 20395:2019*	ISO	Biotechnology – Requirements for evaluating the performance of quantification methods for nucleic acid target sequences – Part 1: qPCR and dPCR	Published 2019	
ISO/DIS 20688-1*	ISO	Biotechnology – Nucleic acid synthesis – Part 1: Requirements for the production and quality control of synthesized oligonucleotides	Published 2020	Published
ISO/PWI 20688-2*	ISO	Biotechnology - Nucleic acid synthesis - Part 2. General definitions and requirements for the production and quality control of synthesized gene fragments, genes and genomes	In development	
ISO 21709*	ISO	Biotechnology – Biobanking – Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines	In development; initiated August 2017	Updated
TR 47*	Parenteral Drug Association (PDA)	Preparation of Virus Spikes Used for Virus Clearance Studies	Published 2010	
USP <130>*	United States Pharmacopeia (USP)	Protein A Quality Attributes	Published; Currently Official USP41-NF36; 2013	
USP <1043>*	USP	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**

GENE THERAPY STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	
USP <1047>*	USP	Gene Therapy Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**

Gene Therapy Logistics and Compliance Criteria Standards

Logistics and compliance involve the coordinated collection, manufacturing, and administration of cells and other therapy products across therapy manufacturers, providers, and receivers. Standards can help to ensure appropriate handling techniques, fixed environmental and storage controls, and unbroken data and product traceability. **Table 13** lists gene therapy standards related to logistics and compliance criteria. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 13. GENE THERAPY SUMMARY: ROLLUP OF LOGISTICS AND COMPLIANCE CRITERIA STANDARDS

16 standards	4 organizations	12 available	4 in development

GENE THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ASTM E1565-00*	ASTM International	Standard Guide for Inventory Control and Handling of Biological Material Maintained at Low Temperatures	Published 2019	
ASTM E1566-00*	ASTM International	Standard Guide for Handling Hazardous Biological Materials in Liquid Nitrogen	Published 2000; revised 2019	New
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	

GENE THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 20387:2018*	International Organization for Standardization (ISO)	Biotechnology - Biobanking - General requirements for biobanking	Published 2018	
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO 21709*	ISO	Biotechnology – Biobanking – Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines	In development; initiated August 2017	Updated
ISO 21899:2020*	ISO	Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks	Published 2020	Published
ISO/ TR 22758:2020*	ISO	Biotechnology - Biobanking - Implementation guide for ISO 20387	Published 2020	Published
ISO/WD TS 23494-1*	ISO	Biotechnology - Provenance information model for biological material and data — Part 1: Design concepts and general requirements	In development	Updated **Expanded Description**
USP <1043>*	United States Pharmacopeia (USP)	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

GENE THERAPY STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <1047>*	USP	Gene Therapy Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**

Gene Therapy Preclinical Study Standards

Preclinical studies test a drug, procedure, or other medical treatment in animals, and are required to take place before clinical trials in humans can be started. Because the preclinical phase of research is critical to decision making about a possible future therapy, experiments done at this stage should be based on best practice methods (e.g., choosing the most appropriate animal model, ensuring that experiments are comparable and reproducible in different labs).

Currently, there are no known gene therapy standards related to preclinical studies.

Gene Therapy Clinical Trial Standards

Clinical trials are research studies that determine whether a regenerative medicine strategy, treatment, or device is safe and effective for human use. These studies must follow strict scientific research standards (e.g., indication-specific endpoints, data collection, analytics) to ensure patients are protected and results are reliable. **Table 14.** Gene Therapy Summary: Rollup of Clinical Trial Standards lists gene therapy standards related to clinical trials. **Click the standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 14. GENE THERAPY SUMMARY: ROLLUP OF CLINICAL TRIAL STANDARDS

4 standards	1 organization	4 available	0 in development

GENE THERAPY STANDARDS ADDRESSING CLINICAL TRIALS
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	Foundation for the Accreditation of Cellular Therapy (FACT)	FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT Standards for Immune Effector Cells (First Edition, Version 1.1)	Published 2018	
N/A*	FACT	FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration (Seventh Edition)	Published 2018	
N/A*	FACT	FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)	Published 2018	

SUMMARY OF TISSUE ENGINEERING STANDARDS

The potential to assemble functional constructs that restore, maintain, or improve damaged tissues or organs offers exciting prospects for changing traditional approaches to clinical treatment but also presents a number of unique challenges. Tissue engineering suffers from a **lack of standards for research and clinical trials**. The tissue engineering sector must overcome challenges with defining and **assessing cell attributes and functions to promote the proliferation of cells** *in vivo* or *in vitro*, **selecting and characterizing biocompatible materials**, and **ensuring long-term product safety**. Guidelines are also needed for current technologies and methods, with insights from manufacturers to develop best practices.

More detailed information for each standard is included in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

NAVIGATING THIS SECTION

The following section contains existing standards in the tissue engineering sector. These standards are summarized in **Table 15**, an infographic rollup table containing information on the following:

- Applicable areas (i.e., what the standards address)
- Functional areas (i.e., to what areas of regenerative medicine therapies the standards apply)
- Publication information (i.e., the number of published standards versus the number of standards in development)
- Developing organizations

This rollup table is followed by detailed tables of standards based on functional areas, with standard names/ID numbers, developing organizations, current status, and information on whether the standard was updated since the last version of this report (e.g., if the standard is new to this version of the report, if it has been published as a final standard, or if it has been updated to a new version).

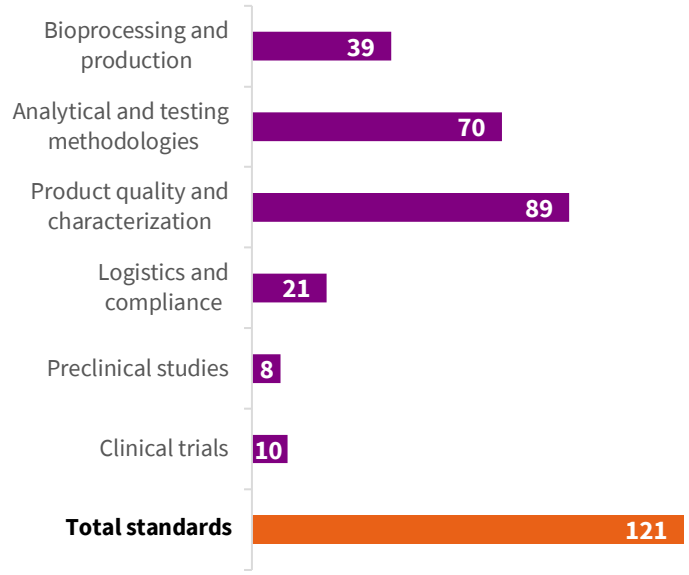
TABLE 15. TISSUE ENGINEERING STANDARDS ROLLUP

STANDARDS AREAS

Tissue engineering standards address:

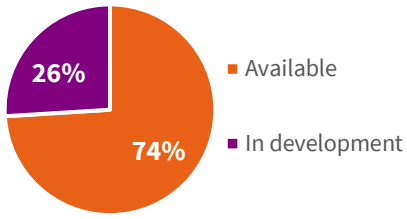
- Assessment of cell viability within scaffolds
- Assessment of tissue-engineered medical products (TEMPs) intended for bone repair and formation
- Characterization and assessment of TEMPs in specific applications (e.g., knee meniscus repair)
- Characterization and testing of TEMP starting materials
- Methods for assessing TEMPs for infectious agents
- Scaffold construction and porousness testing

EXISTING STANDARDS BY FUNCTIONAL AREA*

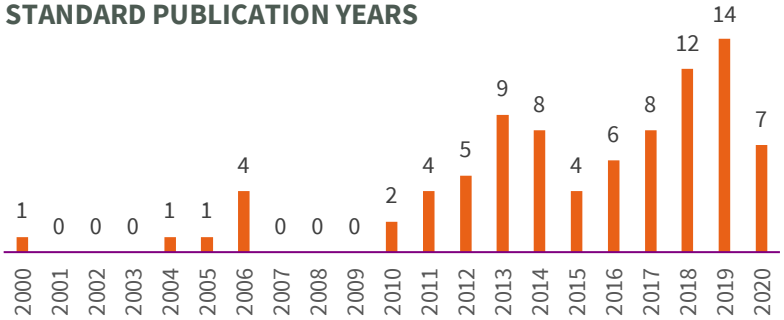


**Standards may apply to multiple functional areas; the bar representing "Total standards" is not a sum of all standards across all functional areas.*

STANDARD STATUS



STANDARD PUBLICATION YEARS



EXISTING TISSUE ENGINEERING STANDARDS BY DEVELOPING ORGANIZATION

1	American Association of Tissue Banking (AATB)
1	American Society of Histocompatibility & Immunogenetics (ASHI)
69	ASTM International
1	European Directorate for the Quality of Medicines and Healthcare (EDQM)
1	European Federation for Immunogenetics (EFI)
2	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)
1	International Council for Commonality in Blood Banking Automation (ICCBBA)
24	International Organization for Standardization (ISO)
1	International Society for Biological and Environmental Repositories (ISBER)
2	Parenteral Drug Association (PDA)
3	Pharmaceuticals and Medical Devices Agency (PMDA), Japan
15	United States Pharmacopeia (USP)

*** Publication years could not be found for 8 standards.*

Tissue Engineering Bioprocessing and Production Standards

Bioprocessing—another way to describe biomanufacturing—involves the design and development of processes, materials, and equipment for manufacturing products from raw/ancillary biological materials (e.g., the characterization of starting materials such as cells, gene therapy vectors, and biomaterials). **Table 16** lists tissue engineering standards related to bioprocessing and production. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 16. TISSUE ENGINEERING SUMMARY: ROLLUP OF BIOPROCESSING AND PRODUCTION STANDARDS

39 standards	7 organizations	29 available	10 in development

TISSUE ENGINEERING STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	American Association of Tissue Banks (AATB)	AATB Standards of Tissue Banking (14th Edition)	Published 2016	
ASTM E2097-00*	ASTM International	Standard Guide for Determining the Impact of Extractables from Non-Metallic Materials on the Safety of Biotechnology Products	Published 2014	New
ASTM F2027-16*	ASTM International	Standard Guide for Characterization and Testing of Raw or Starting Materials for Tissue-Engineered Medical Products	Published 2016	
ASTM F2312-11*	ASTM International	Standard Terminology Relating to Tissue Engineered Medical Products	Published 2011	Updated
ASTM F2383-11*	ASTM International	Standard Guide for Assessment of Adventitious Agents in Tissue Engineered Medical Products (TEMPs)	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F3163-16*	ASTM International	Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds	Published 2016	

TISSUE ENGINEERING STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F3294-18*	ASTM International	Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy	Published 2018	Updated **Expanded Description**
ASTM WK65680	ASTM International	New Test Methods for Printability of Bioinks and Biomaterial Inks	In development; initiated November 2018	
ASTM WK65681	ASTM International	New Guide for Bioinks and biomaterial inks used in bioprinting	In development; initiated November 2018	
ASTM WK66032*	ASTM International	Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment	In development; initiated November 2018	Updated **Expanded Description**
ICH Q7*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ICCBBA ST-002 ISBT 128 global standard*	International Council for Commonality in Blood Banking Automation (ICCBBA)	Standard terminology for medical products of human origin	Published 2017; revised 2020	Updated
ISO/WD TS 20388*	International Organization for Standardization (ISO)	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO/CD 20399*	ISO	Biotechnology — Ancillary materials present during the production of cellular therapeutic products	In development; initiated November 2019	New

TISSUE ENGINEERING STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/TS 20399-1:2018*	ISO	Biotechnology - Ancillary materials present during the production of cellular therapeutic products — Part 1: General requirements	Published 2018	Updated
ISO/TS 20399-2:2018*	ISO	Biotechnology – Ancillary materials present during the production of cellular therapeutic products – Part 2: Best practice guidance for ancillary material suppliers	Published 2018	
ISO/WD TS 20399-3:2018*	ISO	Biotechnology – Ancillary materials present during the production of cellular therapeutic products – Part 3: Best practice guidance for ancillary material users	Published 2018	
ISO/TS 21560:2020*	ISO	General requirements of TEMPs	Published 2020	Published
ISO/WD TS 22859-1	ISO	Biotechnology – Requirements for human mesenchymal stromal cells derived from umbilical cord	In development; initiated July 2018	Updated **Expanded Description**
ISO/WD TS 23565*	ISO	Biotechnology – Bioprocessing – General requirements and considerations for equipment systems used in manufacturing of cellular therapeutic products	In development; initiated September 2018	Updated
ISO/CD 24603*	ISO	Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells	In development; initiated October 2019	New
ISO/CD 24651*	ISO	Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from bone marrow	In development; initiated October 2019	New

TISSUE ENGINEERING STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
N/A	United States Pharmacopeia (USP)	Scaffold Human Amniotic Membrane Allograft	Published; Currently Official USP41-NF36 2S; 2019	
N/A*	USP	Trypsin Recombinant Porcine	Published	
Catalog #1148089*	USP	Collagenase I (2 x 0.5ml) reference material	Released	
Catalog #1148090*	USP	Collagenase II (2 x 0.5ml) reference material	Released	
Catalog #1270548*	USP	Fetal Bovine Serum (10ml) reference material	Released	
Catalog #1311714*	USP	rHuman IL-4 (51mcg) reference material	Released	
USP <89>*	USP	Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing	Published; Currently Official USP41-NF36; 2015	
USP <89.1>*	USP	Collagenase I	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <89.2>*	USP	Collagenase II	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <90>*	USP	Fetal Bovine Serum Quality Attributes & Functionality Tests	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <92>*	USP	Growth Factors and Cytokines Used in Cell Therapy Manufacturing	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1024>*	USP	Bovine Serum	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Tissue Engineering Analytical and Testing Methodologies

Analytical and testing methodologies are used to detect, measure, and/or monitor certain attributes of a material and the state in which it is located (e.g., flow cytometry and microscopy for cell characterization). **Table 17** lists tissue engineering standards related to analytical and testing methodologies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 17. TISSUE ENGINEERING SUMMARY: ROLLUP OF ANALYTICAL AND TESTING METHODOLOGIES STANDARDS

70 standards	6 organizations	56 available	14 in development

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ASTM E3231-19*	ASTM International	Standard Guide for Cell Culture Growth Assessment of Single-Use Material	Published 2019	New
ASTM F2064-17*	ASTM International	Standard Guide for Characterization and Testing of Alginates as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications	Published 2017	
ASTM F2103-18*	ASTM International	Standard Guide for Characterization and Testing of Chitosan Salts as Starting Materials Intended for Use in Biomedical and Tissue-Engineered Medical Product Applications	Published 2011; updated 2018	
ASTM F2131-02*	ASTM International	Standard Test Method for In Vitro Biological Activity of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) Using the W-20 Mouse Stromal Cell Line	Published 2012	

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2212-19*	ASTM International	Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)	Published 2011; updated 2019	Updated
ASTM F2259-10*	ASTM International	e1 Standard Test Method for Determining the Chemical Composition and Sequence in Alginate by Proton Nuclear Magnetic Resonance (1H NMR) Spectroscopy	Published 2012	
ASTM F2260-18*	ASTM International	e1 Standard Test Method for Determining Degree of Deacetylation in Chitosan Salts by Proton Nuclear Magnetic Resonance (1H NMR) Spectroscopy	Published 2012; updated 2018	
ASTM F2312-11*	ASTM International	Standard Terminology Relating to Tissue Engineered Medical Products	Published 2011	Updated
ASTM F2347-15*	ASTM International	Standard Guide for Characterization and Testing of Hyaluronan as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications	Published 2015	
ASTM F2383-11*	ASTM International	Standard Guide for Assessment of Adventitious Agents in Tissue Engineered Medical Products (TEMPs)	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2450-18*	ASTM International	Standard Guide for Assessing Microstructure of Polymeric Scaffolds for Use in Tissue Engineered Medical Products	Published 2010; updated 2018	Updated
ASTM F2451-10*	ASTM International	Standard Guide for in vivo Assessment of Implantable Devices Intended to Repair or Regenerate Articular Cartilage	Published 2010; withdrawn 2019	

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2529-13*	ASTM International	Standard Guide for in vivo Evaluation of Osteoinductive Potential for Materials Containing Demineralized Bone (DBM)	Published 2013	
ASTM F2602-18*	ASTM International	Standard Test Method for Determining the Molar Mass of Chitosan and Chitosan Salts by Size Exclusion Chromatography with Multi-angle Light Scattering Detection (SEC-MALS)	Published 2013; updated 2018	
ASTM F2605-16*	ASTM International	Standard Test Method for Determining the Molar Mass of Sodium Alginate by Size Exclusion Chromatography with Multi-angle Light Scattering Detection (SEC-MALS)	Published 2016	
ASTM F2664-19e1*	ASTM International	Standard Guide for Assessing the Attachment of Cells to Biomaterial Surfaces by Physical Methods	Published 2011; updated 2019	Updated
ASTM F2739-19	ASTM International	Standard Guide for Quantifying Cell Viability within Biomaterial Scaffolds	Published 2016; updated 2019	Updated
ASTM F2791-15	ASTM International	Standard Guide for Assessment of Surface Texture of Non-Porous Biomaterials in Two Dimensions	Published 2015	
ASTM F2883-11*	ASTM International	Standard Guide for Characterization of Ceramic and Mineral Based Scaffolds used for Tissue-Engineered Medical Products (TEMPs) and as Device for Surgical Implant Applications	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2900-11*	ASTM International	Standard Guide for Characterization of Hydrogels used in Regenerative Medicine	Published 2011; withdrawn 2020	**Withdrawn**

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2903-11*	ASTM International	Standard Guide for Tissue Engineered Medical Products (TEMPs) for Reinforcement of Tendon and Ligament Surgical Repair	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2952-14*	ASTM International	Standard Guide for Determining the Mean Darcy Permeability Coefficient for a Porous Tissue Scaffold	Published 2014	
ASTM F2998-14*	ASTM International	Guide for Using Fluorescence Microscopy to Quantify the Spread Area of Fixed Cells	Published 2014	
ASTM F3088-14*	ASTM International	Standard Test Method for Use of a Centrifugation Method to Quantify/Study Cell-Material Adhesive Interactions	Published 2014	
ASTM F3089-14*	ASTM International	Standard Guide for Characterization and Standardization of Polymerizable Collagen-Based Products and Associated Collagen-Cell Interactions	Published 2014	
ASTM F3163-16*	ASTM International	Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds	Published 2016	
ASTM F3223-17*	ASTM International	Standard Guide for Characterization and Assessment of Tissue Engineered Medical Products (TEMPs) for Knee Meniscus Surgical Repair and/or Reconstruction	Published 2017	
ASTM F3224-17*	ASTM International	Standard Test Method for Evaluating Growth of Engineered Cartilage Tissue Using Magnetic Resonance Imaging	Published 2017	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F3259-17*	ASTM International	Standard Guide for Micro-computed Tomography of Tissue Engineered Scaffolds	Published 2017	Updated **Expanded Description**
ASTM F3294-18*	ASTM International	Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy	Published 2018	Updated **Expanded Description**
ASTM F3354-19*	ASTM International	Standard Guide for Evaluating Extracellular Matrix Decellularization Processes	Published 2019	New
ASTM F3368-19*	ASTM International	Standard Guide for Cell Potency Assays for Cell Therapy and Tissue Engineered Products	Published 2019	Published
ASTM WK17329*	ASTM International	New Terminology for Terminology for Cell Signaling Related to Medical and Surgical Devices	In development; initiated November 2007	Updated **Expanded Description**
ASTM WK51697*	ASTM International	Testing and Characterization of Alginate Foam Scaffolds Used in Tissue Engineered Medical Products (TEMPs)	In development; initiated October 2015	
ASTM WK52257*	ASTM International	Characterization and Assessment of Heart Valve Tissue Engineered Medical Products (TEMPs)	In development; initiated November 2015	
ASTM WK55364*	ASTM International	Quantifying Cell Proliferation in 3D-Scaffolds by a Non-Destructive Method	In development; initiated July 2016	
ASTM WK57514	ASTM International	New Guide for Evaluating Extracellular Matrix Decellularization Processes	In development; initiated January 2017	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM WK62115*	ASTM International	New Test Method for Measuring Cell Viability in a Scaffold	In development; initiated January 2018	Updated **Expanded Description**
ASTM WK65476*	ASTM International	New Guide for Characterizing Fiber-Based Constructs for Tissue Engineered Medical Products	In development; initiated October 2018	
ASTM WK72274	ASTM International	New Test Method for Printability of Bioinks for Extrusion-based Bioprinting	In development; initiated March 2020	New
ASTM WK73220*	ASTM International	New Guide for Standard Guide for Characterization and Testing of Mammalian Fibrinogen as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications	In development; initiated June 2020	New
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated **4th Edition**
ISO 13019:2018	International Organization for Standardization (ISO)	Tissue-engineered medical products -- Quantification of sulfated glycosaminoglycans (sGAG) for evaluation of chondrogenesis	Published 2018	
ISO/TR 16379:2014	ISO	Tissue-engineered medical products — Evaluation of anisotropic structure of articular cartilage using DT (Diffusion Tensor) MR Imaging	Published 2014	
ISO 19090:2018	ISO	Evaluation of anisotropic structure of articular cartilage using DT (Diffusion Tensor) MR Imaging	Published 2018	

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO 20391-2:2019*	ISO	Biotechnology - Cell Counting - Part 2: Experimental design and statistical analysis to quantify counting performance	Published 2019	
ISO/TR 20396-1*	ISO	Biotechnology - Data publication - Part 1: Preliminary considerations and concepts	In development	
ISO/TS 21560:2020*	ISO	General requirements of TEMPs	Published 2020	Published
ISO 21899:2020*	ISO	Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks	Published 2020	Published
ISO/WD 24190*	ISO	Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses	In development; initiated 2019	Updated **Expanded Description**
ISO/CD 24603*	ISO	Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells	In development; initiated October 2019	New

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
TR 57*	Parenteral Drug Association (PDA)	Analytical Method Validation and Transfer for Biotechnology Products	Published 2012	
TR 57-2*	PDA	Analytical Method Development and Qualification for Biotechnology Products	Published 2015	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
Catalog #1148089*	United States Pharmacopeia (USP)	Collagenase I (2 x 0.5ml) reference material	Released	
Catalog #1148090*	USP	Collagenase II (2 x 0.5ml) reference material	Released	
Catalog #1270548*	USP	Fetal Bovine Serum (10ml) reference material	Released	
Catalog #1311714*	USP	rHuman IL-4 (51mcg) reference material	Released	
USP <89>*	USP	Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing	Published; Currently Official USP41-NF36; 2015	
USP <89.1>*	USP	Collagenase I	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <89.2>*	USP	Collagenase II	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <90>*	USP	Fetal Bovine Serum Quality Attributes & Functionality Tests	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <92>*	USP	Growth Factors and Cytokines Used in Cell Therapy Manufacturing	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <130>*	USP	Protein A Quality Attributes	Published; Currently Official USP41-NF36; 2013	
USP <1043>*	USP	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Tissue Engineering Product Quality and Characterization Standards

Product quality and characterization standards focus on defining quality attributes (e.g., identity, quantity, purity, sterility, biological activity/potency) of materials used in regenerative medicine therapies and provide a clear understanding of their intended use. These standards provide guidance on topics such as establishing a quality management system or designing measurements with sufficient selectivity, sensitivity, resolution, and robustness to enable subsequent decision making. **Table 18** lists tissue engineering standards related to product quality and characterization. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 18. TISSUE ENGINEERING SUMMARY: ROLLUP OF PRODUCT QUALITY AND CHARACTERIZATION STANDARDS

89 standards	9 organizations	71 available	18 in development

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION

** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	American Association of Tissue Banks (AATB)	AATB Standards of Tissue Banking (14th Edition)	Published 2016	
ASTM E1531-00(2006)*	ASTM International	Standard Practice for Detection of Mycoplasma Contamination of Cell Cultures by Growth on Agarose Medium	Published 2006; withdrawn 2014	New
ASTM E1532-00(2006)*	ASTM International	Standard Practice for Detection of Mycoplasma Contamination of Cell Cultures by Use of Bisbenzamide DNA-Binding Fluorochrome	Published 2006; withdrawn 2014	New
ASTM E1533-00(2006)*	ASTM International	Standard Practice for Indirect Detection of Mycoplasma in Cell Culture by 4`-6-Diamidino-2-2 Phenylindole (DAPI) Staining	Published 2006; withdrawn 2014	New
ASTM E1536-00(2006)*	ASTM International	Standard Practice for Detection of Mycoplasma Contamination of Bovine Serum by Large Volume Method	Published 2006; withdrawn 2014	New

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM E2097-00*	ASTM International	Standard Guide for Determining the Impact of Extractables from Non-Metallic Materials on the Safety of Biotechnology Products	Published 2014	
ASTM F2027-16	ASTM International	Standard Guide for Characterization and Testing of Raw or Starting Materials for Tissue-Engineered Medical Products	Published 2016	
ASTM F2064-17*	ASTM International	Standard Guide for Characterization and Testing of Alginates as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications	Published 2017	
ASTM F2103-18*	ASTM International	Standard Guide for Characterization and Testing of Chitosan Salts as Starting Materials Intended for Use in Biomedical and Tissue-Engineered Medical Product Applications	Published 2011; updated 2018	
ASTM F2131-02*	ASTM International	Standard Test Method for In Vitro Biological Activity of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) Using the W-20 Mouse Stromal Cell Line	Published 2012	
ASTM F2150-19	ASTM International	Standard Guide for Characterization and Testing of Biomaterial Scaffolds Used in Regenerative Medicine and Tissue-Engineered Medical Products	Published 2013; updated 2019	
ASTM F2210-02	ASTM International	Standard Guide for Processing Cells, Tissues, and Organs for Use in Tissue Engineered Medical Products	Published 2010; Withdrawn 2015	

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2211-13	ASTM International	Standard Classification for Tissue Engineered Medical Products (TEMPs)	Published 2013	Updated **Expanded Description**
ASTM F2212-19*	ASTM International	Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)	Published 2011; updated 2019	Updated
ASTM F2260-18*	ASTM International	e1 Standard Test Method for Determining Degree of Deacetylation in Chitosan Salts by Proton Nuclear Magnetic Resonance (1H NMR) Spectroscopy	Published 2012; updated 2018	
ASTM F2312-11*	ASTM International	Standard Terminology Relating to Tissue Engineered Medical Products	Published 2011	Updated
ASTM F2315-18*	ASTM International	Standard Guide for Immobilization or Encapsulation of Living Cells or Tissue in Alginate Gels	Published 2011; updated 2018	
ASTM F2347-15*	ASTM International	Standard Guide for Characterization and Testing of Hyaluronan as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications	Published 2015	
ASTM F2383-11*	ASTM International	Standard Guide for Assessment of Adventitious Agents in Tissue Engineered Medical Products (TEMPs)	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2450-18*	ASTM International	Standard Guide for Assessing Microstructure of Polymeric Scaffolds for Use in Tissue Engineered Medical Products	Published 2010; updated 2018	Updated

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2451-05*	ASTM International	Standard Guide for in vivo Assessment of Implantable Devices Intended to Repair or Regenerate Articular Cartilage	Published 2010; withdrawn 2019	
ASTM F2529-13*	ASTM International	Standard Guide for in vivo Evaluation of Osteoinductive Potential for Materials Containing Demineralized Bone (DBM)	Published 2013	
ASTM F2602-18*	ASTM International	Standard Test Method for Determining the Molar Mass of Chitosan and Chitosan Salts by Size Exclusion Chromatography with Multi-angle Light Scattering Detection (SEC-MALS)	Published 2013; updated 2018	
ASTM F2603-06	ASTM International	Standard Guide for Interpreting Images of Polymeric Tissue Scaffolds	Published 2012; updated 2020	Updated
ASTM F2605-16*	ASTM International	Standard Test Method for Determining the Molar Mass of Sodium Alginate by Size Exclusion Chromatography with Multi-angle Light Scattering Detection (SEC-MALS)	Published 2016	
ASTM F2721-09*	ASTM International	Standard Guide for Pre-clinical in vivo Evaluation in Critical Size Segmental Bone Defects	Published 2014	
ASTM F2883-11*	ASTM International	Standard Guide for Characterization of Ceramic and Mineral Based Scaffolds used for Tissue-Engineered Medical Products (TEMPs) and as Device for Surgical Implant Applications	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2884-12*	ASTM International	Standard Guide for Pre-clinical in vivo Evaluation of Spinal Fusion	Published 2012	

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F2900-11*	ASTM International	Standard Guide for Characterization of Hydrogels used in Regenerative Medicine	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2903-11*	ASTM International	Standard Guide for Tissue Engineered Medical Products (TEMPs) for Reinforcement of Tendon and Ligament Surgical Repair	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2952-14*	ASTM International	Standard Guide for Determining the Mean Darcy Permeability Coefficient for a Porous Tissue Scaffold	Published 2014	
ASTM F2998-14*	ASTM International	Guide for Using Fluorescence Microscopy to Quantify the Spread Area of Fixed Cells	Published 2014	
ASTM F3088-14*	ASTM International	Standard Test Method for Use of a Centrifugation Method to Quantify/Study Cell-Material Adhesive Interactions	Published 2014	
ASTM F3089-14*	ASTM International	Standard Guide for Characterization and Standardization of Polymerizable Collagen-Based Products and Associated Collagen-Cell Interactions	Published 2014	
ASTM F3106-14*	ASTM International	Standard Guide for in vitro Osteoblast Differentiation Assays	Published 2014	
ASTM F3142-16	ASTM International	Standard Guide for Evaluation of in vitro Release of Biomolecules from Biomaterials Scaffolds for TEMPs	Published 2016	Updated **Expanded Description**
ASTM F3163-16*	ASTM International	Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds	Published 2016	
ASTM F3207-17	ASTM International	Standard Guide for in vivo Evaluation of Rabbit Lumbar Intertransverse Process Spinal Fusion Model	Published 2017	

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM F3209-16*	ASTM International	Standard Guide for Autologous Platelet-Rich Plasma for Use in Tissue Engineering and Cell Therapy	Published 2016	
ASTM F3223-17*	ASTM International	Standard Guide for Characterization and Assessment of Tissue Engineered Medical Products (TEMPs) for Knee Meniscus Surgical Repair and/or Reconstruction	Published 2017	
ASTM F3224-17*	ASTM International	Standard Test Method for Evaluating Growth of Engineered Cartilage Tissue Using Magnetic Resonance Imaging	Published 2017	Updated **Expanded Description**
ASTM F3225-17	ASTM International	Standard Guide for Characterization and Assessment of Vascular Graft Tissue Engineered Medical Products (TEMPs)	Published 2017	Updated **Expanded Description**
ASTM F3259-17*	ASTM International	Standard Guide for Micro-computed Tomography of Tissue Engineered Scaffolds	Published 2017	Updated **Expanded Description**
ASTM F3294-18*	ASTM International	Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy	Published 2018	Updated **Expanded Description**
ASTM F3354-19*	ASTM International	Standard Guide for Evaluating Extracellular Matrix Decellularization Processes	Published 2019	New
ASTM F3368-19*	ASTM International	Standard Guide for Cell Potency Assays for Cell Therapy and Tissue Engineered Products	Published 2019	Published
ASTM F3369-19e1*	ASTM International	Standard Guide for Assessing the Skeletal Myoblast Phenotype	Published 2019	

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM WK16591	ASTM International	New Guide for the In Vivo Assessment of Bone Inductive Materials	In development; initiated September 2007	
ASTM WK17329*	ASTM International	New Terminology for Terminology for Cell Signaling Related to Medical and Surgical Devices	In development; initiated November 2007	Updated **Expanded Description**
ASTM WK51697*	ASTM International	Testing and Characterization of Alginate Foam Scaffolds Used in Tissue Engineered Medical Products (TEMPs)	In development; initiated October 2015	
ASTM WK52257*	ASTM International	Characterization and Assessment of Heart Valve Tissue Engineered Medical Products (TEMPs)	In development; initiated November 2015	
ASTM WK62115*	ASTM International	New Test Method for Measuring Cell Viability in a Scaffold	In development; initiated January 2018	Updated **Expanded Description**
ASTM WK65476*	ASTM International	New Guide for Characterizing Fiber-Based Constructs for Tissue Engineered Medical Products	In development; initiated October 2018	
ASTM WK66032*	ASTM International	Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment	In development; initiated November 2018	Updated **Expanded Description**
ASTM WK70143	ASTM International	New Guide for Sampling Methods of Tissue Engineered Medical Products (TEMPs) for Sterility Assurance	In development; initiated October 2019	New

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ASTM WK73220*	ASTM International	New Guide for Standard Guide for Characterization and Testing of Mammalian Fibrinogen as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications	In development; initiated June 2020	New
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated **4th Edition**
ICH Q5E*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Comparability of biotechnological/biological products subject to changes in their manufacturing process	Published 2005	
ICH Q7*	ICH	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ICCBBA ST-002 ISBT 128 global standard*	International Council for Commonality in Blood Banking Automation (ICCBBA)	Standard terminology for medical products of human origin	Published 2017; revised 2020	Updated
ISO 13022:2012*	International Organization for Standardization (ISO)	Medical products containing viable human cells - Application of risk management & requirements for processing practices	Published 2012	
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 20391-2:2019*	ISO	Biotechnology - Cell Counting - Part 2: Experimental design and statistical analysis to quantify counting performance	Published 2019	
ISO/CD 20399*	ISO	Biotechnology — Ancillary materials present during the production of cellular therapeutic products	In development; initiated November 2019	New
ISO/TS 21560:2020*	ISO	General requirements of TEMPs	Published 2020	Published
ISO 21709*	ISO	Biotechnology – Biobanking – Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines	In development; initiated August 2017	Updated
ISO/WD TS 23565*	ISO	Biotechnology – Bioprocessing – General requirements and considerations for equipment systems used in manufacturing of cellular therapeutic products	In development; initiated September 2018	Updated
ISO/WD 24190*	ISO	Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses	In development; initiated 2019	Updated **Expanded Description**
ISO/WD 24421*	ISO	Biotechnology — Minimum requirements for optical signal measurements in photometric methods for biological samples	In development; initiated June 2020	New
ISO/CD 24603*	ISO	Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells	In development; initiated October 2019	New

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/CD 24651*	ISO	Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from bone marrow	In development; initiated October 2019	New
N/A*	International Society for Biological and Environmental Repositories (ISBER)	ISBER Best Practices for Repositories (Fourth Edition)	Published 2018	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
Catalog #1148089*	United States Pharmacopeia (USP)	Collagenase I (2 x 0.5ml) reference material	Released	
Catalog #1148090*	USP	Collagenase II (2 x 0.5ml) reference material	Released	
Catalog #1270548*	USP	Fetal Bovine Serum (10ml) reference material	Released	
Catalog #1311714*	USP	rHuman IL-4 (51mcg) reference material	Released	
USP <89>*	USP	Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing	Published; Currently Official USP41-NF36; 2015	
USP <89.1>*	USP	Collagenase I	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
USP <89.2>*	USP	Collagenase II	Published; Currently Official USP41-NF36; 2017	Updated **Expanded Description**
USP <90>*	USP	Fetal Bovine Serum Quality Attributes & Functionality Tests	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <92>*	USP	Growth Factors and Cytokines Used in Cell Therapy Manufacturing	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <130>*	USP	Protein A Quality Attributes	Published; Currently Official USP41-NF36; 2013	
USP <1024>*	USP	Bovine Serum	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1043>*	USP	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Tissue Engineering Logistics and Compliance Criteria Standards

Logistics and compliance involve the coordinated collection, manufacturing, and administration of cells and other therapy products across therapy manufacturers, providers, and receivers. Standards can help to ensure appropriate handling techniques, fixed environmental and storage controls, and unbroken data and product traceability. **Table 19** lists tissue engineering standards related to logistics and compliance criteria. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 19. TISSUE ENGINEERING SUMMARY: ROLLUP OF LOGISTICS AND COMPLIANCE CRITERIA STANDARDS

21 standards	7 organizations	16 available	5 in development

TISSUE ENGINEERING STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	American Association of Tissue Banks (AATB)	AATB Standards of Tissue Banking (14th Edition)	Published 2016	
ASTM E1565-00*	ASTM International	Standard Guide for Inventory Control and Handling of Biological Material Maintained at Low Temperatures	Published 2019	
ASTM E1566-00*	ASTM International	Standard Guide for Handling Hazardous Biological Materials in Liquid Nitrogen	Published 2000; revised 2019	New
ASTM F2383-11*	ASTM International	Standard Guide for Assessment of Adventitious Agents in Tissue Engineered Medical Products (TEMPs)	Published 2011; withdrawn 2020	**Withdrawn**
ASTM F2386-04	ASTM International	Standard Guide for Preservation of Tissue Engineered Medical Products (TEMPs)	Published 2004; withdrawn 2013	New
ASTM WK66032*	ASTM International	Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment	In development; initiated November 2018	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ICH Q7*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated **Expanded Description**
ISO 20387:2018*	International Organization for Standardization (ISO)	Biotechnology - Biobanking - General requirements for biobanking	Published 2018	
ISO/WD TS 20388*	ISO	Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material	In development; initiated December 2017	Updated **Expanded Description**
ISO/PWI 20389*	ISO	Collection, processing, transportation, and storage criteria for human biological resources	In development	Updated **Expanded Description**
ISO/TS 21560:2020*	ISO	General requirements of TEMPs	Published 2020	Published
ISO 21709*	ISO	Biotechnology – Biobanking – Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines	In development; initiated August 2017	Updated
ISO 21899:2020*	ISO	Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks	Published 2020	Published
ISO/ TR 22758:2020*	ISO	Biotechnology - Biobanking - Implementation guide for ISO 20387	Published 2020	Published

TISSUE ENGINEERING STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/WD TS 23494-1*	ISO	Biotechnology - Provenance information model for biological material and data — Part 1: Design concepts and general requirements	In development	Updated **Expanded Description**
N/A*	International Society for Biological and Environmental Repositories (ISBER)	ISBER Best Practices for Repositories (Fourth Edition)	Published 2018	
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**
USP <1043>*	United States Pharmacopeia (USP)	Ancillary Materials for Cell, Gene, and Tissue-Engineered Products	Published; Currently Official USP41-NF36; 2013	Updated **Expanded Description**
USP <1046>*	USP	Cell and Gene Therapies Products	Published; Currently Official USP41-NF36; 2013	

Tissue Engineering Preclinical Study Standards

Preclinical studies test a drug, procedure, or other medical treatment in animals, and are required to take place before clinical trials in humans can be started. Because the preclinical phase of research is critical to decision making about a possible future therapy, experiments done at this stage should be based on best practice methods (e.g., choosing the most appropriate animal model, ensuring that experiments are comparable and reproducible in different labs). **Table 20** lists tissue engineering standards related to preclinical studies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 20. TISSUE ENGINEERING SUMMARY: ROLLUP OF PRECLINICAL STUDY STANDARDS

8 standards	3 organizations	7 available	in development

TISSUE ENGINEERING STANDARDS ADDRESSING PRECLINICAL STUDIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ASTM F2451-05	ASTM International	Standard Guide for in vivo Assessment of Implantable Devices Intended to Repair or Regenerate Articular Cartilage	Published 2010; withdrawn 2019	
ASTM F2721-09*	ASTM International	Standard Guide for Pre-clinical in vivo Evaluation in Critical Size Segmental Bone Defects	Published 2014	
ASTM F2884-12*	ASTM International	Standard Guide for Pre-clinical in vivo Evaluation of Spinal Fusion	Published 2012	
ASTM WK64460	ASTM International	New Guide for Pre-Clinical Testing Considerations for Materials Used to Regenerate Muscle	In development; initiated August 2018	Updated **Expanded Description**
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated **4th Edition**
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**

TISSUE ENGINEERING STANDARDS ADDRESSING PRECLINICAL STUDIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**

Tissue Engineering Clinical Trial Standards

Clinical trials are research studies that determine whether a regenerative medicine strategy, treatment, or device is safe and effective for human use. These studies must follow strict scientific research standards (e.g., indication-specific endpoints, data collection, analytics) to ensure patients are protected and results are reliable. **Table 21** lists tissue engineering standards related to clinical trials. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 21. TISSUE ENGINEERING SUMMARY: ROLLUP OF CLINICAL TRIAL STANDARDS

10 standards	7 organizations	9 available	1 in development

TISSUE ENGINEERING STANDARDS ADDRESSING CLINICAL TRIALS
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A	American Society of Histocompatibility & Immunogenetics (ASHI)	Standards for Accredited Laboratories	Published 2019	Published
N/A*	European Directorate for the Quality of Medicines and Healthcare (EDQM)	Guidelines on the quality and safety of tissues and cells for human application (4th Edition)	Published 2017; updated 2019	Updated 4th Edition
N/A	European Federation for Immunogenetics (EFI)	Standards for Histocompatibility & Immunogenics Testing, version 8.0	Published 2019	Published
ICH Q5E*	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)	Comparability of biotechnological/biological products subject to changes in their manufacturing process	Published 2005	
ICH Q7*	ICH	Good manufacturing practice guide for active pharmaceutical ingredients	Published 2000	Updated Expanded Description

TISSUE ENGINEERING STANDARDS ADDRESSING CLINICAL TRIALS ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ICCBBA ST-002 ISBT 128 global standard*	International Council for Commonality in Blood Banking Automation (ICCBBA)	Standard terminology for medical products of human origin	Published 2017; revised 2020	Updated
ISO/WD 24190*	International Organization for Standardization (ISO)	Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses	In development; initiated 2019	Updated **Expanded Description**
MHLW No. 266*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	General principles for the handling and use of cellular/tissue-based products	Published	Updated **Expanded Description**
MHLW No. 1314*	PMDA	Guidelines on ensuring the quality and safety of products derived from processed human stem cells	Published	Updated **Expanded Description**
MHLW notifications: autologous No. 0208003, allogenic No. 0912006*	PMDA	Guidelines on ensuring quality and safety of products derived from processed cell/tissue	Published	Updated **Expanded Description**

SUMMARY OF SUPPORTIVE STANDARDS

Supportive standards are not developed specifically for the cell therapy, gene therapy, or tissue engineering sectors, but are applicable to one or more of these sectors. They often can be **used directly in each sector or leveraged when developing sector-specific standards** because they cover many of the same functional areas. As the efforts to develop standards for regenerative medicine continue, there will likely be more supportive standards identified and categorized in the landscape assessment.

More detailed information for each standard is included in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

NAVIGATING THIS SECTION

The following section contains existing supportive standards. These standards are summarized in **Table 22**, an infographic rollup table containing information on the following:

- Applicable areas (i.e., what the standards address)
- Functional areas (i.e., to what areas of regenerative medicine therapies the standards apply)
- Publication information (i.e., the number of published standards versus the number of standards in development)
- Developing organizations

This rollup table is followed by detailed tables of standards based on functional areas, with standard names/ID numbers, developing organizations, current status, and information on whether the standard was updated since the last version of this report (e.g., if the standard is new to this version of the report, if it has been published as a final standard, or if it has been updated to a new version).

TABLE 22. SUPPORTIVE STANDARDS ROLLUP

STANDARDS AREAS

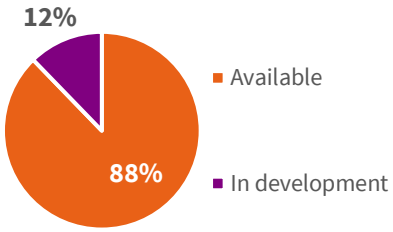
Supportive standards address:

- Data management best practices
- Guidelines for marketing authorizations and accreditation
- How to find relevant legislation and guidance
- Laboratory cleanliness specifications
- Medical device safety
- Specimen container manufacturing and design
- Trial risk management
- Terminology and definitions for medical products of human origin

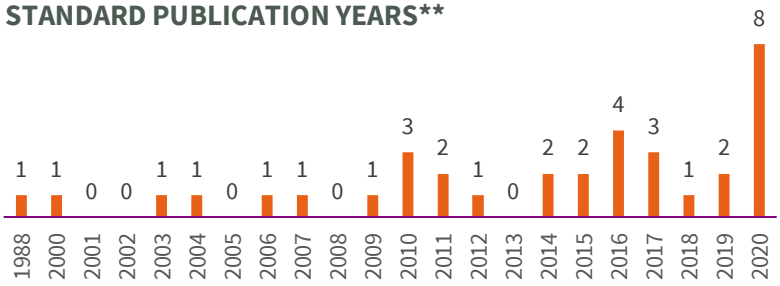
EXISTING STANDARDS BY FUNCTIONAL AREA*

**Standards may apply to multiple functional areas; the bar representing "Total standards" is not a sum of all standards across all functional areas.*

STANDARD STATUS



STANDARD PUBLICATION YEARS**



EXISTING SUPPORTIVE STANDARDS BY DEVELOPING ORGANIZATION

1	AABB
1	Association of German Engineers (VDI)
3	ASTM International
6	Clinical & Laboratory Standards Institute (CLSI)
1	Human Cell Differentiation Molecules
24	International Organization for Standardization (ISO)
1	International Society of Automation (ISA)
6	National Institute for Biological Standards and Control (NIBSC)
1	Parenteral Drug Association (PDA)
3	Pharmaceuticals and Medical Devices Agency (PMDA), Japan

***Publication years could not be found for 8 standards.*

Supportive Bioprocessing and Production Standards

Bioprocessing—another way to describe biomanufacturing—involves the design and development of processes, materials, and equipment for manufacturing products from raw/ancillary biological materials (e.g., the characterization of starting materials such as cells, gene therapy vectors, and biomaterials). **Table 23** lists supportive standards related to bioprocessing and production. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 23. SUPPORTIVE STANDARDS SUMMARY: ROLLUP OF BIOPROCESSING AND PRODUCTION STANDARDS

18 standards	6 organizations	17 available	1 in development

SUPPORTIVE STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
ANSI/ISA-88*	International Society of Automation (ISA)	Batch Control Standard (Parts 1-4)	Published 2010	
N/A*	Association of German Engineers (VDI)	Medical Grade Plastics	Published 2017	
AUTO01-A	Clinical & Laboratory Standards Institute (CLSI)	Laboratory Automation: Specimen Container/Specimen Carrier (1st Edition)	Published 2006	
AUTO02-A2*	CLSI	Laboratory Automation: Bar Codes for Specimen Container Identification; Approved Standard—Second Edition	Published 2016	
ISO 13485:2016*	International Organization for Standardization (ISO)	Medical devices -- Quality management systems -- Requirements for regulatory purposes	Published 2016	
ISO 14644-1:2015*	ISO	Cleanrooms and Associated Controlled Environments - Part 1: Classification of Cleanliness by Particle Concentration	Published 2015	Updated **Expanded Description**

SUPPORTIVE STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/TS 20399-1:2018*	ISO	Biotechnology - Ancillary materials present during the production of cellular therapeutic products — Part 1: General requirements	Published 2018	Updated
ISO 22442-2:2020*	ISO	Medical devices utilizing animal tissues & their derivatives - Part 2: Controls on sourcing, collection, and handling	Published 2015; revised 2020	Updated
ISO 22442-3:2007	ISO	Medical devices utilizing animal tissues & their derivatives - Part 3: Validation of the elimination &/or inactivation of viruses & transmissible spongiform encephalopathy (TSE) agents	Published 2007	
ISO/TR 22442-4:2010*	ISO	Medical devices utilizing animal tissues & their derivatives - Part 4: Principles for elimination &/or inactivation of transmissible spongiform encephalopathy (TSE) agents & validation assays for those processes	Published 2010	
ISO/PWI 22860	ISO	Biotechnology - Data element and metadata specification to describe production management of human isolated cells	In development	
N/A	National Institute for Biological Standards and Control (NIBSC)	Biological reference materials	Released	
N/A	NIBSC	In vitro diagnostic standards including HTLV-1, HIV, Hepatitis A/B/C, flow cytometry, anti-HLA serology, and HLA genotyping (more than 20 CE marked working standards)	Released	

SUPPORTIVE STANDARDS ADDRESSING BIOPROCESSING AND PRODUCTION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
N/A	NIBSC	Influenza reagents	Released	
N/A	NIBSC	Quality control reagents for pathogenic blood virus, cytomegalovirus, malaria, syphilis, rubella, toxoplasma, herpes simplex virus, and varicella zoster virus	Released	
N/A	NIBSC	WHO international standards	Released	
MHLW No. 169*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	Standards for manufacturing and quality control for medical device and in vitro diagnostic reagents	Published 2004; revised 2014	Updated **Expanded Description**
MHLW No. 210*	PMDA	Standards for Biological Materials (in Japanese)	Published 2004	Updated **Expanded Description**

Supportive Analytical and Testing Methodologies Standards

Analytical and testing methodologies are used to detect, measure, and/or monitor certain attributes of a material and the state in which it is located (e.g., flow cytometry and microscopy for cell characterization). **Table 24** lists supportive standards related to analytical and testing methodologies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 24. SUPPORTIVE STANDARDS SUMMARY: ROLLUP OF ANALYTICAL AND TESTING METHODOLOGIES STANDARDS

15 standards	3 organizations	12 available	3 in development

SUPPORTIVE STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
EP21	Clinical & Laboratory Standards Institute (CLSI)	Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures, 2nd Edition	Published 2016	
EP23-A	CLSI	Laboratory Quality Control Based on Risk Management; Approved Guideline	Published 2011	Updated **Expanded Description**
LIS03-A	CLSI	Standard Guide for Selection of a Clinical Laboratory Information Management System	Published 2003	Updated **Expanded Description**
MM19-A	CLSI	Establishing Molecular Testing in Clinical Laboratory Environments (1st Edition)	Published 2011	
ISO 10993-4:2017*	International Organization for Standardization (ISO)	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood	Published 2017	
ISO 10993-5:2009	ISO	Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity	Published 2009	
ISO 10993-6:2016*	ISO	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation	Published 2016	

SUPPORTIVE STANDARDS ADDRESSING ANALYTICAL AND TESTING METHODOLOGIES ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 10993-9:2019*	ISO	Biological evaluation of medical devices - Part 9: Framework for identification & quantification of potential degradation products	Published 2016; revised 2019	Updated
ISO/TR 10993-33:2015*	ISO	Biological evaluation of medical devices - Part 33: Guidance on tests to evaluate genotoxicity - Supplement to ISO 10993-3	Published 2015	Updated **Expanded Description**
ISO/TR 15499:2016*	ISO	Biological evaluation of medical devices - Guidance on the conduct of biological evaluation within a risk management process	Published 2016; withdrawn 2018	**Withdrawn**
ISO/DTR 20386	ISO	Inventory of biotechnology-related terms	Development initiated 2016; abandoned 2019	**Abandoned**
ISO/CD 20691	ISO	Biotechnology – Requirements for data formatting and description in the life sciences for downstream data processing and integration workflows	In development; initiated August 2017	Updated
ISO 21710*	ISO	Biotechnology - Specification on data management and publication in microbial resource centers	In development; initiated July 2017	Updated
IEC 31010:2019*	ISO	Risk management-Risk assessment techniques	Published 2009; revised 2019	Updated
N/A*	National Institute for Biological Standards and Control (NIBSC)	Working and other standards	Released	

Supportive Product Quality and Characterization Standards

Product quality and characterization standards focus on defining quality attributes (e.g., identity, quantity, purity, sterility, biological activity/potency) of materials used in regenerative medicine therapies and provide a clear understanding of their intended use. These standards guide the design of measurements with sufficient selectivity, sensitivity, resolution, and robustness to enable subsequent decision making. **Table 25** lists supportive standards related to product quality and characterization. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 25. SUPPORTIVE STANDARDS SUMMARY: ROLLUP OF PRODUCT QUALITY AND CHARACTERIZATION STANDARDS

22 standards	6 organizations	21 available	1 in development

SUPPORTIVE STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A	AABB	Standards for Relationship Testing Laboratories (14th Edition)	Published 2020	Updated **14th Edition**
ASTM E3251-20	ASTM International	Standard Test Method for Microbial Ingress Testing on Single-Use Systems	Published 2020	New
N/A	Human Cell Differentiation Molecules	A simple guide to the terminology and application of leucocyte monoclonal antibodies	Published 1988	Updated **Expanded Description**
ANSI/ISA-88*	International Society of Automation (ISA)	Batch Control Standard (Parts 1-4)	Published 2010	
ISO 10993-1:2018	International Organization for Standardization (ISO)	Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process	Published 2009; revised 2018	Updated
ISO 10993-3:2014	ISO	Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity & reproductive toxicity	Published 2014	Updated **Expanded Description**

SUPPORTIVE STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 10993-4:2017*	ISO	Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood	Published 2017	
ISO 10993-6:2016*	ISO	Biological evaluation of medical devices - Part 6: Tests for local effects after implantation	Published 2016	
ISO 10993-9:2019*	ISO	Biological evaluation of medical devices - Part 9: Framework for identification & quantification of potential degradation products	Published 2016; revised 2019	Updated
ISO 10993-10:2010	ISO	Biological evaluation of medical devices - Part 10: Tests for irritation & skin sensitization	Published 2010	
ISO 10993-11:2017	ISO	Biological evaluation of medical devices - Part 11: Tests for system toxicity	Published 2017	
ISO 10993-12:2012	ISO	Biological evaluation of medical devices - Part 12: Sample preparation & reference materials	Published 2012	
ISO/TR 10993-33:2015*	ISO	Biological evaluation of medical devices - Part 33: Guidance on tests to evaluate genotoxicity - Supplement to ISO 10993-3	Published 2015	Updated **Expanded Description**
ISO/TR 15499:2016*	ISO	Biological evaluation of medical devices - Guidance on the conduct of biological evaluation within a risk management process	Published 2016	
ISO 21710*	ISO	Biotechnology - Specification on data management and publication in microbial resource centers	In development; initiated July 2017	Updated
ISO 22442-1:2020	ISO	Medical devices utilizing animal tissues & their derivatives - Part 1: Application of risk management	Published 2015; revised 2020	Updated

SUPPORTIVE STANDARDS ADDRESSING PRODUCT QUALITY AND CHARACTERIZATION ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO/TR 22442-4:2010*	ISO	Medical devices utilizing animal tissues & their derivatives - Part 4: Principles for elimination &/or inactivation of transmissible spongiform encephalopathy (TSE) agents & validation assays for those processes	Published 2010	
IEC 31010:2019*	ISO	Risk management-Risk assessment techniques	Published 2009; revised 2019	Updated
N/A*	National Institute for Biological Standards and Control (NIBSC)	Working and other standards	Released	
MHLW No. 169*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	Standards for manufacturing and quality control for medical device and in vitro diagnostic reagents	Published 2004; revised 2014	Updated **Expanded Description**
MHLW No. 210*	PMDA	Standards for Biological Materials (in Japanese)	Published 2004	Updated **Expanded Description**
MHLW notification No. 0327025, 2008 *	PMDA	Points to consider on manufacturing and quality control	Published	

Supportive Logistics Standards and Compliance Criteria

Logistics and compliance involve the coordinated collection, manufacturing, and administration of cells and other therapy products across therapy manufacturers, providers, and receivers. Standards can help to ensure appropriate handling techniques, fixed environmental and storage controls, and unbroken data and product traceability. **Table 26** lists supportive standards related to logistics and compliance criteria. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 26. SUPPORTIVE STANDARDS SUMMARY: ROLLUP OF LOGISTICS AND COMPLIANCE CRITERIA STANDARDS

11 standards	6 organizations	9 available	2 in development

SUPPORTIVE STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
N/A*	Association of German Engineers (VDI)	Medical Grade Plastics	Published 2017	
ASTM E3230-20	ASTM International	Standard Practice for Extraction of Particulate Matter from the Surfaces of Single-Use Components and Assemblies Designed for Use in Biopharmaceutical Manufacturing	Published 2020	New
ASTM WK69660	ASTM International	New Guide for Guidance on Microbiological Quality & Prevention Strategy	In development; initiated August 2019	New
AUTO02-A2*	Clinical & Laboratory Standards Institute (CLSI)	Laboratory Automation: Bar Codes for Specimen Container Identification; Approved Standard—Second Edition	Published 2006	
ISO 13485:2016*	International Organization for Standardization (ISO)	Medical devices -- Quality management systems -- Requirements for regulatory purposes	Published 2016	
ISO 21710*	ISO	Biotechnology - Specification on data management and publication in microbial resource centers	In development; initiated July 2017	Updated

SUPPORTIVE STANDARDS ADDRESSING LOGISTICS AND COMPLIANCE CRITERIA ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
ISO 21973:2020	ISO	Biotechnology – General requirements for transportation of cells for therapeutic use	Published 2020	
ISO 22442-2:2020*	ISO	Medical devices utilizing animal tissues & their derivatives - Part 2: Controls on sourcing, collection, and handling	Published 2015; revised 2020	
TR 67	Parenteral Drug Association (PDA)	Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics	Published 2014	
MHLW No. 169*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	Standards for manufacturing and quality control for medical device and in vitro diagnostic reagents	Published 2004; revised 2014	 **Expanded Description**
MHLW notification No. 0327025, 2008*	PMDA	Points to consider on manufacturing and quality control	Published	

Supportive Preclinical Study Standards

Preclinical studies test a drug, procedure, or other medical treatment in animals, and are required to take place before clinical trials in humans can be started. Because the preclinical phase of research is critical to decision making about a possible future therapy, experiments done at this stage should be based on best practice methods (e.g., choosing the most appropriate animal model, ensuring that experiments are comparable and reproducible in different labs). **Table 27** lists supportive standards related to preclinical studies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 27. SUPPORTIVE STANDARDS SUMMARY: ROLLUP OF PRECLINICAL STUDY STANDARDS

1 standard	1 organization	1 available	0 in development

SUPPORTIVE STANDARDS ADDRESSING PRECLINICAL STUDIES
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
MHLW No. 169*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	Standards for manufacturing and quality control for medical device and in vitro diagnostic reagents	Published 2004; revised 2014	Updated **Expanded Description**

Supportive Clinical Trial Standards

Clinical trials are research studies that determine whether a regenerative medicine strategy, treatment, or device is safe and effective for human use. These studies must follow strict scientific research standards (e.g., indication-specific endpoints, data collection, analytics) to ensure patients are protected and results are reliable. **Table 28** lists supportive standards related to clinical studies. **Click each standard name** to access more information located in **Appendix A. Glossary of Existing Regenerative Medicine Standards**.

TABLE 28. SUPPORTIVE STANDARDS SUMMARY: ROLLUP OF CLINICAL TRIAL STANDARDS

6 standards	3 organizations	6 available	0 in development

SUPPORTIVE STANDARDS ADDRESSING CLINICAL TRIALS
** indicates standards that apply to multiple standards functional areas or sectors*

ID NUMBER	DEVELOPING ORGANIZATION	TITLE	STATUS	UPDATED SINCE LAST REPORT
AUTO02-A2	Clinical & Laboratory Standards Institute (CLSI)	Laboratory Automation: Bar Codes for Specimen Container Identification; Approved Standard—Second Edition	Published 2006	
EP21	CLSI	Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures, 2nd Edition	Published 2016	
EP23-A	CLSI	Laboratory Quality Control Based on Risk Management; Approved Guideline	Published 2011	Updated **Expanded Description**
ISO 14155:2020	International Organization for Standardization (ISO)	Clinical investigation of medical devices for human subjects - Good clinical practice	Published 2011; revised 2020	Updated
ISO 14644-1:2015*	ISO	Cleanrooms and Associated Controlled Environments - Part 1: Classification of Cleanliness by Particle Concentration	Published 2015	Updated **Expanded Description**

SUPPORTIVE STANDARDS ADDRESSING CLINICAL TRIALS ** indicates standards that apply to multiple standards functional areas or sectors*				
ID NUMBER	**DEVELOPING ORGANIZATION**	**TITLE**	**STATUS**	**UPDATED SINCE LAST REPORT**
MHLW No. 169*	Pharmaceuticals and Medical Devices Agency (PMDA), Japan	Standards for manufacturing and quality control for medical device and in vitro diagnostic reagents	Published 2004; revised 2014	Updated **Expanded Description**

APPENDIX A. GLOSSARY OF EXISTING REGENERATIVE MEDICINE STANDARDS

AABB

N/A: Hematopoietic Stem Cell Transplantation: A Handbook for Clinicians (2nd Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2014

Description:
This second edition offers comprehensive and practical information for health-care providers working in the field of hematopoietic stem cell transplantation (HSCT). It provides relevant information on all areas of HSCT, including indications for transplantation; donor and patient evaluation; conditioning regimens; collection, processing, and characterization of stem cell products; management of immunosuppressive therapy; evaluation and management of the most common complications during HSCT; supportive care management; common procedures; and aspects of follow-up care.

How to Access this Standard:
Available for purchase from AABB.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

N/A: Standards for Cellular Therapy Services (9th Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2019

Description:
These documents seek to help maintain and enhance the quality and safety of procurement, processing, storage, and clinical administration of cellular therapy products (CTPs). The standards cover necessary organizational structures, resources, equipment, agreements, process control measures, and document and records procedures. They also provide guidance on how to handle deviations, nonconforming products, or adverse events; conduct internal and external assessments; make process improvements; and maintain safe facilities. The 9th edition includes new standards and requirements for operational continuity, ISBT 128 labeling, and monitoring of oxygen levels, among other topics.

How to Access this Standard:
Available for purchase from AABB.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: Standards for Molecular Testing for Red Cell Platelet and Neutrophil Antigens (4th Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2018

Description:
These documents of practice are for facilities using molecular methods to predict ABO, Rh, and other blood group antigens on red blood cells, platelets, and neutrophils. These standards also contain quality system requirements, operational standards, and a detailed list of inventory resources necessary to identify targeted nucleotides that encode these antigens.

How to Access this Standard:
Available for purchase from AABB.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

N/A: Standards for Patient Blood Management Program (2nd Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2018

Description:
These documents can help establish a solid foundation for maintaining and optimizing patient care for facilities that are implementing or enhancing patient blood management efforts. The documents include overarching quality standards as well as specific technical standards, and cover topics including demonstrating blood use in an evidence-informed manner with supporting metrics on appropriateness and safety; proving processes are in place to minimize blood loss in surgical and medical patients; treating presurgical anemia proactively; and having processes in place to identify and manage patients at risk for or with hemorrhage, as well as patients for whom transfusion is not a therapeutic option.

How to Access this Standard:
Available for purchase from AABB.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: Standards for Relationship Testing Laboratories (14th Edition)

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2020

Description:
These documents outline the requirements for relationship testing laboratories in areas including employee qualification, facility monitoring of potentially fabricated documents, and identification of non-chain-of-custody cases. The standards are intended to aid materially in developing and maintaining policies, processes, and procedures that will contribute to acceptable results as well as to a safe work environment for laboratory personnel.

How to Access this Standard:
Available for purchase from AABB.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

American Association of Tissue Banks (AATB)

N/A: AATB Standards of Tissue Banking (14th Edition)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2016

Description:
This document provides guidance on tissue-banking best practices and considerations, including general institutional requirements; functional components; records management; authorization and consent practices; donor screening, testing, and suitability assessment; parameters surrounding tissue recovery operations; tissue processing, packaging, labeling, storage and distribution; and establishment and maintenance of a quality program.

How to Access this Standard:
Access to these standards requires AATB membership.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

American Society of Histocompatibility & Immunogenetics (ASHI)

N/A: Standards for Accredited Laboratories

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2019

Description:
This document sets forth the conditions that a laboratory must satisfy in order to be accredited by the American Society for Histocompatibility and Immunogenetics (ASHI) to perform testing on human specimens. The standard includes requirements for proficiency testing, laboratory quality systems, and personnel qualifications and responsibilities.

How to Access this Standard:
Proposed revisions to the 2019 standards are available on the ASHI website.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

American Type Culture Collection (ATCC)

ASN-0002-2011: Authentication of Human Cell Lines: Standardization of STR Profiling

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2011

Description:
This document provides a standardized procedure for unambiguous authentication and identification of human cell lines using short tandem repeat (STR) profiling. The objective of this standard is to specify the methodologies for DNA extraction and STR profiling, data analyses, quality control of the data, interpretation of results, and implementation of a searchable public database.

How to Access this Standard:
Available for purchase from ANSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC CRL-2972: HeLa RC32 cell line

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This standard reference material is a clone of HeLa cells that harbors one to two rep-cap gene copies per cell. Upon vector transfection and adenovirus infection, efficient rAAV assembly correlated with a 100-fold amplification of the integrated rep-cap sequence with the inverted terminal repeats (ITRs) deleted.

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC MBA-331: TR-UF-11 vector plasmid

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This standard reference material is the pTR-UF-11 vector plasmid in E. coli. This vector plasmid is used in SmaI cuts in both adeno-associated virus (AAV) inverted terminal repeat sequences (ITRs) and as a diagnostic that the ITRs are intact.

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC RSM VR-1516: Adenovirus Type 5 Reference Material

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This standard reference material is a dose of adenovirus reference material (ARM), which consists of purified Adenovirus, Type 5 (wild type adenovirus) formulated as a sterile liquid in 20 mM TRIS, 25 mM NaCl, 2.5% glycerol, pH 8.0 at room temperature, and stored frozen at –70°C. The configuration is 0.5-mL in a Type II glass vial with a Teflon-coated gray butyl stopper, plus an aluminum seal and crimp closure. The U.S. Food and Drug Administration (FDA) has made recommendations for the use of the ARM when characterizing adenoviral gene therapy products.

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC VR-539D: Molecular Standards for Herpes Simplex Virus (HSV-1)

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This standard reference material is genomic DNA (gDNA) isolated from a preparation of cell lysate and supernatant from Vero cells (ATCC® CCL-81™) infected with human herpesvirus 1 (HSV-1) strain McIntyre (ATCC® VR-539™). This product was prepared using methods known to inactivate viruses. It is suitable for use in polymerase chain reactions (PCR) or other molecular-based procedures.

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC VR-540DQ: Molecular Standards for Herpes Simplex Virus (HSV-2)

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This standard reference material is genomic DNA (gDNA) isolated from a preparation of cell lysate and supernatant from Vero cells (ATCC® CCL-81™) infected with human herpesvirus 2, strain MS (ATCC® VR-540™). This product was prepared using methods known to inactivate viruses. It is suitable for use in polymerase chain reactions (PCR) and other molecular-based applications.

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC VR-1616: Recombinant Adeno-Associated Virus 2 Reference Standard Material (AAV2 RSM)

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This standard reference material is a dose of recombinant Adeno-associated Virus 2 Reference Standard Stock (rAAV2 RSS), consisting of highly purified preparation formulated as a sterile liquid in phosphate buffered saline (PBS) + 135 mM NaCl at room temperature, and stored frozen at –80°C. The purpose of the rAAV2 RSS is to define the particle, vector genome, and infectious units for adeno-associated virus (AAV) 2-based gene vectors and establish a reference point for comparisons. It was developed at the recommendation of the U.S. Food and Drug Administration (FDA) and the National Institutes of Health (NIH) Recombinant DNA Advisory Committee, under the guidance of the Adeno-Associated Virus (AAV) Reference Standard Working Group (AAVRSWG) and the U.S. Food and Drug Administration (FDA).

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ATCC VR-1816: Adeno-Associated Virus 8 Reference Standard Material (AAV8 RSM)

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This standard reference material is a dose of recombinant Adeno-associated Virus 8 Reference Standard Stock (rAAV8 RSS), consisting of a highly purified preparation formulated as a sterile liquid in Dulbecco's phosphate-buffered saline (dPBS) at room temperature, and stored frozen at –80°C. The configuration is 0.125 ml per vial in polypropylene cryogenic vials. The purpose of the rAAV8 RSS is to define the particle, vector genome, and infectious units for adeno-associated virus (AAV) 8-based gene vectors and establish a reference point for comparisons. It was developed under the guidance of the Adeno-Associated Virus (AAV) Reference Standard Working Group (AAVRSWG), the U.S. Food and Drug Administration (FDA), and the European Directorate for the Quality of Medicines and Healthcare (EDQM).

How to Access this Reference Material:
Available for purchase from ATCC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

Association of German Engineers (VDI)

N/A: Medical Grade Plastics

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2017

Description:
This standard defines and describes what is meant by Medical Grade Plastics and which properties and requirements for plastics are relevant for use in medical devices. The application of the guideline helps raw material manufacturers and producers of plastic products to ensure the consistency of the recipe, quality, biocompatibility, and delivery reliability of such products.

How to Access this Standard:
Available for purchase from VDI.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ASTM International

ASTM E1531-00(2006): Standard Practice for Detection of Mycoplasma Contamination of Cell Cultures by Growth on Agarose Medium

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published 2006; withdrawn 2014

Description:
This standard outlines the procedures used for detection of mycoplasma contamination by direct microbiological culture.

This standard was withdrawn in 2014.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E1532-00(2006): Standard Practice for Detection of Mycoplasma Contamination of Cell Cultures by Use of Bisbenzamide DNA-Binding Fluorochrome

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published 2006; withdrawn 2014

Description:
This standard outlines the use of cell cultures and DNA-binding flurorochrome techniques to detect mycoplasma contamination of cell cultures.

This standard was withdrawn in 2014.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E1533-00(2006): Standard Practice for Indirect Detection of Mycoplasma in Cell Culture by 4`-6-Diamidino-2-2 Phenylindole (DAPI) Staining

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	⊘ Published 2006; withdrawn 2014

Description:
This standard outlines procedures used for the detection of mycoplasma contamination by indirect DNA staining.

This standard was withdrawn in 2014.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E1536-00(2006): Standard Practice for Detection of Mycoplasma Contamination of Bovine Serum by Large Volume Method

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	⊘ Published 2006; withdrawn 2014

Description:
This standard outlines procedures used for detection of mycoplasma contamination in serum by direct microbiological culture.

This standard was withdrawn in 2014.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E1565-00: Standard Guide for Inventory Control and Handling of Biological Material Maintained at Low Temperatures

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	Published 2019

Description:
This guide covers recommended procedures for handling material stored at low temperatures in mechanical freezers and liquid nitrogen freezers. It includes recommendations for implementing procedures to ensure adequate inventory control and safeguarding material stored at low temperatures.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E1566-00: Standard Guide for Handling Hazardous Biological Materials in Liquid Nitrogen

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	Published 2000; revised 2019

Description:
This guide is intended for use by individuals maintaining and handling hazardous biological material in liquid nitrogen freezers. It covers recommended procedures and safety precautions for maintaining and handling hazardous biological materials at liquid nitrogen temperatures.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2027-16: Standard Guide for Characterization and Testing of Raw or Starting Materials for Tissue-Engineered Medical Products

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2016

Description:
This document provides guidance on writing a materials specification for raw or starting materials intended for use in tissue engineering scaffolds for growth, support, or delivery of cells and/or biomolecules. This guide provides a compendium of relevant existing standards and test methods for materials already commonly used within medical products and includes characterization guidance for interim use of raw materials for which a standard does not exist.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2064-17: Standard Guide for Characterization and Testing of Alginates as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2017

Description:
This document contains a listing of characterization parameters directly related to the functionality of alginate. This guide can aid in the selection and characterization of an appropriate alginate for a particular application. The alginate covered by this guide may be gelled, extruded, or otherwise formulated into biomedical devices for use in tissue-engineered medical products (TEMPs) or drug delivery devices for implantation as determined to be appropriate, based on supporting biocompatibility and physical test data.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E2097-00: Standard Guide for Determining the Impact of Extractables from Non-Metallic Materials on the Safety of Biotechnology Products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2014

Description:
This guide covers procedures and test methods for process component qualification by the end user. The goal is to assess the safety impact of extractables from non-metallic process components used in contact with bioprocessing solutions. This encompasses the impact of extractables on the safety of the final product as it passes through the various stages of the manufacturing process.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E3230-20: Standard Practice for Extraction of Particulate Matter from the Surfaces of Single-Use Components and Assemblies Designed for Use in Biopharmaceutical Manufacturing

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2020

Description:
This practice describes the requirements for development, qualification, and routine application of a procedure for the effective liquid extraction of particulate matter from the surfaces of single-use components and assemblies designed for use in biopharmaceutical manufacturing processes. The extraction generates a suspension of particulate matter in liquid, which makes the particulate matter readily available for analytical characterization.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E3231-19: Standard Guide for Cell Culture Growth Assessment of Single-Use Material

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Published 2019

Description:
This guide outlines best practices to consider when setting up a representative leachable test method to detect if a material is compatible with cell culture media or manufacturing processes. This guide does not replace or supersede cell growth tests like USP <87>, USP <88> (plastic/elastomeric materials), or ISO 10993 (medical device materials), which are used in assessing biological reactivity in humans. Polymeric materials that have passed these tests have been found to leach compounds under normal process conditions that can inhibit cell culture growth for some cell lines.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM E3251-20: Standard Test Method for Microbial Ingress Testing on Single-Use Systems

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2020

Description:
The microbial test method outlined in this document applies to microbial ingress risk assessment of a single-use system (SUS) or its individual components that require integrity testing either by the assembly supplier or the end user of the assembly based on a potential risk of a breach to the product or manufacturing process. Microbial ingress testing helps evaluate the ability of an SUS fluid path to remain sterile after microbial exposure and can help determine the maximum allowable leakage limit (MALL) that does not allow microbial ingress under specific test conditions.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2103-18: Standard Guide for Characterization and Testing of Chitosan Salts as Starting Materials Intended for Use in Biomedical and Tissue-Engineered Medical Product Applications

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2011; updated 2018

Description:
This document lists characterization parameters directly related to the functionality of chitosan. This standard can aid in the selection and characterization of the appropriate chitosan or chitosan salt for a particular application. This standard is intended to give guidance in the methods and types of testing necessary to properly characterize, assess, and ensure consistency in the performance of a particular chitosan.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2131-02: Standard Test Method for In Vitro Biological Activity of Recombinant Human Bone Morphogenetic Protein-2 (rhBMP-2) Using the W-20 Mouse Stromal Cell Line

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published 2012

Description:
This document describes a standard test method and standard method for calculating results for the determination of the in-vitro biological activity of recombinant human bone morphogenetic protein-2 (rhBMP-2) using the mouse stromal cell line W-20 clone 17 (W-20-17). This clone was derived from bone marrow stromal cells of the W++ mouse strain. Although the test method can be used for assessment of the bioactivity of crude preparations of rhBMP-2, it has only been validated for use with highly pure (>98 % by weight protein purity) preparations of rhBMP-2.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2149-16: Standard Test Method for Automated Analyses of Cells—the Electrical Sensing Zone Method of Enumerating and Sizing Single Cell Suspensions

APPLICABLE SECTOR(S):
Cell therapy

STATUS:
Published 2016

Description:
This document details a standard procedure for enumeration and measurement of size distribution of most cell types. The instrumentation allows for user-selectable cell size settings and is appropriate for suspension as well as adherent cell cultures. This method works best for spherical cells and may be less accurate if cells are not spherical (e.g., discoid cells, budding yeast).

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2150-19: Standard Guide for Characterization and Testing of Biomaterial Scaffolds Used in Regenerative Medicine and Tissue-Engineered Medical Products

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2013; updated 2019

Description:
This document is a resource of currently available test methods for the characterization of the compositional and structural aspects of biomaterial scaffolds used to develop and manufacture tissue-engineered medical products (TEMPs). This guide addresses natural, synthetic, or combination scaffold materials with or without bioactive agents or biological activity.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2210-02: Standard Guide for Processing Cells, Tissues, and Organs for Use in Tissue Engineered Medical Products

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2010; withdrawn 2015

Description:
This document describes the processing, characterization, production, and quality assurance of cells, tissues, and organs used for tissue-engineered medical products (TEMPs). It concerns aspects of processing activities for cells, tissues, and organs, including: 1) cell, tissue, and organ processing (i.e., facilities, reagents, and procedures for receipt, inspection, and storage; tissue culture components, biological risk factors; and processing area); 2) human and nonhuman donor screening; and 3) cell, tissue, and organ characterization.

This document was withdrawn without replacement due to its limited use by industry.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2211-13: Standard Classification for Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2013

Description:
This classification outlines key aspects of TEMPs and their individual components. The categories outlined in this classification are intended to list, identify, and group the areas pertinent to TEMPs to help subcommittees for the organization of the development of tissue engineering standards. The classification outlines the aspects of TEMPS that will be developed as standards.

This classification excludes traditional transplantation of organs and tissues as well as transplantation of living cells alone as cellular therapies. The classification does not apply to any medical products of human origin regulated by FDA under 21 CFR Parts 16 and 1270 and 21 CFR Parts 207, 807, and 1271. The standard does not address specific components covered in other standards. Any safety areas associated with the medical product's use are not addressed in the standard.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2212-19: Standard Guide for Characterization of Type I Collagen as Starting Material for Surgical Implants and Substrates for Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2011; updated 2019

Description:
This document provides guidance in the characterization of type I collagen as a starting material for surgical implants and substrates for TEMPs. This document contains a list of physical and chemical parameters that are directly related to the function of collagen. This document can aid in the selection and characterization of the appropriate collagen starting material for a specific use.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2259-10: e1 Standard Test Method for Determining the Chemical Composition and Sequence in Alginate by Proton Nuclear Magnetic Resonance (1H NMR) Spectroscopy

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2012

Description:
This document denotes a test method using high-resolution proton nuclear magnetic resonance (1H NMR) to determine the composition and monomer sequence of alginate intended for use in biomedical and pharmaceutical applications as well as in tissue-engineered medical products (TEMPs). This document will assist end users in choosing the correct alginate for their particular application. Knowledge of alginate parameters is necessary to understand the functionality of alginate in TEMP formulations and applications.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2260-18: e1 Standard Test Method for Determining Degree of Deacetylation in Chitosan Salts by Proton Nuclear Magnetic Resonance (1H NMR) Spectroscopy

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2012; updated 2018

Description:

This document denotes a simple, rapid test method using high-resolution proton nuclear magnetic resonance (1H NMR) to determine the degree of deacetylation (DA) in chitosan and chitosan salts intended for use in biomedical and pharmaceutical applications as well as in tissue-engineered medical products (TEMPs). The method is applicable for determining the degree of DA (percent DA) of chitosan chloride and chitosan glutamate salts and is valid for percent DA values from 50 up to and including 99. Knowledge of the degree of DA is important for an understanding of the functionality of chitosan salts in TEMP formulations and applications.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2312-11: Standard Terminology Relating to Tissue Engineered Medical Products

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2011

Description:

This terminology defines basic terms and presents the relationships of the scientific fields related to Tissue Engineered Medical Products (TEMPs). Committee F04 has defined these terms for the specific purpose of unifying the language used in standards for TEMPs.

A revision of this standard is in progress (ASTM WK71984).

How to Access this Standard:

ASTM F2312-11 is available for purchase from ASTM. ASTM WK71984 is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ASTM F2315-18: Standard Guide for Immobilization or Encapsulation of Living Cells or Tissue in Alginate Gels

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2011; updated 2018

Description:
This document presents information on the immobilization or encapsulation of living cells or tissue in alginate gels. Immobilized or encapsulated cells are suitable for use in biomedical and pharmaceutical applications, including, but not limited to, tissue-engineered medical products (TEMPs). This document addresses key parameters for successful immobilization and encapsulation in alginate gels.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2347-15: Standard Guide for Characterization and Testing of Hyaluronan as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2015

Description:
This document lists characterization parameters directly related to the functionality of hyaluronan. This document can aid in the selection and characterization of the appropriate hyaluronan for a particular application and is intended to provide guidance on the methods and types of testing necessary to properly characterize, assess, and ensure consistency in the performance of a particular hyaluronan.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2383-11: Standard Guide for Assessment of Adventitious Agents in Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2011; withdrawn 2020

Description:
This guide is intended as a resource for individuals and organizations involved in the production, delivery, and regulation of TEMPs. Safety from contamination by potentially infectious adventitious agents is important in the development of all TEMPs as well as their components. This guide addresses how to assess safety risks associated with adventitious agents and their byproducts.

This standard was withdrawn in 2020.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ASTM F2386-04: Standard Guide for Preservation of Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2004; withdrawn 2013

Description:
This guide covers the development of standards related to the preservation of cells, tissues, and TEMPs. Preservation techniques include freezing, vitrification, and hypothermic preservation. This guide discusses preservation, including issues of pre-preservation processing, the process of preservation, storage, transport, recovery, post-preservation processing, quality assurance, and process control.

This standard was withdrawn in 2013.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2450-18: Standard Guide for Assessing Microstructure of Polymeric Scaffolds for Use in Tissue Engineered Medical Products

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2010; updated 2018

Description:
This document provides an overview of test methods for obtaining information on the dimensions of pores, the pore size distribution, the degree of porosity, interconnectivity, and measures of permeability for porous materials used as polymeric scaffolds in the development and manufacture of tissue-engineered medical products (TEMPs). This information is key to optimizing the structure for a particular application, developing robust manufacturing routes, and providing reliable quality control data.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2451-05: Standard Guide for in vivo Assessment of Implantable Devices Intended to Repair or Regenerate Articular Cartilage

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2010; withdrawn 2019

Description:

This document provides general guidelines for the *in vivo* assessment of implantable devices intended to repair or regenerate articular cartilage. Devices included in this guide may be composed of natural or synthetic biomaterials (biocompatible and biodegradable) or composites thereof and may contain cells or biologically active agents such as growth factors, synthetic peptides, plasmids, or complementary DNA (cDNA). The document includes a description and rationale for use of animal models.

This guide was withdrawn in January 2019 in accordance with section 10.6.3 of the Regulations Governing ASTM Technical Committees, which requires that standards shall be updated by the end of the eighth year since the last approval date.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ✓ Preclinical studies
- ○ Clinical trials

ASTM F2529-13: Standard Guide for in vivo Evaluation of Osteoinductive Potential for Materials Containing Demineralized Bone (DBM)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2013

Description:

This document covers animal implantation methods and analysis of the explanted DBM-containing material to determine whether a material or substance possesses osteoinductive potential, as defined by its ability to cause bone to form *in vivo* at a site that would otherwise not support bone formation (e.g., heterotopically in a skeletal muscle implant site). This document applies to products that may be composed of one or more of the following components: natural biomaterials (such as demineralized bone), and synthetic biomaterials (such as calcium sulfate, glycerol, and reverse phase polymeric compounds) that act as additives, fillers, and/or excipients (radioprotective agents, preservatives, and/or handling agents) to make the demineralized bone easier to manipulate.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2602-18: Standard Test Method for Determining the Molar Mass of Chitosan and Chitosan Salts by Size Exclusion Chromatography with Multi-angle Light Scattering Detection (SEC-MALS)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2013; updated 2018

Description:
This document covers the determination of the molar mass of chitosan and chitosan salts intended for use in biomedical and pharmaceutical applications as well as in tissue-engineered medical products (TEMPs) by size exclusion chromatography with multi-angle light scattering detection (SEC-MALS). This document will assist end users in choosing the correct chitosan for their particular application. Chitosan may have utility as a scaffold or matrix material for TEMPs, in cell and tissue encapsulation applications, and in drug delivery formulations.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2603-06: Standard Guide for Interpreting Images of Polymeric Tissue Scaffolds

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2012; updated 2020

Description:
This document covers the factors that need to be considered when obtaining and interpreting images of tissue scaffolds, including technique selection, instrument resolution and image quality, quantification, and sample preparation. The information in this document is intended to be applicable to porous polymer-based tissue scaffolds, including naturally derived materials such as collagen. However, some materials (both synthetic and natural) may require unique or varied sample preparation methods that are not specifically covered in this guide.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2605-16: Standard Test Method for Determining the Molar Mass of Sodium Alginate by Size Exclusion Chromatography with Multi-angle Light Scattering Detection (SEC-MALS)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2016

Description:
This document provides a standard method for using size exclusion chromatography with multi-angle light scattering detection (SEC-MALS) to determine the molar mass (typically expressed as grams/mole) of sodium alginate intended for use in biomedical and pharmaceutical applications as well as in tissue-engineered medical products (TEMPs). This document will assist end users in choosing the correct alginate for their particular application. Alginate may have utility as a scaffold or matrix material for TEMPs, in cell and tissue encapsulation applications, and in drug delivery formulations.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F2664-19e1: Standard Guide for Assessing the Attachment of Cells to Biomaterial Surfaces by Physical Methods

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2011; updated 2019

Description:
This document describes protocols that can be used to measure the strength of the adhesive bond that develops between a cell and a surface as well as the force required to detach cells that have adhered to a substrate. Controlling the interactions of mammalian cells with surfaces is fundamental to the development of safe and effective medical products. The information generated by these methods can be used to obtain quantitative measures of the susceptibility of surfaces to cell attachment as well as measures of the adhesion of cells to a surface. This document also highlights the importance of cell culture history and influences of cell type.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2721-09: Standard Guide for Pre-clinical in vivo Evaluation in Critical Size Segmental Bone Defects

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2014

Description:
This document covers general guidelines for the *in vivo* assessment of tissue-engineered medical products (TEMPs) intended to repair or regenerate bone. TEMPs included in this guide may be composed of natural or synthetic biomaterials (biocompatible and biodegradable) or composites thereof, and may contain cells or biologically active agents such as growth factors, synthetic peptides, plasmids, or complementary DNA (cDNA). The document includes a description and rationale for use of animal models, including species such as rat (murine), rabbit (leporine), dog (canine), goat (caprine), and sheep (ovine). The standard also briefly describes outcome measures based on histologic, radiographic, and mechanical analyses.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Logistics and compliance criteria
- ✓ Preclinical studies
- ○ Clinical trials

ASTM F2739-19: Standard Guide for Quantifying Cell Viability within Biomaterial Scaffolds

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2016; updated 2019

Description:
This document is a resource of cell viability test methods that can be used to assess the number and distribution of viable and non-viable cells within porous and non-porous, hard or soft biomaterial scaffolds, such as those used in tissue-engineered medical products (TEMPs). In addition to providing a compendium of available techniques, this document describes materials-specific interactions with the cell assays that can interfere with accurate cell viability analysis and includes guidance on how to avoid and/or account for scaffold material/cell viability assay interactions.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ASTM F2791-15: Standard Guide for Assessment of Surface Texture of Non-Porous Biomaterials in Two Dimensions

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2015

Description:
This document describes some of the more common methods that are available for measuring the topographical features of a surface and provides an overview of the parameters that are used to quantify them. Being able to reliably derive a set of parameters that describe the texture of biomaterial surfaces is a key aspect in the manufacture of safe and effective implantable medical devices that have the potential to trigger an adverse biological reaction in situ.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Preclinical studies
- ○ Clinical trials

ASTM F2883-11: Standard Guide for Characterization of Ceramic and Mineral Based Scaffolds used for Tissue-Engineered Medical Products (TEMPs) and as Devices for Surgical Implant Applications

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2011; withdrawn 2020

Description:
This document covers the chemical, physical, biological, and mechanical characterization requirements for biocompatible mineral- and ceramic-based scaffolds used solely as a device or to manufacture TEMPs. This document may be used as guidance in the selection of test methods for the comprehensive characterization of raw materials, granules, or pre-shaped blocks, or as an original equipment manufacturer (OEM) specification. This document may also be used to characterize the scaffold component of a finished medical product.

This standard was withdrawn in 2020.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2884-12: Standard Guide for Pre-clinical in vivo Evaluation of Spinal Fusion

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2012

Description:

This document covers general guidelines for the preclinical *in vivo* assessment of tissue-engineered medical products (TEMPs) intended to repair or regenerate bone in an interbody and/or posterolateral spinal environment. TEMPs included in this guide may be composed of, but are not limited to, natural or synthetic biomaterials or composites thereof, and may contain cells or biologically active agents such as growth factors, synthetic peptides, plasmids, or complementary DNA (cDNA). Guidelines include a description of and rationale for various animal models for the *in vivo* assessment of the TEMP.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F2900-11: Standard Guide for Characterization of Hydrogels used in Regenerative Medicine

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2011; withdrawn 2020

Description:
This document provides an overview of test methods suitable for characterizing hydrogels used in regenerative medicine as matrix substitutes, delivery vehicles for drugs and/or biologics, and environments for cell culture. Specifically, this guide describes methods to assess hydrogel biological properties, kinetics of formation, degradation and agent release, physical and chemical stability, and mass transport capabilities.

This standard was withdrawn in 2020.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2903-11: Standard Guide for Tissue Engineered Medical Products (TEMPs) for Reinforcement of Tendon and Ligament Surgical Repair

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2011; withdrawn 2020

Description:
This document is intended as a resource for individuals and organizations involved in the development, production, and delivery of TEMPs intended to provide a mechanical (functional) reinforcement of the surgical repair of tendons and ligaments.

This standard was withdrawn in 2020.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Logistics and compliance criteria
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- ○ Clinical trials

ASTM F2944-20: Standard Practice for Automated Colony Forming Unit (CFU) Assays—Image Acquisition and Analysis Method for Enumerating and Characterizing Cells and Colonies in Culture

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	Published 2012; updated 2020

Description:
This document describes a procedure for quantitative measurement of the number and biological characteristics of colonies derived from a stem cell or progenitor population using image analysis. This document applies to *in vitro* laboratory settings and utilizes (a) standardized protocols for image capture of cells and colonies derived from *in vitro* processing of a defined population of starting cells in a defined field of view (FOV), and (b) standardized protocols for image processing and analysis.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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ASTM F2952-14: Standard Guide for Determining the Mean Darcy Permeability Coefficient for a Porous Tissue Scaffold

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2014

Description:
This document describes test methods suitable for determining the mean Darcy permeability coefficient for a porous tissue scaffold, which is a measure of the rate at which a fluid, typically air or water, flows through it in response to an applied pressure gradient. This information can be used to optimize the structure of tissue scaffolds and develop a consistent manufacturing process and can also be used for quality assurance purposes.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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ASTM F2997-13: Standard Practice for Quantification of Calcium Deposits in Osteogenic Culture of Progenitor Cells Using Fluorescent Image Analysis

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2013

Description:
This document defines an estimation method for calcium content at multiple time points in living cell cultures that have been cultured under conditions known to promote mineralization. The practice involves applying a fluorescent calcium chelating dye that binds to the calcium phosphate mineral crystals present in the live cultures, followed by image analysis of fluorescence microscopy images of the stained cell cultures. Calcium deposition in a secreted matrix is one of several features that characterize bone formation (*in vitro* and *in vivo*) and is therefore a parameter that may indicate bone formation and osteoblast function (i.e., osteoblastic differentiation).

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F2998-14: Guide for Using Fluorescence Microscopy to Quantify the Spread Area of Fixed Cells

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2014

Description:
This document describes several measurement and technical issues involved in quantifying the spread area of fixed cells and is meant to serve as a guide for developing methods to reliably measure the area to which cells spread at a surface. Cell spreading and the distribution of cell spread areas of a population of cells are the result of a biological response dependent on intracellular signaling mechanisms and the characteristics of cell adhesion to a surface.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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ASTM F3088-14: Standard Test Method for Use of a Centrifugation Method to Quantify/Study Cell-Material Adhesive Interactions

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2014

Description:
This document describes a centrifugation cell adhesion assay that can be used to detect changes in adhesive characteristics of cells with passage or treatments. This approach measures the force required to detach cells from a substrate. The cells may include adult, progenitor, or stem cells from any species, and the types of cells may include chondrocytes, fibroblasts, osteoblast, islet cells, or other relevant adherent cell types.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Preclinical studies
- ○ Clinical trials

ASTM F3089-14: Standard Guide for Characterization and Standardization of Polymerizable Collagen-Based Products and Associated Collagen-Cell Interactions

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2014

Description:

This document provides guidance in the production, characterization, testing, and standardization of: (a) collagen polymers as a starting material for surgical implants, substrates for tissue-engineered medical products (TEMPs), vehicles for therapeutic cells and molecules, and 3D *in vitro* tissue systems for basic research, drug development, and toxicity testing; and (b) self-assembled collagen-based materials produced with collagen polymer formulations. This document can aid in the selection, characterization, and standardization of the appropriate collagen polymer starting material as well as associated self-assembled collagen-based products for a specific use. Not all tests or parameters are applicable to all uses of collagen.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F3106-14: Standard Guide for in vitro Osteoblast Differentiation Assays

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Published 2014

Description:
This document describes the components and conditions used for *in vitro* osteoblast differentiation assays used to screen for the osteogenic capability of progenitor stem cells from various human or animal sources. These sources include mixed tissue-derived connective tissue progenitor populations and cell populations that may be selectively isolated or manipulated through culture expansion, processing, transfection, or genetic modification.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Preclinical studies
- ○ Clinical trials

ASTM F3142-16: Standard Guide for Evaluation of in vitro Release of Biomolecules from Biomaterials Scaffolds for TEMPs

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2016

Description:

The European Pharmacopoeia (Ph. Eur.) and the United States Pharmacopeia (USP) describe several dissolution and drug release setups for tablets, capsules, transdermal patches, and suppositories (USP <711>, USP <724>, Ph. Eur. 2.9.3, Ph. Eur. 2.9.4). However, previously no pharmacopoeia-standardized *in vitro* release test has been established for parenteral dosage forms providing sustained drug release (e.g., implants). An appropriately designed *in vitro* release test would be favorable in the early stage of development of biomolecule-releasing scaffolds for tissue-engineered medical products (TEMPs), as well as in quality control, and may help to reduce the number of animal experiments.

This standard provides a tabulated overview of published *in vitro* release studies performed with biomaterial scaffolds loaded with biomolecules. It describes general principles of developing and/or using an *in vitro* assay to evaluate biomolecule release from biomaterials scaffolds for TEMPs, with examples from the literature. The guide will address scaffolds that do not contain seeded cells; general principles may still apply but may need to be modified if cells are part of the TEMPs.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Preclinical studies
- ○ Clinical trials

ASTM F3163-16: Standard Guide for Classification of Cellular and/or Tissue-Based Products (CTPs) for Skin Wounds

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2016

Description:
This guide defines terminology for description of CTPs for skin wounds. CTPs are defined primarily by their composition and comprise cells and/or the extracellular components of tissue. CTPs may contain cells (viable or nonviable), tissues, proteins, and other materials for which there is a rationale for benefit beyond that achievable with conventional wound coverings. CTPs may additionally include synthetic components.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Clinical trials

ASTM F3206-17: Standard Guide for Assessing Medical Device Cytocompatibility with Delivered Cellular Therapies

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	Published 2017

Description:
This document is designed to assist medical device manufacturers as they develop new devices or qualify existing devices (e.g., catheters, needles) for delivering clinical cell therapies. This document outlines the parameters to consider when designing *in vitro* tests to assess the potential impact of a delivery device on a cellular product being dispensed. This document does not provide specific protocols, but rather suggests what should be considered the minimum characterization necessary to assess device cytocompatibility. Topics discussed include selecting an appropriate cell line(s), cell physiology parameters to measure, and relevant test procedure variables. Only cells suspended in liquid and infused through a device are considered.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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ASTM F3207-17: Standard Guide for in vivo Evaluation of Rabbit Lumbar Intertransverse Process Spinal Fusion Model

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2017

Description:

This document covers general guidelines to evaluate the effectiveness of products intended to cause and/or promote bone formation in the lumbar intertransverse process spinal fusion model *in vivo*. The primary purpose of this document is to facilitate the equitable comparison of bone void fillers and/or autograft extender products *in vivo*. This document is applicable to products that may be composed of natural biomaterials (such as demineralized bone) and/or synthetic biomaterials (such as calcium sulfate, glycerol, and reverse phase polymeric compounds) that act as additives, fillers, and/or excipients (radioprotective agents, preservatives, and/or handling agents).

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F3209-16: Standard Guide for Autologous Platelet-Rich Plasma for Use in Tissue Engineering and Cell Therapy

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2016

Description:
This document defines terminology and identifies key fundamental properties of autologous platelet-rich plasma (PRP) and PRP-derived platelet gels intended to be used for tissue-engineered medical products (TEMPs) or for cell therapy applications. This document provides a common nomenclature and basis for describing notable properties and processing parameters for PRP and platelet gels that may have utility for manufacturers, researchers, and clinicians. Further discussion is also provided on certain aspects of PRP processing techniques, characterization, and quality assurance and how those considerations may impact key properties.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F3223-17: Standard Guide for Characterization and Assessment of Tissue Engineered Medical Products (TEMPs) for Knee Meniscus Surgical Repair and/or Reconstruction

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2017

Description:
This document is intended as a resource for individuals and organizations involved in the production, delivery, and regulation of TEMPs and other tissues intended for use in the surgical repair, replacement, and/or reconstruction of the knee meniscus. Complete or near complete excision of the meniscus in a young individual is associated with an early increased risk of knee osteoarthritis due to the loss of the meniscus's chondroprotective effects. The potential of TEMPs to enhance the outcome of the surgical meniscus repair and/or reconstruction has been recognized.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F3224-17: Standard Test Method for Evaluating Growth of Engineered Cartilage Tissue Using Magnetic Resonance Imaging

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2017

Description:

In tissue-engineered cartilage, it is expected that the cells will differentiate towards chondrogenic lineage and produce an ample amount of cartilage extracellular matrix proteins, proteoglycans, and collagen type-II. Traditional testing methods such as histological staining, mechanical testing, and quantitative Polymerase Chain Reaction (qPCR) are invasive, destructive, and cannot be performed *in vivo* after the transplantation of engineered tissue as a regenerative treatment. It is important to evaluate whether the implanted tissue regenerates as an articular cartilage over time. Magnetic resonance imaging (MRI) is utilized for post-operative monitoring and assessment of cartilage regeneration in clinics. Therefore, it is important to evaluate tissue-engineered cartilage using MRI at the preclinical stage as well.

This standard is intended as a standard test method for engineered cartilage tissue growth evaluation using MRI. It is intended for use in the development of tissue engineering regenerative medical products for cartilage damages, such as in knee, hip, or shoulder joints. The standard has been prepared for evaluation of engineered cartilage tissue growth at the preclinical stage and summarizes results from tissue growth evaluation of tissue-engineered cartilage in a few notable cases using water spin-spin relaxation time, T2, *in vitro*, and *in vivo* in small animal models. It uses the change in mean T2 values as a function of growth time to evaluate the tissue growth of engineered cartilage. It also provides a method to remove the scaffold contribution to the tissue growth evaluation.

Information in this standard is applicable to most porous natural and synthetic polymers used as a scaffold in engineered cartilage, such as alginate, agarose, collagen, chitosan, and poly-lactic-co-glycolic acid (PLGA). However, some materials (both synthetic and natural) may require unique or varied methods of MRI evaluation that are not covered in this test method.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F3225-17: Standard Guide for Characterization and Assessment of Vascular Graft Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2017

Description:

Rerouting blood flow around diseased vascular regions is a common therapy to mitigate the pathological effects of blood vessel occlusion or aneurysm-related vascular wall weakening. Autologous and non-autologous grafts are often used surgically as vascular substitutes to achieve this therapeutic intervention. Vascular graft TEMPs may also be used for these purposes. They may also be used to create or revise arteriovenous shunts.

This guide is intended as a resource for individuals and organizations involved in the development, production, delivery, and regulation of TEMPs intended for use in the surgical repair, replacement, shunting and/or bypass of blood vessels. This guide is intended for use related to the *in vitro* assessment of TEMP vascular grafts. *In vitro* cellular characterization and *in vivo* testing are not within scope for this standard guide.

How to Access this Standard:

Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F3259-17: Standard Guide for Micro-computed Tomography of Tissue Engineered Scaffolds

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2017

Description:
This guide is a resource for conducting micro-computed tomography (microCT) imaging and analysis of porous scaffolds for tissue engineering applications. It provides considerations for sample preparation, image acquisition parameter selection, post-processing, and data interpretation.

The information in this guide applies to products that include a porous scaffold component and are designed for tissue engineering repair strategies. The scaffolds may be fabricated from synthetic polymers (e.g., absorbable polyesters) or natural materials (e.g., calcium phosphates), mammalian or human derived materials (e.g., demineralized bone) or combinations of these. While some considerations are provided for imaging of materials that are of moderate to high radiodensity, specific guidelines are not provided for imaging metallic scaffolds.

Applicability of the guidelines will depend on scaffold material type and the user's application (e.g., experimental design, as manufactured characterization) as appropriate.

The guidelines for microCT are most suitable for specimen scanning *in vitro*. Specific guidelines relevant to direct *in vivo* imaging of scaffolds are not included because the imaging parameters will be dependent on the implantation site, animal size, breathing, etc.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

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- ○ Clinical trials

ASTM F3294-18: Standard Guide for Performing Quantitative Fluorescence Intensity Measurements in Cell-based Assays with Widefield Epifluorescence Microscopy

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2018

Description:

Relative intensity measurements made by widefield epifluorescence microscopy are used as part of cell-based assays to quantify attributes such as the abundance of probe molecules (see ASTM F2997), fluorescently labeled antibodies, or fluorescence protein reporter molecules. The general procedure for quantifying relative intensities is to acquire digital images, then to perform image analysis to segment objects and compute intensities. The raw digital images acquired by epifluorescence microscopy are not typically amenable to relative intensity quantification. This guide offers a checklist of potential sources of bias that are often present in fluorescent microscopy images and suggests approaches for storing and normalizing raw image data to assure that computations are unbiased.

Widefield fluorescence microscopy is frequently used to measure the location and abundance of fluorescent probe molecules within or between cells. In instances where Random Illumination Microscopy (RIM) comparisons are made between a region of interest (ROI) and another ROI, accurate normalization procedures are essential to the measurement process to minimize biased results. Example use cases where this guidance document may be applicable include:

- Characterization of cell cycle distribution by quantifying the abundance of DNA in individual cells
- Measuring the area of positively stained mineralized deposits in cell cultures (ASTM F2997)
- Quantifying the spread area of fixed cells (ASTM F2998)
- Determining DNA damage in eukaryotic cells using the comet assay (ASTM E2186)
- The quantitation of a secondary fluorescent marker that provides information related to the genotype, phenotype, biological activity, or biochemical features of a colony or cell (ASTM F2944)

This guidance document was developed to facilitate the collection of microscopy images with an epifluorescence microscope allowing quantitative fluorescence measurements to be extracted from the images. The document is tailored to cell biologists who often use fluorescent staining techniques to visualize components of a cell-based experimental system. Quantitative comparison of the intensity data available in these images is only possible if the images are quantitative based on sound experimental design and appropriate operation of the digital array detector, such as a charge coupled device (CCD) or a scientific complementary metal oxide semiconductor (sCMOS) or similar camera. The document considers issues involving the array detector and controller software settings, including collection of dark count images to estimate the offset, flat-field correction, background correction, benchmarking of the excitation lamp, and the fluorescent collection optics.

This document was developed around epifluorescence microscopy but may also be applicable to quantitative imaging in other fluorescence microscopy systems such as fluorescence confocal microscopy. This guide was developed around single-color fluorescence microscopy imaging or multi-color imaging where the measured fluorescence is spectrally well separated. This document also discusses metrology issues related to relative measurements and experimental designs that

may be required to ensure quantitative fluorescence measurements are comparable after changing microscope, sample, and lamp configurations.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F3354-19: Standard Guide for Evaluating Extracellular Matrix Decellularization Processes

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published 2019

Description:
This document provides guidance on the characterization and evaluation of the decellularization processes used to produce decellularized extracellular matrix (dECM) materials that will be used as medical products in direct or indirect contact with the body. This standard details recommendations for the following steps in evaluating an extracellular matrix decellularization process: selecting attributes and test methods for characterization, developing decellularization acceptance criteria for selected attributes, documenting and analyzing the decellularization process flow, and performing a characterization of the decellularization process by testing dECM materials using the selected attributes, methods, and acceptance criteria.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F3368-19: Standard Guide for Cell Potency Assays for Cell Therapy and Tissue Engineered Products

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Published 2019

Description:
This document provides guidance to those developing cell therapy and cell-containing tissue-engineered products on potency assay requirements during development of a product and as an approved product.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM F3369-19e1: Standard Guide for Assessing the Skeletal Myoblast Phenotype

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Published 2019

Description:
This document describes the stages for multipotent stem cell differentiation toward myoblasts and myotubes. The purpose of the document is to aid researchers working in the area of skeletal myogenesis. Using this document, researchers should be able to understand which skeletal muscle markers are best suited for experiments.

How to Access this Standard:
Available for purchase from ASTM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK16591: New Guide for the In Vivo Assessment of Bone Inductive Materials

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	In development; initiated September 2007

Description:

This document covers general guidelines for evaluating the effectiveness of devices intended to cause and/or promote bone formation when implanted or injected *in vivo*. This document is applicable to devices that may be composed of one or more of the following components: natural biomaterials (such as demineralized bone), synthetic biomaterials (such as calcium sulfate), cells, growth factors, cytokines, synthetic peptides, or DNA. It should not be assumed that the devices producing a positive outcome from this assessment will form bone when used in a clinical setting. The primary purpose of this document is to facilitate the equitable comparison of unique bone forming devices in heterotopic *in vivo* models of osteoconductivity/osteoinductivity/osteogenic activity.

How to Access this Standard:

This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
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- ○ Clinical trials

ASTM WK17329: New Terminology for Terminology for Cell Signaling Related to Medical and Surgical Devices

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated November 2007

Description:
This standard provides definitions of cell signaling terms to facilitate communication and understanding. These terms may be found in standards and documents prepared by Subcommittee F04.46 on Cell Signaling. This terminology document is intended for this emerging signaling field and for describing the biocompatibility and other interactions between cells and biomaterials/medical devices

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):
- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
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- ○ Clinical trials

ASTM WK51697: Testing and Characterization of Alginate Foam Scaffolds Used in Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated October 2015

Description:
This document provides information for the physical testing of alginate foam scaffolds such as mechanical properties, hydration properties, pore structure, and scaffold degradation. In addition, it outlines issues related to biological properties such as elemental impurities, bacterial bioburden, bacterial endotoxins, sterility, and biocompatibility.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):
- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK52257: Characterization and Assessment of Heart Valve Tissue Engineered Medical Products (TEMPs)

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated November 2015

Description:
This document is intended as a resource for individuals and organizations involved in the development, production, delivery, and regulation of TEMPs intended for use in the surgical repair and/or replacement of heart valves. This document is intended for use related to the *in vitro* assessment of TEMP heart valves.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK55364: Quantifying Cell Proliferation in 3D-Scaffolds by a Non-Destructive Method

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated July 2016

Description:
This document describes how to conduct a nondestructive proliferation test for mammalian cells based on metabolic activity that can be used to assess the number of viable cells within 3D-scaffolds for regenerative medicine and in tissue-engineered medical products (TEMPs). This document provides a detailed explanation of the resazurin cell metabolic activity method in terms of reagent concentrations, incubation times, cell culture media composition, calibration curve, assay linearity, and limitations of the assay, and describes factors that can interfere with accurate cell proliferation assessment.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK57514: New Guide for Evaluating Extracellular Matrix Decellularization Processes

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated January 2017

Description:

This standard provides guidance on the characterization and evaluation of the decellularization processes used to produce decellularized extracellular matrix (dECM) materials that will be used as implanted medical products. The decellularization process may be performed on tissue from human or other mammalian sources or produced *in vitro* from human or other mammalian cells. The dECM may or may not be recellularized before use. dECM material derived from non-mammalian tissue or cells and decellularized ECM material used for non-medical purposes may follow the framework provided but will require additional considerations outside the scope of this guide.

Biological tissues are composed of a structural ECM and embedded cells. The intent of a decellularization process is to disrupt or remove or both cells and cellular components from an ECM material while maintaining the material's key structural and/or compositional properties. Decellularization comprises process steps intended or expected to result or aid in the disruption of source tissue cells and/or removal of cellular content from the material undergoing decellularization. Actions that are intended to rinse or otherwise remove decellularization reagents or byproducts should also be considered in that context as part of the decellularization process. Purifications or other isolations of specific ECM components are not considered decellularization and would be outside the scope of this guide.

This guide describes relevant parameters of decellularization processes used to prepare ECM materials as medical products. The guide provides guidance on the measurement of specific and general properties of dECM. This includes both the analysis of cellular material as well as the assessment of the effects of decellularization on dECM properties such as composition, structure, and material properties. This guide does not provide guidance on the assessment of the host response subsequent to the implantation of dECM medical products. It provides guidance on determining pertinent quality attributes as well as developing and assessing targets (acceptance criteria) related to the use of decellularization in manufacturing medical products. This guide also provides recommendations on developing process parameters and associated process controls.

No consensus has been established regarding decellularization thresholds or classifications. This guide, therefore, cannot suggest targets and instead recommends commonly measured attributes to develop targets specific to the design of each unique material and its intended use.

How to Access this Standard:

This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Preclinical studies
- ○ Clinical trials

ASTM WK62115: New Test Method for Measuring Cell Viability in a Scaffold

APPLICABLE SECTOR(S):
Tissue engineering

STATUS:
In development; initiated January 2018

Description:
This standard will be a protocol for measuring cell viability in a tissue engineering scaffold. The working group will select an appropriate test system, including the assay, scaffold, and cell type. They will then select a scaffold system that can be disassembled to release the cells. This will enable comparison of assays conducted on scaffolds containing cells to results on the released cells. The working group will aim to use a higher order measurement to verify results, such as electron paramagnetic resonance, to assess partial oxygen pressure in the scaffold. The working group will assess reproducibility of the test method through an inter-laboratory test. Results of these studies will be used to support an ASTM standard test method.

The inability to adequately assess cell viability in a scaffold has been a major impediment to the tissue engineering industry's growth. Typically, metabolic assays developed for cells cultured on planar substrates, such as tissue culture polystyrene, are used to assess cells in 3D scaffolds. There are two issues with this approach. First, the scaffold may impede the diffusion of assay reactants and products into and out of the scaffold, yielding inaccurate results. Second, there are many sample handling issues that arise from seeding cells onto scaffolds or conducting assays on cells in scaffolds that affect the measurement uncertainty in unknown ways.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK63854: New Practice for Material Biocompatibility

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	In development; initiated June 2018

Description:
This standard outlines a test designed to determine the biological reactivity of mammalian cell cultures following the exposure to extracts from polymeric materials used in the manufacture and processing of cell-based therapeutics. The test is intended as a screening tool to indicate the likelihood that extractables from the test article will impact *in vitro* cell culture performance.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Preclinical studies
- ○ Clinical trials

ASTM WK64460: New Guide for Pre-Clinical Testing Considerations for Materials Used to Regenerate Muscle

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	In development; initiated August 2018

Description:
This guide will provide scientifically based information concerning muscle grafts and will present the strengths and weaknesses of animal models used to demonstrate effectiveness. Materials used to support muscle regeneration are comparatively new but are very much needed. There is not agreement on the best animal models for assessing effectiveness or whether materials that are used in one model will be successful in a different model. Users will include academic scientists and industry scientists.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
- ✓ Preclinical studies
- ○ Clinical trials

ASTM WK65476: New Guide for Characterizing Fiber-Based Constructs for Tissue Engineered Medical Products

APPLICABLE SECTOR(S):
Tissue engineering

STATUS:
In development; initiated October 2018

Description:
This guide will focus on fiber-based constructs made by methods including, but not limited to, electrospinning, forcespinning, meltspinning, pneumatospinning, and extrusion. The guide will focus on the fiber diameter range of 10 nm to 100 m. It is anticipated that the guide will provide a list of common measurements and discuss caveats, best practices, controls, reference standards if available, and reasons for doing the measurement.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK65680: New Test Methods for Printability of Bioinks and Biomaterial Inks

APPLICABLE SECTOR(S):
Tissue engineering

STATUS:
In development; initiated November 2018

Description:
This specification covers a method to evaluate printability of bioinks and biomaterial inks used in automated biofabrication technology. This specification is intended for use by manufacturers and researchers that produce bioinks and biomaterial inks to assess and compare properties of bioinks or biomaterial inks, which is important for precision manufacturing of 3D bioprinted parts. This proposed standard would provide a test method to specify printability as a means to help establish reproducibility and quality control between material lots or manufacturers.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK65681: New Guide for Bioinks and biomaterial inks used in bioprinting

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated November 2018

Description:
This document describes bioinks and biomaterial inks used in biofabrication technology to create living constructs for tissue regeneration or drug testing. This guidance document lists ranges of material compositions and properties that promote survival of living cells in bioinks. This document also describes compositions and properties of materials that can be printed without cells in parallel with bioinks to provide mechanical support or as sacrificial materials to create boundaries or porosity within the bioprinted constructs. Methods of 3D bioprinting that this standard may apply to include laser-assisted bioprinting, inkjet bioprinting/droplet bioprinting, and extrusion-based bioprinting.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ASTM WK66032: Revision of E2500-13 Standard Guide for Specification, Design, and Verification of Pharmaceutical and Biopharmaceutical Manufacturing Systems and Equipment

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated November 2018

Description:
This guide is applicable to all elements of pharmaceutical and biopharmaceutical manufacturing systems that have the potential to affect product quality and patient safety, including facility equipment, process equipment, supporting utilities, associated process monitoring and control systems, and automation systems. The standard is undergoing revision.

This is the first major revision of the popular and well received E-2500 (Risk Based Qualification). This version is updated to: Include a reference Annex 21, clarify guidance on quality assurance's (QA's) role within the process, and clarify and add detail to help distinguish that only Critical Aspects as derived from the Risk Assessment (which by definition affect Patient Safety and Product Quality) should be qualified.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
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- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK69660: New Guide for Guidance on Microbiological Quality & Prevention Strategy

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	In development; initiated August 2019

Description:
This guide will aid biomanufacturers in preparing a microbiological control strategy for a site.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
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- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK70143: New Guide for Sampling Methods of Tissue Engineered Medical Products (TEMPs) for Sterility Assurance

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated October 2019

Description:
This guide covers general guidelines for sampling methods for subsequent sterility assurance testing in biological scaffold, cell scaffold, and related TEMPs. It includes a description and rationale for the various sampling methods and conditions for sterility assurance testing. Specific rationales for sampling of final container material for sterility assurance are generally discussed.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Preclinical studies
- ○ Clinical trials

ASTM WK72274: New Test Method for Printability of Bioinks for Extrusion-based Bioprinting

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated March 2020

Description:
This standard describes procedures to evaluate printability of bioinks, including material inks without cells used during extrusion-based bioprinting. This test method is intended for use by manufacturers and researchers to assess and compare printability of bioinks, including material inks without cells that can be printed in air without requiring any support medium.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ASTM WK73220: New Guide for Standard Guide for Characterization and Testing of Mammalian Fibrinogen as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	In development; initiated June 2020

Description:
This guide covers the evaluation of fibrinogen suitable for use in biomedical or pharmaceutical applications, or both, including, but not limited to, tissue engineered medical products (TEMPs). This guide addresses key parameters relevant for functionality, characterization, and purity of fibrinogen.

How to Access this Standard:
This standard is currently in development. To comment on the draft, become an ASTM member.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

British Standards Institution (BSI)

PAS 83:2012: Developing human cells for clinical applications in the European Union and the United States of America

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2012

Description:
This document is a reference source designed to increase clarity for users on the requirements needed for exploitation of cell therapy products. The main focus of this publicly available specification (PAS) is cell-based medicinal products (CBMPs) that are regulated as advanced therapy medicinal products (ATMP) in the EU and biologics (351 HCT/P) in the United States. For completeness, aspects of minimally manipulated, homologous use products (also known as 361 HCT/P in the United States) are also covered. This PAS will help users find relevant EU and U.S. legislation, guidance documents, pharmacopeia chapters, and monographs.

How to Access this Standard:
Available for purchase from BSI.

STANDARD FUNCTIONAL AREA(S):

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- ✓ Analytical and testing methodologies
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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

PAS 84:2012: Cell therapy and regenerative medicine: Glossary

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2012

Description:
This document has been developed to encourage the use of common terms and definitions within the field of regenerative medicine. It defines the terms commonly used in the field of regenerative medicine, providing clear guidance on the meaning of terminology currently used in the UK by industry, regulators, government, and academia. It is designed to help the key stakeholders to communicate more effectively and allow the commercialization of the new technology to take place more efficiently and safely.

How to Access this Standard:
Available for purchase from BSI.

STANDARD FUNCTIONAL AREA(S):

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- ○ Preclinical studies
- ○ Clinical trials

PAS 93:2011: Characterization of human cells for clinical applications: Guide

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2011

Description:
This document is a best practice guide for organizations that use human cells as the building blocks of products for clinical applications, including regenerative products based on stem cells. The recommendations and guidance in PAS 93 will assist developers in understanding the importance of characterizing the behavior of their cells, which in turn will help them take a comprehensive approach to the quality of the cell therapy product.

How to Access this Standard:
Available for purchase from BSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Preclinical studies
- ○ Clinical trials

Clinical & Laboratory Standards Institute (CLSI)

AUTO01-A: Laboratory Automation: Specimen Container/Specimen Carrier (1st Edition)

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2000

Description:
This document provides standards for the design and manufacture of specimen containers and carriers used for collecting and processing liquid samples, such as blood and urine, for clinical testing in laboratory automation systems. Though this document is no longer being reviewed as part of CLSI's consensus process, CLSI is continuing to make the document available for its informational content because of its usefulness to a limited segment of the healthcare community.

How to Access this Standard:
Available for purchase from CLSI.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

AUTO02-A2: Laboratory Automation: Bar Codes for Specimen Container Identification; Approved Standard—Second Edition

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2006

Description:
This document provides specifications for the use of linear bar codes on specimen container tubes in the clinical laboratory and for use with laboratory automation systems. Though this document is no longer being reviewed as part of CLSI's consensus process, CLSI is continuing to make the document available for its informational content because of its usefulness to a segment of the healthcare community.

How to Access this Standard:
Available for purchase from CLSI.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

EP21: Evaluation of Total Analytical Error for Quantitative Medical Laboratory Measurement Procedures, 2nd Edition

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2016

Description:
This document provides manufacturers and end users with an understanding of concepts related to total analytical error (TAE) for quantitative measurement procedures. An experimental protocol and data analysis method are provided to estimate TAE based on a comparison of methods from experiments with patient specimens, and to assess it relative to a pre-established goal for clinical acceptability.

How to Access this Standard:
Available for purchase from CLSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

EP23-A: Laboratory Quality Control Based on Risk Management; Approved Guideline

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2011

Description:
This document provides guidance on risk management for laboratories to help them develop quality control plans tailored to the particular combination of measuring system, laboratory setting, and clinical application of the test. The document describes good laboratory practice for developing and maintaining a quality control plan for medical laboratory testing using internationally recognized risk-management principles. An individual quality control plan should be established, maintained, and modified as needed for each measuring system. The quality control plan is based on the performance required for the medical application of the test results. Risk mitigation information obtained from the manufacturer and identified by the laboratory, applicable regulatory and accreditation requirements, and the individual health care and laboratory setting are considered in the development of the quality control plan. This document is intended to guide laboratories in determining quality control procedures that are both appropriate and effective for the test being performed.
Use EP23 to help create an individualized quality control plan based on risk management.

How to Access this Standard:
Available for purchase from CLSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

LIS03-A: Standard Guide for Selection of a Clinical Laboratory Information Management System

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2003

Description:

This guide covers the selection, purchase, use, enhancement, and updating of computer technology supplied by a vendor as a complete system in the clinical laboratory. The purpose of the guide is to assist hospitals, clinics, and independent laboratories through the entire automation project in order to minimize the risks and maximize the benefits. It provides a process that may be used by the medical institution to carry out laboratory information projects in a rational and orderly manner. It also includes checklists of items to consider at each stage of planning to help guard against oversights. It includes planning and design aids to assist in carrying out the project. In addition, there is information about enhancement and updates after the system is purchased.

This guide is not concerned with digital or computer electronics used only within instrumentation. Rather, it deals with the application of information systems to a large segment of the laboratory operation, and generally is concerned with how Information and Communications Technology (ICT) can be used to enhance the interaction of the laboratory with the rest of the institution, improve workflow in the laboratory, and help keep records. Such systems will normally include segments for patient biographical information, test ordering, specimen collection, workstations, worklists, test result entry, result verification, patient result reporting, management reports, archiving, and other special functions.

How to Access this Standard:

Available for purchase from ANSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

MM09-A2: Nucleic Acid Sequencing Methods in Diagnostic Laboratory Medicine; Approved Guideline—Second Edition

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2014

Description:
This document addresses diagnostic sequencing using both automated capillary-based sequencers and massively parallel sequencing instruments. Topics include specimen collection and handling; isolation and extraction of nucleic acid; template preparation; sequence generation, alignment, and assembly; validation and verification; ongoing quality assurance; and reporting results.

How to Access this Standard:
Available for purchase from CLSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

MM19-A: Establishing Molecular Testing in Clinical Laboratory Environments (1st Edition)

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2011

Description:
This document provides comprehensive guidance for planning and implementation of molecular diagnostic testing, including strategic planning, regulatory requirements, implementation, quality management, and special considerations for the subspecialties of molecular genetics, infectious diseases, oncology, and pharmacogenetics. Though this document is no longer being reviewed as part of CLSI's consensus process, CLSI is continuing to make the document available for its informational content because of its usefulness to a segment of the healthcare community.

How to Access this Standard:
Available for purchase from CLSI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EuroFlow Consortium

N/A: EuroFlow standardization of flow cytometer instrument settings and immunophenotyping protocols

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2012

Description:
The EU-supported EuroFlow Consortium aimed at innovation and standardization of immunophenotyping for diagnosis and classification of hematological malignancies by introducing 8-color flow cytometry with fully standardized laboratory procedures and antibody panels in order to achieve maximally comparable results among different laboratories. This required the selection of optimal combinations of compatible fluorochromes and the design and evaluation of adequate standard operating procedures (SOPs) for instrument setup, fluorescence compensation and sample preparation. Additionally, the consortium developed software tools for the evaluation of individual antibody reagents and antibody panels.

How to Access this Standard:
Free access available from The National Center for Biotechnology Information (NCBI).

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

European Directorate for the Quality of Medicines and Healthcare (EDQM)

N/A: Guidelines on the quality and safety of tissues and cells for human application (4th Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2017; updated 2019

Description:
These documents ensure the quality and safety of tissues and cells for human application, whether for transplantation or clinical use (including insemination and fertilization). The information in it will support professionals involved in identifying potential donors, transplant coordinators managing the process of donation after death, bone marrow and cord blood collection centers, tissue establishments processing and storing tissues and cells, testing laboratories, fertility clinics, organizations responsible for human application, inspectors auditing the establishments, and Health Authorities responsible for tissues and cells for human application.

How to Access this Standard:
Available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

EP 2.6.27: Microbiological examination of cell-based preparations

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2017

Description:
This general chapter addresses sterility testing for cell-based preparations for which it is not possible to use traditional sterility following the recommended methodology of Chapter 2.6.1: Sterility, for reasons related to the sample's shelf life, size, or composition. The chapter provides risk-analysis procedures and rationale for choosing alternate test methods.

How to Access this Standard:
The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EP 2.6.34: Host-cell protein assays

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2017

Description:
This general chapter provides guidance for the development and validation of assays used to test products obtained by recombinant DNA technology for acceptable levels of residual host-cell proteins. It provides assay selection criteria and validation methods to determine assay accuracy, specificity, precision, range, and robustness; quantitation and detection limits; and linearity.

How to Access this Standard:
The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EP 2.6.35: Quantification and characterisation of residual host-cell DNA

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2019

Description:

This general chapter provides analytical methods for quantifying residual host-cell DNA in biological products produced in cell substrates, including characterization of size. The document can be used in the development of gene therapy and cell therapy products. Analytical methods for residual DNA quantification and size characterization in biologicals produced in cell substrates are critical for product safety and efficacy. This guidance is intended to aid in regulatory approval of these products.

This chapter focuses on the most widely used techniques: quantitative Polymerase Chain Reaction (qPCR) and the Threshold method. It does not exclude the use of alternative approaches that are acceptable to the competent authority.

How to Access this Standard:

The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EP 2.7.23: Numeration of CD34/CD45+ cells in haematopoietic products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published

Description:
This general chapter provides methods for enumerating cells possessing the CD34 and CD45 antigens on their surface as a measure of the presence of hematopoietic stem/progenitor cells in a product sample. Quantification of peripheral blood CD34+ progenitor cells is a strong predictor of effectiveness to guide stem cell harvesting and is often used in cell and gene therapy production. This chapter is indented for manufacturers of cell and gene therapy products. This guidance is intended to aid in regulatory approval of these products.

How to Access this Standard:
The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EP 2.7.28: Colony-forming cell assay for human haematopoietic progenitor cells

APPLICABLE SECTOR(S):
Cell therapy

STATUS:
Published

Description:
This general chapter provides a method for studying the proliferation and differentiation patterns of hematopoietic stem/progenitor cells through their ability to form colonies in a semisolid medium. Hematopoietic stem cells (HSCs) present in small numbers in adult bone marrow (BM), peripheral blood (PB), and umbilical cord blood (CB) produce a heterogeneous pool of progenitors that can be detected *in vitro* using colony forming cell (CFC) assays. This chapter is intended for manufacturers of cell and gene therapy products. The guidance is intended to aid in regulatory approval of these products. It describes protocols for the detection and enumeration of myeloid multipotential progenitors and committed progenitors of the erythroid, monocyte, and granulocyte lineages.

How to Access this Standard:
The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EP 2.7.29: Nucleated cell count and viability

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published

Description:
This general chapter addresses methods for obtaining a total nucleated cell count and assessing the viability of the cells in a sample to determine cell dose/concentration. Many labs processing samples for allogeneic transplantation rely on the traditional methods of staining with Trypan Blue and manually counting cells on a hemacytometer. Alternatively, 7-AAD fluorescence is characterized flow cytometrically to determine cell concentration and viability. As these factors are critical for cell and gene therapy product manufacturing, standardization of these assays helps to ensure product quality. This chapter is intended for manufacturers of cell and gene therapy products. This guidance is intended to aid in regulatory approval of these products.

How to Access this Standard:
The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

EP 5.2.12: Raw materials of biological origin for the production of cell-based and gene therapy medicinal products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published 2017

Description:
This general chapter provides a framework for assuring the quality and safety of raw materials (e.g., cells, proteins, vectors) used in the production of cell and gene therapy products. It identifies critical quality attributes of raw materials of biological origin and provides criteria for risk assessment and selection of appropriate assays.

How to Access this Standard:
The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

EP 5.14: Gene transfer medicinal products for human use

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2008

Description:

This general chapter offers best practices for the development and quality control of gene therapy products. It is intended for manufacturers of cell and gene therapy products and is intended to aid in regulatory approval of these products. The objective of this guideline is to provide recommendations on the quality, non-clinical, and clinical studies that should be performed in order to obtain marketing authorization of a live recombinant viral vectored vaccine intended for use in humans. This guideline is intended for products entering the marketing authorization procedure. However, the principles laid down in the guideline should also be considered by applicants entering into clinical trials. Live recombinant vectored vaccines are live viruses (the vector) that express a heterologous antigen(s). A live recombinant vectored vaccine may also have been genetically modified for other reasons (e.g., attenuation).

How to Access this Standard:

The complete European Pharmacopoeia is available for purchase from EDQM.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

European Federation for Immunogenetics (EFI)

N/A: Standards for Histocompatibility & Immunogenics Testing, version 8.0

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2019

Description:
These Standards establish minimal criteria for accurate and dependable histocompatibility testing consistent with the current state of technological procedures and reagent availability, which all histocompatibility laboratories must meet if their services are to be considered acceptable. The standards include personnel qualifications, quality assurance testing methods, accessibility to different facilities, preanalytical sampling, external proficiency testing, and reagents, among other topics.

How to Access this Standard:
Free access available from EFI.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

Foundation for the Accreditation of Cellular Therapy (FACT)

N/A: FACT Common Standards for Cellular Therapies (Second Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2019

Description:
These standards represent basic principles of quality in cellular therapy that can be applied to any cell source or therapeutic application and are intended to be used throughout product development and clinical trials. In early stage product development and early phase clinical trials, these standards provide the quality management infrastructure to facilitate patient and data accrual to advance the therapy. Ideally, disease, discipline, or product-specific standards will be added in the future through collaboration with experts in those specialties where clinical teams and products are ready for additional standardization and voluntary accreditation.

How to Access this Standard:
Free access available from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: FACT Standards for Immune Effector Cells (First Edition, Version 1.1)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published 2018

Description:
The objective of these Standards is to promote quality practice in immune effector cell therapy. These Standards apply to immune effector cells used to modulate an immune response for therapeutic intent, such as dendritic cells, natural killer cells, T cells, and B cells. This includes, but is not limited to, genetically engineered chimeric antigen receptor T cells (CAR-T cells) and therapeutic vaccines.

How to Access this Standard:
Free access available from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: FACT Immune Effector Cells Accreditation Manual (First Edition, Version 1.1)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published 2018

Description:
This manual accompanies the FACT Standards for Immune Effector Cells, First Edition. While this manual is not a standard, it provides supplemental guidance to applicants for accreditation and to on-site inspectors, explaining the intent and rationale for specific standards and offering explanations, examples, and alternative approaches helpful in the accreditation process.

How to Access this Standard:
Free access available from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: FACT Quality Handbook (Second Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2015

Description:
This handbook provides practical advice and examples from quality experts in the cellular therapy and cord blood bank communities. While this handbook is not a standard, it supplements existing standards with fundamental information about quality systems, with chapters on document control elements, outcome analysis, and validation and verification of critical procedures.

How to Access this Standard:
Available for purchase from FACT.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

N/A: FACT-JACIE International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, & Administration (Seventh Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published 2018

Description:
These documents are designed to provide minimum guidelines for programs, facilities, and individuals performing hematopoietic cell transplantation and therapy or providing support services for such procedures. These documents apply to hematopoietic progenitor cells (HPCs), defined as self-renewing and/or multi-potent stem cells capable of maturation into any of the hematopoietic lineages, lineage-restricted pluripotent progenitor cells, and committed progenitor cells from hematopoietic sources (bone marrow, umbilical cord blood, peripheral blood, or other tissue source). These standards also apply to immune effector cells collected, processed, or administered in HPC transplant programs. The standards cover clinical programs, marrow collection facilities, apheresis collection facilities, and cell processing facilities.

How to Access this Standard:
Available for purchase from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: FACT-JACIE Hematopoietic Cellular Therapy Accreditation Manual (Seventh Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published 2018

Description:
This manual provides guidance to applicants for accreditation and to on-site inspectors. While this manual is not a standard, it explains the intent and rationale for specific standards for hematopoietic cellular therapy and provides explanations, examples, and alternative approaches helpful in the accreditation process. The standards cover clinical programs, cell collection, and cell processing facilities.

How to Access this Standard:
Available for purchase from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: NetCord-FACT International Standards for Cord Blood Collection, Banking, & Release for Administration (Seventh Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2019

Description:
The major objective of these documents is to promote quality medical and laboratory practices throughout all phases of cord blood (CB) collection, banking, and release to achieve consistent production of quality placental and umbilical CB units for administration. These documents cover 1) collection of CB cells, regardless of the methodology or site of collection; 2) screening, testing, and eligibility determination of the maternal and infant donor according to applicable law; 3) all phases of processing, cryopreservation, and storage, including quarantine, testing, and characterization of the CB unit; 4) making the CB unit available for administration, either directly or through listing with a search registry; 5) the search process for selection of specific CB units; 6) reservation and release of CB units for clinical use; and 7) all transport or shipment of CB units, whether fresh or cryopreserved.

How to Access this Standard:
Available for purchase from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

N/A: NetCord-FACT Cord Blood Accreditation Manual (Seventh Edition)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2019

Description:
These documents are designed to provide minimum guidelines for cord blood (CB) banks, facilities, and individuals performing CB donor management, collection, processing, testing, cryopreservation, storage, listing, search, selection, reservation, release, and distribution, or providing support services for such procedures. While it is not a standard, this manual explains the intent and rationale for specific standards and provides explanations, examples, and alternative approaches helpful in the accreditation process.

How to Access this Standard:
Available for purchase from FACT.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

Human Cell Differentiation Molecules

N/A: A simple guide to the terminology and application of leucocyte monoclonal antibodies

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 1988

Description:
This is a simple guide and quick reference to the terminology and diagnostic applications of leucocyte monoclonal antibodies. The differentiation cluster terminology, where applicable, is used throughout. Differentiation is a critical step in many cell and gene therapies, and monoclonal antibodies are critical in assessing the differentiation. For many therapies that involve differentiation into leucocyte lineage, there is a need for clear communication and understanding throughout the entire manufacturing process. The standardization of terminology in this area aims to allow for comparison and quality across the field.

How to Access this Standard:
Available for purchase from *Histopathology*.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Preclinical studies
- ○ Clinical trials

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

ICH Q5A (R1): Guideline for viral safety evaluation of biotechnology products derived from cell lines of human or animal origin quality of biotechnological products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 1997

Description:
This document is concerned with testing and evaluation of the viral safety of biotechnology products derived from characterized cell lines of human or animal origin (i.e., mammalian, avian, insect) and outlines data that should be submitted in a marketing application/registration package. The purpose of this document is to provide a general framework for virus testing, experiments for the assessment of viral clearance, and a recommended approach for the design of viral tests and viral clearance studies.

How to Access this Standard:
Free access available from ICH.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

ICH Q5E: Comparability of biotechnological/biological products subject to changes in their manufacturing process

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Published 2005

Description:
This document provides principles for assessing the comparability of biotechnological/biological products before and after changes are made in the manufacturing process for the drug substance or drug product. Thus, this guideline is intended to assist in the collection of relevant technical information which serves as evidence that the manufacturing process changes will not have an adverse impact on the quality, safety, and efficacy of the drug product.

How to Access this Standard:
Free access available from ICH.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

ICH Q7: Good manufacturing practice guide for active pharmaceutical ingredients

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2000

Description:
This document is intended to provide guidance regarding good manufacturing practice (GMP) for the manufacturing of active pharmaceutical ingredients (APIs) under an appropriate system for managing quality. It is also intended to help ensure that APIs meet the quality and purity characteristics that they purport, or are represented, to possess. In this guidance, the term manufacturing is defined to include all operations of receipt of materials, production, packaging, repackaging, labeling, relabeling, quality control, release, storage, and distribution of APIs and the related controls. The guidance treats the terms “current GMPs” and “GMPs” as equivalent.

How to Access this Standard:
Free access available from ICH.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

ICH Q8 (R2): Pharmaceutical development

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	Published 2009

Description:
This document is intended to provide guidance on the contents of Section 3.2.P.2 (Pharmaceutical Development) for drug products as defined in the scope of Module 3 of the Common Technical Document (ICH guideline M4). The Pharmaceutical Development section provides an opportunity to present the knowledge gained through the application of scientific approaches and quality risk management to the development of a product and its manufacturing process.

How to Access this Standard:
Free access available from ICH.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

ICH Q9: Quality Risk Management

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	Published 2005

Description:
This document offers a systematic approach to quality risk management. It specifically provides guidance on the principles and some of the tools of quality risk management that can enable more effective and consistent risk-based decisions, both by regulators and industry, regarding the quality of drug substances and drug (medicinal) products across the product life cycle.

How to Access this Standard:
Free access available from ICH.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

ICH Q10: Pharmaceutical quality system

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	Published 2008

Description:
This document establishes a new ICH tripartite guideline describing a model for an effective quality management system for the pharmaceutical industry, referred to as the Pharmaceutical Quality System. This guideline applies to the systems supporting the development and manufacture of pharmaceutical drug substances (i.e., active pharmaceutical ingredients [API]) and drug products, including biotechnology and biological products, throughout the product life cycle.

How to Access this Standard:
Free access available from ICH.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

International Council for Commonality in Blood Banking Automation (ICCBBA)

ICCBBA ST-002 ISBT 128 global standard: Standard terminology for medical products of human origin

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2017; revised 2020

Description:
This document provides a standard terminology for describing transfusion and transplantation products. Although primarily developed to ensure standard labeling of products, the terminology has a wider application in ensuring a common international understanding of specialized terms. Other professional and accreditation bodies have adapted their terminology to be consistent with this document.

How to Access this Standard:
Free access available from ICCBBA.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- ✓ Clinical trials

International Organization for Standardization (ISO)

ISO/DIS 5058-1: Biotechnology — Genome Editing — Part 1: Terminology

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	In development; initiated May 2020

Description:
This document defines terms related to genome editing technology. The definitions are worded with the intention that additional context can be added with supplementary language when they are used. The document is applicable to general use of genome editing across species.

While genome editing technology is being actively utilized, there is no standardization in terms and definitions for this field, which can lead to misinterpretation and miscommunication of concepts, data, and results. This document was developed to provide a unified, standard set of terms and definitions that serve the needs of biotechnology stakeholders and act as a reference for genome editing technology.

Standards in the field of genome editing will harmonize and accelerate effective communication, technology development, qualification, and evaluation of genome editing products. This document is expected to improve confidence in and clarify scientific communication, data reporting, and data interpretation in the genome editing field. This document provides a vocabulary that standardizes the use and meaning of terms associated with genome editing. This document is organized into the categories of Genome Editing Concepts, Genome Editing Tools, General, CRISPR, Meganuclease, megaTAL, TALEN, ZFN, and Genome Editing Outcomes.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 10993-1:2018: Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2009; revised 2018

Description:
This document describes the general principles governing the biological evaluation of medical devices within a risk management process. It includes general device categorization based on the nature and duration of their contact with the body; methods for evaluating existing relevant data from all sources, identifying any data gaps, and identifying additional data sets necessary to analyze the biological safety of the medical device; and guidance on assessing the biological safety of a medical device.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO 10993-3:2014: Biological evaluation of medical devices - Part 3: Tests for genotoxicity, carcinogenicity, & reproductive toxicity

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2014

Description:

This part of ISO 10993 specifies strategies for risk estimation, selection of hazard identification tests, and risk management for the following potentially irreversible biological effects from exposure to medical devices: genotoxicity, carcinogenicity, and reproductive and developmental toxicity. The standard is applicable when the need to evaluate a medical device for potential genotoxicity, carcinogenicity, or reproductive toxicity has been established.

The basis for biological evaluation of medical devices is often empirical and driven by the relevant concerns for human safety. The assessment of mutagenic, carcinogenic, and reproductive hazards is an essential component of the control of these risks. Not all test methods for the assessment of genotoxicity, carcinogenicity, or reproductive toxicity are equally well developed, nor is their validity well established for the testing of medical devices.

In the selection of tests needed to evaluate a particular medical device, there is no substitute for a careful assessment of expected human uses and potential interactions of the medical device with various biological systems. These considerations will be particularly important in such areas as reproductive and developmental toxicology. This part of ISO 10993 presents test methods for the detection of specific biological hazards and strategies for the selection of tests, where appropriate, that will assist in hazard identification.

How to Access this Standard:

Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO 10993-4:2017: Biological evaluation of medical devices - Part 4: Selection of tests for interactions with blood

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2017

Description:
This document specifies general requirements for evaluating the interactions of medical devices with blood. It describes a) a classification of medical devices that will come in contact with blood based on the intended use and duration of contact as defined in ISO 10993-1; b) the fundamental principles governing the evaluation of device interaction with blood; and c) the rationale for a structured selection of tests according to specific categories, combined with the principles and scientific bases of these tests.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 10993-5:2009: Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2009

Description:
This part of ISO 10993 describes test methods to assess the *in vitro* cytotoxicity of medical devices. These methods specify the incubation of cultured cells in contact with a device and/or extracts of a device either directly or through diffusion. These methods are designed to determine the biological response of mammalian cells *in vitro* using appropriate biological parameters.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 10993-6:2016: Biological evaluation of medical devices - Part 6: Tests for local effects after implantation

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2016

Description:
This part of ISO 10993 specifies test methods for the assessment of the local effects after implantation of biomaterials intended for use in medical devices. This part of ISO 10993 applies to materials that are solid and non-absorbable; non-solid, such as porous materials, liquids, gels, pastes, and particulates; and degradable and/or absorbable, which may be solid or non-solid. This part of ISO 10993 can also be applied to medical devices intended for topical use in clinical indications to evaluate local tissue responses where the surface or lining might have been breached.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Preclinical studies
- ○ Clinical trials

ISO 10993-9:2019: Biological evaluation of medical devices - Part 9: Framework for identification & quantification of potential degradation products

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2016; revised 2019

Description:
This part of ISO 10993 provides general principles for the systematic evaluation of the potential and observed biodegradation of medical devices and for the design and performance of biodegradation studies. Information obtained from these studies can be used in the biological evaluation described in the ISO 10993 series. This part of ISO 10993 considers both non-resorbable and resorbable materials, and can be applied to the degradation of materials used in any kind of product that falls within the definition of "medical device" in ISO 10993-1, even if such products are subject to different regulations from those applying to medical devices (e.g., the scaffold in a tissue-engineered medical product [TEMPs], or a carrier matrix to deliver drugs or biologics).

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO 10993-10:2010: Biological evaluation of medical devices - Part 10: Tests for irritation & skin sensitization

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2010

Description:
This part of ISO 10993 describes the procedure for the assessment of medical devices and their constituent materials with regard to their potential to produce irritation and skin sensitization. It includes pretest considerations for irritation, including *in silico* and *in vitro* methods for dermal exposure; details of *in vivo* (irritation and sensitization) test procedures; and key factors for the interpretation of the results.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 10993-11:2017: Biological evaluation of medical devices - Part 11: Tests for system toxicity

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2017

Description:
This part of ISO 10993 specifies requirements and gives guidance on procedures for evaluating medical device materials for their potential to cause adverse systemic reactions. This part of ISO 10993 addresses the evaluation of generalized systemic toxicity rather than specific target organ or organ system toxicity, even though these effects may result from the systemic absorption and distribution of toxicants.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 10993-12:2012: Biological evaluation of medical devices - Part 12: Sample preparation & reference materials

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2012

Description:
This part of ISO 10993 specifies requirements and gives guidance on procedures for preparing samples and selecting reference materials for medical device testing in biological systems in accordance with one or more parts of ISO 10993. Specifically, this part of ISO 10993 addresses the following: test sample selection; selection of representative portions from a device; test sample preparation; experimental controls; selection of and requirements for reference materials; and preparation of extracts. While it is not applicable to live cells, it can be relevant to the material or device components of combination products containing live cells.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
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- ○ Clinical trials

ISO/TR 10993-33:2015: Biological evaluation of medical devices - Part 33: Guidance on tests to evaluate genotoxicity - Supplement to ISO 10993-3

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2015

Description:
This Technical Report describes the differing views between regulatory bodies on the subject of genotoxicity testing. It provides background information to facilitate the selection of tests and guidance on the performance of tests. Specifically, it includes information on a variety of testing methodologies, including: *in vitro* tests to detect genotoxicity; *in vivo* tests to detect genotoxicity; bacterial reverse mutation assays; *in vitro* mammalian chromosome aberration tests; *in vitro* mammalian micronucleus tests; *in vitro* mammalian cell gene mutation tests using mouse lymphoma (L5178Y) cells; *in vivo* mammalian erythrocyte micronucleus tests; and *in vivo* chromosome aberration tests.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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ISO 13019:2018: Tissue-engineered medical products -- Quantification of sulfated glycosaminoglycans (sGAG) for evaluation of chondrogenesis

APPLICABLE SECTOR(S):	STATUS:
Tissue engineering	Published 2018

Description:
This document specifies test methods for the quantification of sulfated glycosaminoglycans (sGAG), one of the major extracellular matrix components in articular, meniscal, and elastic cartilages, and tissue-engineered cartilage constructs.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Clinical trials

ISO 13022:2012: Medical products containing viable human cells - Application of risk management & requirements for processing practices

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2012

Description:
This document specifies requirements and guidance for processing practices and managing risks associated with viable cellular components of products regulated as medicinal products, biologics, medical devices and active implantable medical devices, or combinations thereof. It covers viable human materials of autologous and allogeneic human origin, obtained from living or deceased donors.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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ISO 13485:2016: Medical devices -- Quality management systems -- Requirements for regulatory purposes

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2016

Description:
This document specifies requirements for a quality management system where an organization needs to demonstrate its ability to provide medical devices and related services that consistently meet customer and applicable regulatory requirements. ISO 13485:2016 can also be used by suppliers or external parties that provide products, including quality management system-related services for such organizations.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO 14155:2020: Clinical investigation of medical devices for human subjects - Good clinical practice

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2011; revised 2020

Description:
This document addresses good clinical practice for designing, conducting, recording, and reporting clinical investigations carried out in human subjects to assess the safety or performance of medical devices for regulatory purposes. ISO 14155:2011 specifies general requirements intended to protect the rights, safety, and well-being of human subjects; ensure the scientific conduct of the clinical investigation and the credibility of the results; define the responsibilities of the sponsor and principal investigator; and assist sponsors, investigators, ethics committees, regulatory authorities, and other bodies involved in the conformity assessment of medical devices.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

ISO 14644-1:2015: Cleanrooms and associated controlled environments - Part 1: Classification of cleanliness by particle concentration

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2015

Description:
This document specifies the classification of air cleanliness in terms of concentration of airborne particles in cleanrooms, clean zones, and separative devices (e.g., clean air hoods, gloveboxes, isolators, and minienvironments). The use of light scattering (discrete) airborne particle counters (LSAPC) is the basis for determination of the concentration of airborne particles, equal to and greater than the specified sizes, at designated sampling locations.

Only particle populations having cumulative distributions based on threshold (lower limit) particle sizes ranging from 0,1 µm to 5 µm are considered for classification purposes. ISO 14644-1:2015 cannot be used to characterize the physical, chemical, radiological, viable, or other nature of airborne particles.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- Logistics and compliance criteria
- Preclinical studies
- ✓ Clinical trials

ISO/TR 15499:2016: Biological evaluation of medical devices - Guidance on the conduct of biological evaluation within a risk management process

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2016; withdrawn 2018

Description:
This document provides guidance on biological evaluations of medical devices according to the requirements of ISO 10993-1 (regarding potential human biological risks from the use of medical devices). This document can be used to better understand the requirements of ISO 10993-1 and to illustrate some of the variety of methods and approaches available for meeting the requirements of ISO 10993-1.

This standard was withdrawn in 2018.

How to Access this Standard:
Previously available for purchase from ISO; the standard is now withdrawn.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Clinical trials

ISO/TR 16379:2014: Tissue-engineered medical products — Evaluation of anisotropic structure of articular cartilage using Diffusion Tensor (DT) MR Imaging

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2014

Description:
This document evaluates regenerative medicine therapies for articular cartilage disease and summarizes results from structural evaluation of knee joint cartilage by diffusion tensor (DT) imaging, a magnetic resonance imaging (MRI)-applied technology allowing non-invasive observation of soft tissue morphology *in vivo*.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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ISO 19090:2018: Tissue-engineered medical products - Bioactive ceramics - Method to measure cell migration in porous materials

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2018

Description:
This document specifies cell migration ability testing methods for porous bioactive ceramics. This standard is not applicable to porous materials that have low or no cell adhesion properties (e.g., synthetic polymers and metals) where the transfer of cells from a culture dish to a test specimen can take longer to occur.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO/DTR 20386: Inventory of biotechnology-related terms

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	⊘ Development initiated 2016; abandoned 2019

Description:
This inventory of biotechnology-related terms and definitions serves as a source of information for interested parties working in the field of biotechnology.

This in-development standard was abandoned in 2019.

How to Access this Standard:
Previously in development by ISO but is now deleted.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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ISO 20387:2018: Biotechnology - Biobanking - General requirements for biobanking

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy, Tissue engineering	Published 2018

Description:
This document specifies general quality control requirements for the competence, impartiality, and consistent operation of biobanks, including quality control requirements to ensure biological material and data collections are of appropriate quality. This document is applicable to all organizations performing biobanking activities, including biobanking of human, animal, plant, protist, and multicellular organism and microorganism material for research and development. Biobank users, regulatory authorities, organizations and schemes using peer assessment, accreditation bodies, and others can also use this document to help confirm or recognize the competence of their biobanks.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO/WD TS 20388: Biotechnology – Biobanking – Requirements for the collection, processing, storage and transportation of animal biological material

APPLICABLE SECTOR(S):
Cell therapy, Gene therapy, Tissue engineering

STATUS:
In development; initiated December 2017

Description:
As a technical specification and substandard, this document will continuously supplement the general requirements of ISO 20387, Biotechnology — Biobanking — General requirements for biobanking. This document specifies methods and general requirements for collection, processing, storage, and transportation of animal genetic resources (e.g., tissues, blood). This document is applicable to all biobanks, institutions, and researchers collecting and storing vertebrate and invertebrate genetic resources.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/PWI 20389: Collection, processing, transportation, and storage criteria for human biological resources

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	In development

Description:
As a technical specification and substandard, this document will continuously supplement the general requirements of ISO 20387, Biotechnology — Biobanking — General requirements for biobanking. This document specifies requirements for the collection, processing, transport, and storage of human biological material.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 20391-1:2018: Biotechnology - Cell Counting - Part 1: General guidance on cell counting methods

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2018

Description:
ISO 20391-1:2018 defines terms related to cell counting for biotechnology. It describes counting of cells in suspension (generally cell concentration) and cells adhered to a substrate (generally area density of cells). It provides key considerations for general counting methods (including total and differential counting, and direct and indirect counting) as well as for method selection, measurement process, and data analysis and reporting.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Clinical trials

ISO 20391-2:2019: Biotechnology - Cell Counting - Part 2: Experimental design and statistical analysis to quantify counting performance

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2019

Description:
This document provides a method for evaluating the quality of a cell counting measurement process through a set of quality indicators derived from a dilution series experimental design and statistical analysis. The quality indicators are based on repeatability of the measurement and the degree to which the results conform to an ideal proportional response to dilution. This method is most suitable during cell counting method development, optimization, validation, and/or evaluation of established, routine cell counting measurement processes.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO 20395:2019: Biotechnology – Requirements for evaluating the performance of quantification methods for nucleic acid target sequences – Part 1: qPCR and dPCR

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2019

Description:
This document describes the quality, reliability, and reproducibility of targeted nucleic acid quantification measurements employed in bioproduct development and characterization and in bioprocesses, supporting the regulatory-driven requirements of the biotechnology industry.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

ISO/TR 20396-1: Biotechnology - Data publication - Part 1: Preliminary considerations and concepts

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy, Tissue engineering	In development

Description:
This document specifies key aspects of data description and publication for biological data. Specifically, it defines best practices that respect the existing standardization efforts of biotechnology research communities, normalize key aspects of data description at the level of the biology being studied and shared across biotechnology communities, ensure that data is accessible and usable by other researchers, and provide concrete guidance and metrics for judging the applicability of a particular data sharing plan.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

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ISO/CD 20397-1: Biotechnology - General requirements for massive parallel sequencing - Part 1: Nucleic acid and library preparation

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	In development

Description:
This document provides requirements on quality evaluation and assessment for the upstream process of massive parallel sequencing, including process workflow, quality control checkpoints, barcoding, reference materials, and contaminations.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Preclinical studies
- ○ Clinical trials

ISO/FDIS 20397-2: Biotechnology – Massively parallel sequencing – Part 2: Quality evaluation of sequencing data

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	In development; initiated July 2017

Description:
This document specifies minimum requirements and quality evaluation methods of massive sequencing data, including base quality control, cross-species contamination evaluation, and index-adapter contamination evaluation.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/CD 20399: Biotechnology — Ancillary materials present during the production of cellular therapeutic products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated November 2019

Description:

This document provides guidance to suppliers and users of ancillary materials to improve the consistency and quality of ancillary materials of biological (human and animal) and chemical origin used in the production of cell-based medicinal products for human use. This document is intended to help the suppliers and users of ancillary materials to achieve and maintain an appropriate level of documented lot-to-lot consistency in the aspects of identity, purity, storage and stability, biosafety, and performance.

This document is intended to provide confidence to the users, developers and/or suppliers of ancillary materials so that the quality of any such material will lead to final products that are safe and effective. Cells that are either starting materials and/or final therapeutic products are not within scope. Agents for cryopreservation, beads, scaffolds, feeder cells, apparatus and instruments, or additives used post bioprocessing are not within scope.

This standard will combine ISO/TS 20399-1, ISO/TS 20399-2, and ISO/TS 20399-3 into an international standard.

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/TS 20399-1:2018: Biotechnology - Ancillary materials present during the production of cellular therapeutic products — Part 1: General requirements

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering, Supportive standard	Published 2018

Description:
This document specifies definitions and general requirements for ancillary materials used in cell processing of cellular therapeutic products. This document is applicable to cellular therapeutic products, including those gene therapy products whereby cells form part of the final product.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/ TS 20399-2:2018: Biotechnology – Ancillary materials present during the production of cellular therapeutic products – Part 2: Best practice guidance for ancillary material suppliers

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Published 2018

Description:
This document provides guidance for ancillary material suppliers to maintain a high level of lot-to-lot consistency in the aspects of identity, purity, stability, biosafety, and performance, as well as the accompanying documentation. This document is applicable to cellular therapeutic products, including gene therapy products whereby cells form part of the final product. It does not apply to products without cells.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/TS 20399-3:2018: Biotechnology – Ancillary materials present during the production of cellular therapeutic products – Part 3: Best practice guidance for ancillary material users

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published 2018

Description:
This document provides guidance for ancillary material users. It is applicable to cellular therapeutic products, including those gene therapy products whereby cells form part of the final product. It does not apply to products without cells. This document focuses primarily on ancillary materials of biological (human and animal) origin and their potential impurities and contaminants.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/AWI 20404: Biotechnology — Bioprocessing — General requirements for packaging to contain cells for therapeutic use

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	In development; initiated October 2020

Description:

This document provides terms and definitions, minimum requirements, and general considerations for packaging used to fill or wrap cells for therapeutic use. This document is intended to help the users of packaging to design and employ packaging in consideration of filling, wrapping, storage, transportation, and utilization processes of cells for therapeutic use. This document is also intended to help the suppliers of packaging to design and manufacture packaging in consideration of the above-mentioned processes. This document is applicable to packaging intended to fill or wrap starting materials and intermediate materials of cells for therapeutic use.

This document does not specify:

- Packages, which consist of both packaging and its content (cell and/or cell solution)
- Shipping containers, which contain packages for transportation
- Services performed with the package (e.g. storage service)

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 20688-1: Biotechnology – Nucleic acid synthesis – Part 1: Requirements for the production and quality control of synthesized oligonucleotides

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Published 2020

Description:
This document specifies general definitions and minimum requirements for production and quality control processes of synthetic oligonucleotides (nominally up to 250 bases). Manufacturers of synthesized oligonucleotides can use this document to develop or improve their quality management. This document is applicable to anyone using synthesized oligonucleotides for the selection of quality indicators to evaluate a manufacturer's products.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/PWI 20688-2: Biotechnology - Nucleic acid synthesis - Part 2. General definitions and requirements for the production and quality control of synthesized gene fragments, genes and genomes

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	In development

Description:
This standard specifies the general definitions and requirements for production and quality control of synthesized double-stranded DNA, including synthetic gene fragments, genes, and genomes with a length below 107bp in the form of non-clonal fragments and clonal genes in plasmid. It covers the requirements for biosecurity evaluation, the quality control requirements in the production process, and the quality attributes and assessing methods for the final product of synthesized gene fragments, genes, and genomes.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/CD 20691: Biotechnology – Requirements for data formatting and description in the life sciences for downstream data processing and integration workflows

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	In development; initiated August 2017

Description:
This document specifies requirements and rules for the specific application of dedicated community standards for formatting and documenting data captured in biotechnology and general life sciences, as well as of secondary data and computer models (and their context) derived from the original data through computational processing. The document also contains recommended workflows for the structured processing, storage, and integration of data and corresponding computer models in the above-mentioned fields.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/TS 21560:2020: General requirements of TEMPs

APPLICABLE SECTOR(S):	**STATUS:**
Tissue engineering	Published 2020

Description:
This document specifies general requirements for tissue engineered medical products (TEMPs). With regard to safety, this document outlines requirements for materials, manufacture, quality control, and unintentional biological effects elicited by TEMPs. 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 non-human cells, or 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.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

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

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy, Tissue engineering	In development; initiated August 2017

Description:
This document specifies processes and quality requirements for the biobanking of mammalian (including human) cell lines. This document outlines requirements for the fundamental procedures of the biobank and provides guidelines regarding establishment, reception, preservation, storage, quality control, and distribution of cell lines.

How to Access this Standard:
This standard is approved and pending publication and will be available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 21710: Biotechnology - Specification on data management and publication in microbial resource centers

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	In development; initiated July 2017

Description:
This document specifies requirements for data management and publication in microbial biological resource centers (MRCs) to enable consistent formatting as well as how to establish a quality control workflow to improve the overall data quality. It also provides recommendations for MRCs to improve data sharing and integration of microbial material and associated data. The specifications in this standard will influence procedures such as accessioning, acquisition, authentication, preservation, storage, distribution, and disposal.

How to Access this Standard:
This standard is approved and pending publication and will be available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 21899:2020: Biotechnology — Biobanking - General requirements for the validation and verification of processing methods for biological material in biobanks

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy, Tissue engineering	Published 2020

Description:
This document specifies the requirements necessary for a biobank to be able to demonstrate that it operates its production of biological materials with validated and/or verified methods. This document is intended for use by biobank laboratories in the implementation and validation of their processing methods for quality, administrative, and technical operations. It can also be used by biological material end users, regulatory authorities, and accreditation bodies.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 21973:2020: Biotechnology – General requirements for transportation of cells for therapeutic use

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2020

Description:
This document provides general definitions and requirements for transportation of cellular therapeutic products. It specifies general requirements and reviews the points to consider for the transportation of cells for therapeutic use, including storage during transportation. Transportation starts with the transfer of the packaged cells by the sender to the transportation service provider and ends when the package is delivered to the receiver at its destination. This document does not apply to transportation of cells within one facility.

This document includes the development of a transportation plan, including verification and validation, communication between the client and the transportation service provider, and associated documentation. This document does not specify particular conditions for transportation such as specification for shipping container, ambient temperature control, etc.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 22442-1:2020: Medical devices utilizing animal tissues & their derivatives - Part 1: Application of risk management

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2015; revised 2020

Description:
This part of ISO 22442 applies to medical devices—other than *in vitro* diagnostic medical devices—manufactured using non-viable materials of animal origin. It specifies, in conjunction with ISO 14971, a procedure to identify the hazards and hazardous situations associated with such devices; to estimate, evaluate, and control the resulting risks; and to monitor the effectiveness of risk control. Furthermore, it outlines the decision process for residual risk acceptability, accounting for the balance of residual risk as defined in ISO 14971 and the expected medical benefit compared to available alternatives.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO 22442-2:2020: Medical devices utilizing animal tissues & their derivatives - Part 2: Controls on sourcing, collection, and handling

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	Published 2015; revised 2020

Description:
This part of ISO 22442 specifies requirements for controls on the sourcing, collection, and handling (which includes storage and transport) of animals and tissues for the manufacture of medical devices utilizing materials of animal origin, excluding *in vitro* diagnostic medical devices. It applies where required by the risk management process as described in ISO 22442-1.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO 22442-3:2007: Medical devices utilizing animal tissues & their derivatives - Part 3: Validation of the elimination &/or inactivation of viruses & transmissible spongiform encephalopathy (TSE) agents

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	Published 2007

Description:
This part of ISO 22442 specifies requirements for validating the elimination and/or inactivation of viruses and TSE agents during the manufacture of medical devices (excluding *in vitro* diagnostic medical devices) utilizing non-viable animal tissue or products derived from non-viable animal tissue. It applies where required by the risk management process as described in ISO 22442-1.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/TR 22442-4:2010: Medical devices utilizing animal tissues & their derivatives - Part 4: Principles for elimination &/or inactivation of transmissible spongiform encephalopathy (TSE) agents & validation assays for those processes

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2010

Description:
This document offers suggestions for designing and conducting validation assays to determine if manufacturing processes of medical devices derived from non-viable animal tissues might serve to reduce the risk of iatrogenic transmission of TSEs. This document builds upon the specific discussion in ISO 22442-3 relative to TSE agents and attempts to summarize the current state of the art in the arena of TSE agent elimination.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
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- ○ Clinical trials

ISO/TR 22758:2020: Biobanking - Implementation guide for ISO 20387

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	Published 2020

Description:
This document provides guidance to biobanks on how to meet the requirements for competence and quality contained in ISO 20387. This document provides clarifications, explanations, examples, and exclusions that can be used to implement these requirements into a biobank's quality management system. This document is equally applicable to newly established and existing biobanks and encompasses both the management and technical requirements of ISO 20387. This document can be used by all organizations performing biobanking, including biobanking of human, animal, plant, fungi, and microorganism material for research and development.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/WD TS 22859-1: Biotechnology – Requirements for human mesenchymal stromal cells derived from umbilical cord

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy, Tissue engineering	In development; initiated July 2018

Description:
This document provides general guidelines and definitions for the processing of human mesenchymal stem cells / human mesenchymal stromal cells derived from umbilical cord (hUC-MSCs) tissue for biobanking and defines quality control criteria for these cells.

The document specifies requirements for the collection, isolation, culture, expansion, cryopreservation, transport, and characterization of hUC-MSCs (Wharton's jelly [WJ]) for biobanking. The document is applicable to all organizations performing biobanking of hUC-MSCs used for research and development. It does not apply to human MSCs for clinical applications or therapeutic uses and is not intended for application to human subjects.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/PWI 22860: Biotechnology - Data element and metadata specification to describe production management of human isolated cells

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	In development

Description:
This document defines the structure of isolated and cultured cells production management, including required data fields and their metadata for human isolated and cultured cell production management and optional data. It also covers the processes of donor management, biological material origin management, cell production management, and storage and transportation management.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/DIS 23033: Biotechnology — Analytical methods — General guidelines for the characterization and testing of cellular therapeutic products

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	In development; initiated November 2017

Description:

This standard is currently in development. It defines terms related to characterization of human cells for therapeutic applications. It also provides a general description of cell characteristics and common cell measurement methods. This document defines terms and provides general requirements for the testing of cellular therapeutic products intended for human use.

This document also provides considerations for the characterization and testing of cellular therapeutic products, including approaches to select and design analytical methods that are fit-for purpose and considerations for setting specifications for the analytical methods. Such considerations can be used to establish critical quality attributes (CQAs) for a cellular therapeutic product.

Aspects of this document are applicable to starting materials (including those for tissue-engineered products) and intermediates of cellular therapeutic products. This document excludes tissues used in transplantation.

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/WD TS 23494-1: Biotechnology - Provenance information model for biological material and data — Part 1: Design concepts and general requirements

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy, Tissue engineering	In development

Description:
This standard serves as a general guidance for provenance information management in biotechnology. The standard will address reproducibility concerns and data integration in biotechnology by defining a common model for provenance generated and consumed by various stakeholders involved in research, including support for provenance distributed across different organizations. The common provenance model can be viewed as a backbone making independently generated provenance information interoperable.

The common provenance model will support interlinking of opaque parts of provenance information maintained by different organizations, without disclosing detailed information (which may be sensitive for various reasons). The respective part of the provenance may be resolved after granting authorization by the responsible organization. This document defines serialization guidelines for the common provenance model.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/NP 23511: Biotechnology - General guidance on detection methods of cell cross-contamination

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy	In development

Description:
This guidance outlines appropriate procedures for determining cell cross-contamination for biotechnology applications. It describes the general principles, detection strategies, and analytical methods for cell line authentication. The standard also provides key considerations for cell line authentication-related detection technical methods, method selection, application scenarios, quality standards, data analysis, and reporting.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/WD TS 23565: Biotechnology – Bioprocessing – General requirements and considerations for equipment systems used in manufacturing of cellular therapeutic products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated September 2018

Description:
This standard is currently in development. The document defines relevant cell therapy manufacturing terms, minimum equipment requirements, and general considerations for equipment involved in cell procurement, isolation/selection, expansion, washing and volume reduction, in-line monitoring, and cryopreservation.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/CD 24088-1: Biotechnology — Biobanking — Requirements for the collection, processing, storage and transportation of microorganisms — Part 1: Bacteria and archaea

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	In development; initiated October 2019

Description:

This document specifies requirements for biobanking of bacteria and archaea, including acquisition, microbial culture, identification, quality control, preservation, storage, and distribution. It includes management of microbial material-associated data as well as biosafety and biosecurity requirements. This document is applicable to all organizations performing biobanking of bacteria and archaea used for research and development. This document does not apply to processing methods for microbial materials intended for food/feed production, laboratories undertaking food/feed analysis, or therapeutic use.

Many countries around the world have microbial biobanks that perform biobanking activities according to their own guidelines. Microbial biobanks face challenges such as the genetic mutation of strains, microbial contamination, misidentification, and loss of viability. These challenges can impact users' research results, with consequent serious socio-economic losses, affecting the bioindustry, society in general, and other stakeholders. It is imperative that international standardized operational and management requirements address these common problems.

This document has been developed to promote confidence in microbial biobanking. It contains the requirements to enable biobanks to demonstrate their competent operation and the ability to provide authenticated microbial materials and associated data of appropriate quality for research and development. This is intended to be achieved by the planning and implementation of policies, processes, and procedures relevant to the life cycle of microbial material and associated data within the scope/control of the microbial biobank.

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/WD 24190: Biotechnology -- Analytical Methods -- Risk based approach for design and validation of methods for rapid microbial detection in bioprocesses

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
In development; initiated 2019

Description:
This standard is currently in development. The standard will offer a flexible, risk-based framework for validating rapid microbial test methods (RMTMs). This document provides definitions, guidelines, a framework, and a risk-based approach for the design, validation, and use of methods for rapid microbial detection in cell-based therapy manufacturing. It is based on the generalized requirements and risk associated with cell-based therapy manufacturing, with flexibility to address the specific manufacturing process and location of each unique therapeutic product. This document addresses safety of cell-based therapies.

The validation of RMTMs will enable technology providers to develop standard analytical products that can be used in routine testing of biological therapeutics. This document provides guidance on validation of RMTM products intended to significantly speed cell therapies to market by shortening testing times and reducing the use of resources. The standard is intended to help accelerate development timelines for cell-based therapies and aid in meeting the short shelf lives of some cell-based therapies.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

ISO/WD TS 24420: Biotechnology — Massively parallel DNA sequencing — General requirements for data processing of shotgun metagenomics

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	In development; initiated June 2020

Description:

This document illustrates the workflow of shotgun metagenomic data processing. It specifies the requirements for quality control of shotgun metagenomic data processing for massively parallel DNA sequencing. This document provides guidelines for data directory, data archive, and metadata for shotgun metagenomic data. It applies to shotgun metagenomic data processing and analyses but excludes functional analysis. This document also applies to data storage, sharing, and interoperability of shotgun metagenomic data.

Based on massive parallel sequencing technology and other technological advances, metagenomics research has been widely conducted in life science and clinical testing, such as human complex disease association analysis and environmental microecology. To meet such increasing demand, specifications for data processing, data format and quality control are becoming more and more urgent. In metagenomics analysis, standardized processing and quality control of sequencing data are essential in the identification and analysis of species in complex ecological community and significantly affect the reliability of the results. Data format standardization is crucial to promote data sharing. However, there is no unified upstream data processing process, data quality assessment method, reference materials, or data format standards in metagenomics. As academic research is developing closer links with the industry, many challenges are emerging, such as the extreme data complexity from high-depth sequencing, the pressure of data processing, and management from extra-large cohort studies. This proposal will provide general requirements and recommendations in these areas.

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/WD 24421: Biotechnology — Biotechnology — Minimum requirements for optical signal measurements in photometric methods for biological samples

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated June 2020

Description:
This document provides minimum requirements for ensuring reliable and accurate detection of optical signals in photometric methods used for qualitative or quantitative characterization of biological samples. The optical signal can be generated by bioluminescence, chemiluminescence, fluorescence, and in absorption measurements. This document defines terms and provides general guidance for reliable and accurate detection of optical signals used for measurements of biological samples. These photometric methods can involve measurement of bioluminescence, chemiluminescence, fluorescence, or absorption, which can be applied to measurements of biological samples in toxicity testing, environmental risk assessment, biomanufacturing, drug development, regenerative medicine, and biobanking.

There are significant needs, however, for high-quality photometric methods in industry to increase confidence in the repeatability, intermediate precision, and reproducibility for measurement of biological samples. While repeatability of the photometric method is already sufficient for qualitative characterization of biological samples, quantitative characterization requires more accurate intermediate precision and reproducibility, and it also requires assessment of deviations from the ideal proportionality of the optical signal and the output of the photometric method.

This document will provide a general framework for ensuring proper measurement of optical signal in these photometric methods. This includes procedures for instruments qualification and the use of optical references, including reference light sources. Optical references can be used to calibrate instruments to increase confidence in the repeatability, intermediate precision, and reproducibility of optical signal measurement. For example, light intensity emitted from luminescent products can be compared on a common measurement scale between manufacturer and manufacturer, manufacturer and user, or user and user. This document also provides points to consider regarding biological samples, apparatus, and reagents for ensuring optical signal measurements.

This document can be used by manufacturers who provide products such as instruments, reagents, measurement kits, and cells to ensure product performance. This document can be also used by the users, including testing laboratories, who perform measurements of biological samples by means of photometric methods with increased need for confidence in measurement results.

How to Access this Standard:
This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

ISO/CD 24603: Biotechnology — Biobanking — Requirements for the establishment, maintenance, characterization and distribution of pluripotent stem cells

APPLICABLE SECTOR(S):

Cell therapy, Tissue engineering

STATUS:

In development; initiated October 2019

Description:

This document specifies establishment, expansion, preservation, maintenance, characterization, quality control, storage, distribution, and transport requirements for the biobanking of mouse and human pluripotent stem cells (PSCs). This document is applicable to all organizations performing biobanking with mouse and human PSCs used for research and development, excluding cell lines used for *in vivo* application in humans, clinical applications, or therapeutic use.

Thousands of PSC lines have been established in laboratories around the world. PSC lines hold unique characteristics and behavior due to their capability for both self-renewal and differentiation into multiple cell types. However, the stem cell phenotype can be changed by suboptimal cell culture technique, prolonged passage, or changing the culture conditions. Accordingly, mouse PSCs have been used to establish our fundamental understanding of PSC biology, and these discoveries have been translated into human PSC research to drive the development of new human cell-based *in vitro* assays and potential regenerative medicines. Mouse PSCs and human PSCs have become the most widely studied species in this field, and many significant scientific advances have been made by using PSCs from these two species.

Human PSCs developed in research environments will give the clues to the development of cell therapies. Thus, it is critical to ensure that cell lines used in this dynamic field have been prepared and documented appropriately and have the correct identity and characteristics to help assure reproducibility in PSC-based research. This document aims to meet the current demand for the standardized PSC procedures of biobanks and builds on international consensus agreed by PSC resource centers (International Stem Cell Banking Initiative [ISCBI], 2009). This document specifies the establishment, maintenance, characterization, storage and distribution requirements for mouse and human PSCs, providing a general guideline for both biobanking and fundamental research of PSCs.

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ISO/CD 24651: Biotechnology — Biobanking — Requirements for human mesenchymal stromal cells derived from bone marrow

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	In development; initiated October 2019

Description:

This document specifies requirements for the collection, isolation, culture, expansion, characterization, quality control, cryopreservation, storage, distribution, and transport of human mesenchymal stromal cells derived from bone marrow (hBM-MSCs) for biobanking. This document is applicable to all organizations performing biobanking with hBM-MSCs used for research. This document does not apply to hBM-MSCs for the purpose of *in vivo* application in humans, cell therapy, clinical applications, tissue engineering or therapeutic use.

Mesenchymal stromal cells may contain a sub-population of stem or progenitor cells that demonstrate *in vivo* self-renewal and differentiation, as has been rigorously demonstrated for bone marrow-derived progenitor cells. The functional definition of mesenchymal stromal cells 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 proposed by the International Society of Cell and Gene Therapy (ISCT) and require careful characterization by a matrix of functional assays. 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.

The aim of this document is to provide a consensual general guideline for biobanking of mesenchymal stromal cells derived from human bone marrow (hBM-MSCs) for research purposes. This document is applicable for academic centers and public and private institutions performing a biobanking service of hBM-MSCs for R&D (Research & Development) and preclinical studies, but not for clinical use. Importantly, this document is focused on MSCs that have been isolated, manipulated and/or propagated in culture for research purposes.

How to Access this Standard:

This standard is currently in development. To comment on the draft, contact the U.S. Technical Advisory Group (TAG) to ISO/TC 276. If you are not a U.S. stakeholder, please contact your national ISO member about joining an ISO technical committee at the organization-level.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

IEC 31010:2019: Risk management-Risk assessment techniques

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	Published 2009; revised 2019

Description:
This document provides guidance on selection and application of systematic techniques for risk assessment. This standard does not deal specifically with safety; it is a generic risk management standard and any references to safety are purely of an informative nature.

How to Access this Standard:
Available for purchase from ISO.

STANDARD FUNCTIONAL AREA(S):

- Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- Preclinical studies
- Clinical trials

International Society for Advancement of Cytometry (ISAC)

FCS 3.1: Flow Cytometry Standard (FCS) Implementation Guidance

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2012

Description:
This document on the flow cytometry standard (FCS) format provides guidance and data file examples from instrument vendors to prevent potential compatibility issues identified during discussion with implementers that could be faced when implementing the FCS spillover and preferred display keywords that have arisen during discussions among some implementers. The FCS format was established in 1984 (Murphy, R.F., Chused, T.M. A proposal for a flow cytometric data file standard. *Cytometry* 5:553–555, 1984).

How to Access this Standard:
Free access available from ISAC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Preclinical studies
- ○ Clinical trials

N/A: Gating-ML 2.0 data exchange standard for gating description

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2015

Description:
The lack of software interoperability with respect to gating has traditionally been a bottleneck preventing the use of multiple analytical tools and reproducibility of flow cytometry data analysis by independent parties. To address this issue, ISAC developed Gating-ML, a computer file format to encode and interchange gates. Gating-ML 1.5 was adopted and published as an ISAC Candidate Recommendation in 2008. Feedback during the probationary period from implementors, including major commercial software companies, instrument vendors and the wider community, has led to a streamlined Gating-ML 2.0.

How to Access this Standard:
Free access available from ISAC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Preclinical studies
- ○ Clinical trials

N/A: Minimum Information about a Flow Cytometry Experiment

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2008

Description:
The Minimum Information about a Flow Cytometry Experiment (MIFlowCyt) establishes criteria for recording and reporting information about the flow cytometry experiment overview, samples, instrumentation and data analysis. It promotes consistent annotation of clinical, biological and technical issues surrounding a flow cytometry experiment by specifying the requirements for data content and by providing a structured framework for capturing information.

How to Access this Standard:
Free access available from ISAC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
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- ○ Preclinical studies
- ○ Clinical trials

N/A: Image Cytometry Experiment Format

APPLICABLE SECTOR(S):
Cell therapy

STATUS:
Published 2011

Description:
This document represents the Image Cytometry Experiment Format (the ICEFormat), an open file format to capture image cytometry data, metadata and features in a standardized manner allowing these to be processed by independently developed software application. The adoption of the ICEFormat can facilitate the interchange and validation of data between different software packages with the potential of significant interoperability increase. It supports various use cases including individual and composite images, masks with a variety of bit depths, features of multiple data types and high throughput plate-based experiments.

How to Access this Standard:
Published in *Cytometry Part A*; free access available.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Clinical trials

N/A: Mean Equivalent Soluble Fluorophores (MESF) and Equivalent Reference Fluorophore (ERF)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2008

Description:
Mean Equivalent Soluble Fluorophores (MESF) can be used as an intensity measurement standard for calibrating fluorescence and flow cytometry measurements. Reference particles with intensities calibrated in MESF units are available for a few of the most frequently used fluorophores, but there are not many reference materials for highly multiparameter measurements. An alternative approach is to use the Equivalent Reference Fluorophore (ERF) unit, a calibration particle with a broad emission spectrum and referenced to a single reference fluorophore to calibrate the response of multiple fluorescence channels over defined spectral ranges. The ERF unit will complement the MESF unit by providing practical and accurate calibration of absolute intensities.

How to Access this Standard:
Free access available from ISAC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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- ○ Clinical trials

N/A: Classification Results File Format (CLR)

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2015

Description:
Identifying homogenous sets of cell populations in flow cytometry is an important process for sorting and selecting populations of interest for further data acquisition and analysis. ISAC's Classification Results File Format (CLR) was developed to exchange the results of both manual gating and algorithmic classification approaches in a standardized way based on per event-based classifications, including the potential for soft classifications expressed as the probability of an event being a member of a class.

How to Access this Standard:
Published in *Cytometry Part A*; free access available.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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International Society of Automation (ISA)

ANSI/ISA-88: Batch Control Standard (Parts 1-4)

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	Published 2010

Description:
This standard addresses batch process control and serves as a design philosophy for describing equipment and procedures. The standard provides a consistent set of standards and terminology for batch control and defines the physical model, procedures, and recipes. This standard was originally published in 1995.

How to Access this Standard:
Available for purchase from ANSI/ISA.

- Part 1
- Part 2
- Part 3
- Part 4

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
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International Society for Biological and Environmental Repositories (ISBER)

N/A: ISBER Best Practices for Repositories (Fourth Edition)

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published 2018

Description:
This document provides guidance on the most effective practices for the management of biological and environmental specimen collections and repositories. While this document is not a standard, it includes evidence-based and consensus-based practices for collection, long-term storage, retrieval and distribution of specimens. These guidelines promote the availability of high-quality biological and environmental specimens for future research.

How to Access this Standard:
Free access available from ISBER.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Clinical trials

International Society for Cellular Therapy (ISCT)

N/A: Minimal criteria for defining multipotent mesenchymal stromal cells

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2009

Description:
This document details the International Society for Cellular Therapy (ISCT)'s Mesenchymal and Tissue Stem Cell Committee's proposed minimal criteria to define human multipotent mesenchymal stromal cells (MSC). This minimal set of standard criteria will foster a more uniform characterization of MSC and facilitate the exchange of data among investigators.

How to Access this Standard:
Published in *Cytotherapy;* available for purchase.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Preclinical studies
- ○ Clinical trials

N/A: Potency assay development for cellular therapy products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2011

Description:
This document summarizes the outcomes of the ISCT Process and Product Development Subcommittee's potency working group at the 17th annual ISCT meeting in Rotterdam, the Netherlands, in 2011. The document explains the need to provide a broader explanation of why potency assessment is a critical part of characterization and the control of product quality and consistency during development and over the entire product life cycle. This document also provides examples of potency strategies that have been developed for a range of patient-specific and off-the-shelf cellular therapy products (CTPs).

How to Access this Standard:
Published in Cytotherapy; available for purchase.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
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- ○ Preclinical studies
- ○ Clinical trials

N/A: Stromal cells from the adipose tissue-derived stromal vascular fraction and culture expanded adipose tissue-derived stromal/stem cells – IFATS/ISCT statement

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2013

Description:
Under the authority of the International Federation of Adipose Therapeutics (IFATS) and International Society for Cellular Therapy (ISCT), this paper sets out to establish minimal definitions of stromal cells both as uncultured stromal vascular fraction (SVF) and as an adherent stromal/stem cells population. The goal of this paper is to provide initial guidance for the scientific community working with adipose-derived cells and to facilitate development of international standards based on reproducible parameters.

How to Access this Standard:
Published in *Cytotherapy*; available for purchase.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
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- ○ Preclinical studies
- ○ Clinical trials

International Society for Stem Cell Research (ISSCR)

ISSCR 2016: Guidelines for STEM cell research and clinical translation

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2016

Description:
The International Society for Stem Cell Research (ISSCR)'s guidelines pertain to human stem cell research, clinical translation, and related research activities. These guidelines promote an efficient, appropriate, and sustainable research enterprise for stem cell research and medical interventions that will improve human health.

How to Access this Standard:
Free access available from ISSCR.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ✓ Clinical trials

National Institute for Biological Standards and Control (NIBSC)

04/224: Factor V Leiden, Human gDNA

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference panel of genomic samples intended for use in genetic tests for the blood clotting disorder Factor V Leiden.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

05/130: WHO International Genetic Reference Panel for Prothrombin Mutation G20210A, Human gDNA

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference panel of genomic samples intended for use in genetic tests for Prothrombin gene mutation G20210A.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

07/222: WHO International Reference Reagent: RhD/SRY plasma DNA sensitivity standard

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released 2012

Description:
This is a World Health Organization (WHO) international standard reference reagent of RhD-positive male plasma diluted in an excess of RhD-negative female plasma intended for use as a reference reagent for minimum acceptable potency for the detection of RhD and sex-determining region Y (SRY) sequences in cell-free plasma DNA.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

08/158: WHO International Genetic Reference Panel for Fragile X Syndrome, Human DNA

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference panel of genomic samples intended for use in genetic tests for Fragile X Syndrome.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

08/160: WHO International Genetic Reference Panel for Hemophilia A Intron 22 inversion

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference panel of genomic samples intended for use in genetic tests for Hemophilia A, intron 22 inversion.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

09/138: WHO International Genetic Reference Panel for the quantitation of BCR-ABL translocation by RQ-PCR

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a human genomic DNA (gDNA) reference standard of chronic myelogenous myeloid leukemia for *in vitro* diagnostic quantitation of the BCR-ABL fusion gene via real-time polymerase chain reaction (RQ-PCR). It is intended to be used as a primary standard for calibrating secondary standards by RQ-PCR.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

09/140: WHO International Genetic Reference Panel, Prader Willi and Angelman Syndromes, Human gDNA

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference panel of genomic samples intended for use in genetic testing for Prader Willi and Angelman syndromes.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

10/136-001: HLA-DRB1 Genotyping Reference panel - CE marked material

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a standard genotyping reference panel for use as positive controls in DNA-based low-resolution human leukocyte antigen class II histocompatibility antigen D related beta chain (HLA-DRB1) typing using sequence-specific oligonucleotide polymerase chain reaction (SSO-PCR) and single specific primer polymerase chain reaction (SSP-PCR) techniques. The panel is intended to act as a validator of assay function.

How to Access this Standard:
Previously released by NIBSC; currently unavailable.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

10/232: International Reference Reagent: Genomic DNA (gDNA) for blood group genotyping RBC1(AR1R1)

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference reagent of genomic DNA (gDNA) for use in standardizing and controlling blood group genotyping procedures for common Caucasian and Black African alleles (RBC1[AR1R1]).

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

10/234: International Reference Reagent: Genomic DNA (gDNA) for blood group genotyping RBC12(ODΨ)

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference reagent of genomic DNA (gDNA) for use in standardizing and controlling blood group genotyping procedures for common Caucasian and Black African alleles (RBC12[ODΨ]).

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

10/236: International Reference Reagent: Genomic DNA for blood group genotyping RBC4 (AR1R1)

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference reagent of genomic DNA (gDNA) for use in standardizing and controlling blood group genotyping procedures for common Caucasian and Black African alleles (RBC4[AR1R1]).

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

10/238: International Reference Reagent: Genomic DNA (gDNA) for blood group genotyping RBC5(Brr)

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference reagent of genomic DNA (gDNA) for use in standardizing and controlling blood group genotyping procedures for common Caucasian and Black African alleles (RBC5[Brr]).

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

11/214: International Reference Reagent: Blood Group Genotyping Reference Panel

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard blood group genotyping reference panel.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

11/218: MLH1/MSH2 Exon Copy Number Reference Panel

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Released

Description:
This is an DNA mismatch repair protein MutL homolog 1 (MLH1) / DNA mismatch repair protein MutL homolog 2 (MSH2) exon copy genomic reference panel intended as a single-use control in multiplex ligation-dependent probe amplification (MLPA)-based dosage analyses of hereditary nonpolyposis colorectal cancer (HNPCC; Lynch Syndrome)-associated mutations in MLH1 and MSH2.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

N/A: Biological reference materials

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Released

Description:
The National Institute for Biological Standards and Control (NIBSC) offers a collection of standard biological reference materials and reagents—including WHO international standards, influenza reagents, Quality Control Reagents Unit (QCRU) reagents, and other CE-marked *in vitro* diagnostic device (IVD) reagents—for research and testing purposes.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: Clinical virology standards (nearly 20 clinical virology network reference materials)

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
These are 19 clinical virology standards that the National Institute for Biological Standards and Control (NIBSC) offers for use in research, including influenza and parainfluenza viruses, human rhinovirus, human measles, norovirus, and zika virus.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: In vitro diagnostic standards including HTLV-1, human immunodeficiency virus (HIV), Hepatitis A/B/C, flow cytometry, anti-HLA serology, and HLA genotyping (more than 20 CE marked working standards)

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Released

Description:
These are 25 *in vitro* diagnostic reference standards the National Institute for Biological Standards and Control (NIBSC) offers for use in research, including a human T-lymphotropic virus (HTLV-1) antibody monitor sample, anti-rubella serum, and human immunodeficiency virus (HIV)-1 working reagents and antibodies.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: Influenza reagents

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Released

Description:
These are more than 300 *in vitro* influenza reagents that the National Institute for Biological Standards and Control (NIBSC) offers for use in research.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: Quality control reagents for pathogenic blood virus, cytomegalovirus, malaria, syphilis, rubella, toxoplasma, herpes simplex virus, and varicella zoster virus

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Released

Description:
These are 40 quality control reagents that the National Institute for Biological Standards and Control (NIBSC) offers for use in research.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: WHO 1st International Reference Panel for Genomic JAK2 V617F

APPLICABLE SECTOR(S):	STATUS:
Gene therapy	Released

Description:
This is a World Health Organization (WHO) international standard reference panel of genomic Janus kinase 2 (JAK2) V617F mutation. The panel is intended for use as a primary standard for calibrating secondary standards, assays, and kits for JAK2 V617F detection.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: WHO international standards

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Released

Description:
These are more than 350 World Health Organization (WHO)-determined international standards of various vaccines, serums, antibodies, and reagents that the National Institute for Biological Standards and Control (NIBSC) offers for use in research.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: Working and other standards

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Released

Description:
These are more than 200 working standards and other biological reference materials for use in research and testing.

How to Access this Standard:
Available for purchase from NIBSC.

STANDARD FUNCTIONAL AREA(S):

- Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

ONE Study Consortium

N/A: Standardization of whole blood immune phenotype monitoring by flow cytometry for clinical trials: panels and methods from the ONE study

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published 2013

Description:
This document describes a standardized method for monitoring patients in clinical trials involving transplants—particularly trials of novel tolerance-promoting therapies—to facilitate fair and meaningful comparisons between trials.

How to Access this Standard:
Published in *Transplantation Research*; free access available.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

Parenteral Drug Association (PDA)

N/A: Cryopreservation of Cells

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	In development

Description:
This standard establishes a common framework for selecting minimally damaging cryopreservation methods. The standard provides evidence-based best practices for process variables including media choice, freezing rates, and thaw temperatures.

How to Access this Standard:
This standard is currently in development with PDA. Free access to the draft standard is available during public comment periods.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 33: Evaluation, Validation, and Implementation of Alternative and Rapid Microbiological Methods

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Gene therapy	Published 2013

Description:
This technical report, though not an official standard, was written to establish industry-wide criteria on what constitutes an acceptable alternative or rapid microbiology test to the compendial or classical method and how to prove it to the satisfaction of quality organizations and regulatory agencies. It intends to provide guidance for the successful evaluation, validation, and implementation of alternative and rapid microbiological methods needed by the pharmaceutical, biotechnology, and medical device industries to assure product quality.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 42: Process Validation of Protein Manufacturing

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Published 2005

Description:
This technical report, though not an official standard, focuses on validation of biopharmaceutical processes used to manufacture therapeutic proteins and polypeptides produced from recombinant or non-recombinant cell-culture expression systems. Selected principles may also apply to other product types, such as proteins and polypeptides isolated from tissues and body fluids. The technical report provides practical guidance for compliance with current good manufacturing practices (cGMPs) and ICH guidance's for the validation of biopharmaceutical processes to the drug substance stage.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

TR 47: Preparation of Virus Spikes Used for Virus Clearance Studies

APPLICABLE SECTOR(S):
Cell therapy, Gene therapy

STATUS:
Published 2010

Description:
This technical report represents the efforts of an international task force to define the quality attributes that may be applied to virus and bacteriophage spike preparations, as well as to cell lines used for virus propagation and sample testing. While this report is not a standard, it presents principles important in selecting and defining appropriate quality attributes for selected model viruses, with an emphasis on minimizing the impact of the virus spike itself on the results of validation studies (viral clearance) conducted on scaled-down models of the process unit operation.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 50: Alternative Methods for Mycoplasma Testing

APPLICABLE SECTOR(S):
Cell therapy, Gene therapy

STATUS:
Published 2010

Description:
This technical report discusses alternative methods for mycoplasma detection, though it is not considered an official standard. It focuses on non-culture testing methodology, including Nucleic Acid Amplification Technique assays and enzyme activity-based assays. Representatives of the U.S. FDA and the U.S. Pharmacopeia contributed to the report.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 57: Analytical Method Validation and Transfer for Biotechnology Products

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	Published 2012

Description:
This technical report, though not an official standard, provides practical and strategic guidance for stakeholders to efficiently use historical data and knowledge to design suitable risk-based Analytical Method Validation (AMV) studies and to set appropriate protocol acceptance criteria. The document provides an illustrated map of the typical method lifecycle steps prior, during and beyond the AMV studies to help users visualize their AMV program. The typical sequence of all pre-validation, validation and post-validation steps is reflected in the sequence of sections in the technical report.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 57-2: Analytical Method Development and Qualification for Biotechnology Products

APPLICABLE SECTOR(S):
Cell therapy, Gene therapy, Tissue engineering

STATUS:
Published 2015

Description:
This technical report, though not an official standard, provides practical, risk-based guidance for the development and qualification portions of the analytical method lifecycle for biotechnology products. Method development begins with defining the requirements for the analytical method and leads to, but does not necessarily finish with, its qualification, which is a documented assessment of method performance. Guidance for analytical method development and analytical method qualification studies, such as risk-based strategies and priorities, analytical target profile and quality-by-design concepts, target performance criteria, and modern quality expectations is also included in this report.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 67: Exclusion of Objectionable Microorganisms from Nonsterile Pharmaceuticals, Medical Devices, and Cosmetics

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	Published 2014

Description:
This technical report provides guidance to the nonsterile product manufacturing industry on how to manage the microbial risks associated with manufacturing and storage, as well as how to determine what isolates would be deemed objectionable microorganisms in nonsterile products. This document is intended to be globally applicable, though it is not considered a standard. When country-specific regulations are cited, they serve as examples of such and are not binding to industry stakeholders outside the country's jurisdiction.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 75: Consensus Method for Rating 0.1µm Mycoplasma Reduction Filters

APPLICABLE SECTOR(S):
Cell therapy, Gene therapy

STATUS:
Published 2016

Description:
This technical report, though not an official standard, educates users and filter manufacturers about best practices for mycoplasma reduction filtration and suggests the implementation of a specific filtration testing method and positive controls for establishing a manufacturer's claims of mycoplasma reduction. This technical document recommends a consistent method that filter manufacturers can use to test and rate the effectiveness of mycoplasma reduction filters. The consensus method also provides cultivation parameters for *Acholeplasma laidlawii* as a challenge microorganism, if a risk assessment determines that process-specific evaluation is appropriate.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

TR 81: Cell-Based Therapy Control Strategy

APPLICABLE SECTOR(S):
Cell therapy

STATUS:
Published 2019

Description:
This technical report focuses on the development of a risk-based control strategy adapted to cell-based therapy to mitigate the risk of generating a product of poor quality. This report is not considered a standard but provides best practices on control strategy development.

How to Access this Standard:
Available for purchase from PDA.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

Pharmaceuticals and Medical Devices Agency (PMDA), Japan

MHLW No. 169: Standards for manufacturing and quality control for medical device and in vitro diagnostic reagents

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published 2004; revised 2014

Description:
This Ordinance issued by the Japanese Ministry of Health, Labor, and Welfare describes standards applicable to marketing approval holders, with basic manufacturing control and quality control requirements identical to clauses 4–8 of ISO 13485:2003. That document specifies requirements for a quality management system (QMS) in which an organization must demonstrate its ability to provide medical devices and related services that consistently meet customer and applicable regulatory requirements.

How to Access this Standard:
Free access available from PMDA.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

MHLW No.210: Standards for Biological Materials (in Japanese)

APPLICABLE SECTOR(S):	**STATUS:**
Supportive standard	Published 2004

Description:
This standard covers pharmaceuticals, quasi-drugs, cosmetics, and medical devices, as well as ingredients or materials (e.g., additives, media) derived from humans or other organisms (excluding plants) used in the manufacturing process. This includes raw materials used for *in vitro* diagnostic drugs and other products that are not directly used by the human body and blood products. This standard does not apply to microorganisms and viruses used in the manufacture of materials and vaccines, etc. The standard establishes the necessary measurements to be taken to ensure integrity, quality, effectiveness, and safety of pharmaceutical products.

How to Access this Standard:
Free access available from PMDA (link in Japanese).

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

MHLW No. 266: General principles for the handling and use of cellular/tissue-based products

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published

Description:
The objective of this guideline is to show the basic requirements for handling cells/tissues and to ensure scientific and ethical validity in handling cells/tissues. The major elements addressed in the document are: technological requirements for securing product quality and safety, requirements to be met by medical institutions at the cell/tissue collection stage, review by the Institutional Review Board (IRB), explanation to and informed consent from the donor, matters relating to donor selection criteria and eligibility, and ensuring the appropriateness of the cell/tissue collection process. The document also covers the preparation of the cell/tissue collection record and storage, explanation to and consent from the patient for product application, and matters relating to protection of personal data.

How to Access this Standard:
Developed by PMDA; no link currently available.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

MHLW notifications: autologous No. 0208003, allogenic No. 0912006: Guidelines on ensuring quality and safety of products derived from processed cell/tissue

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published

Description:
This document includes guidelines on ensuring the quality and safety of human or animal cells that have been processed and will be used for the purpose of gene therapy. These cells can be used in the reconstruction, restoration, or formation of body structures, or for the purpose of treating or preventing diseases.

How to Access this Standard:
Free access available from PMDA (links in Japanese).

STANDARD FUNCTIONAL AREA(S):
- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

MHLW No. 1314: Guidelines on ensuring the quality and safety of products derived from processed human stem cells

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published

Description:
This document presents the basic requirements for handling cells and tissues to ensure the quality and safety of drugs derived from these materials. Its purpose is to ensure scientific and ethical validity.

How to Access this Standard:
Free access available from PMDA (link in Japanese).

STANDARD FUNCTIONAL AREA(S):
- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ✓ Preclinical studies
- ✓ Clinical trials

N/A: Points to consider on manufacturing and quality control (MHLW notification No. 0327025, 2008)

APPLICABLE SECTOR(S):	STATUS:
Supportive standard	Published

Description:
A description is unavailable for this standard; however, it was deemed relevant to regenerative medicine therapies and is therefore included as an existing standard.

How to Access this Standard:
Developed by PMDA; no link currently available.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

United States Pharmacopeia (USP)

Catalog #1084292: CD34+ Cell Enumeration System Suitability (1.24 x 10^4 cells) reference material

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Released

Description:
This is a system suitability standard of CD34+ cells. This known amount of cells is used to ensure that cell counting methods (e.g., flow cytometric enumeration methods) produce accurate counts.

How to Access this Standard:
Available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

Catalog #1148089: Collagenase I (2 x 0.5ml) reference material

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Released

Description:
This is a physical reference material of collagenase I. Collagenase can be used to digest connective components in tissue to liberate individual cells for tissue culture studies.

How to Access this Standard:
Available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

Catalog #1148090: Collagenase II (2 x 0.5ml) reference material

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Released

Description:
This is a physical reference material of collagenase II. Collagenase can be used to digest connective components in tissue to liberate individual cells for tissue culture studies. Collagenase II is used to digest lung, kidney, liver, thymus, endothelial, and mesenchymal stem cells.

How to Access this Standard:
Available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

Catalog #1270548: Fetal Bovine Serum (10ml) reference material

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Tissue engineering	Released

Description:
This is a physical reference material of fetal bovine serum. Fetal bovine serum is a growth supplement for cell culture media with a high content of embryonic growth promoting factors.

How to Access this Standard:
Available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

Catalog #1311714: rHuman IL-4 (51mcg) reference material

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Released

Description:
This is a physical reference material of recombinant human IL-4, which is used as an ancillary material in the manufacturing of some cell therapy products.

How to Access this Standard:
Available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: Scaffold Human Amniotic Membrane Allograft

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published; Currently Official USP41-NF36 2S; 2019

Description:
This monograph describes the sourcing, isolation, sterilization, and testing of Scaffold Human Amniotic Membrane Allografts, a human tissue that is composed predominantly of collagen and elastin.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

N/A: Trypsin Recombinant Porcine

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published

Description:
This document details a standard amount of trypsin, recombinant porcine, used as raw material for the production of active pharmaceutical ingredients (APIs).

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- Analytical and testing methodologies
- Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

USP <89>: Enzymes Used as Ancillary Materials in Pharmaceutical Manufacturing

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published; Currently Official USP41-NF36; 2015

Description:
The purpose of this chapter is to describe the quality attributes and associated tests with acceptance criteria for enzymatic preparations used in biopharmaceutical manufacturing. The quality of ancillary materials, including enzymes, used in biopharmaceutical manufacturing can have an impact on the therapeutic products. Several enzymes are used in this type of cell processing. Examples include trypsin, collagenase, pepsin, and papain. This chapter does not discuss applications of these enzymes but rather focuses on tests to assess their quality as process materials.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

USP <89.1>: Collagenase I

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published; Currently Official USP41-NF36; 2017

Description:
USP <89> describes the quality attributes and associated tests with acceptance criteria for enzymatic preparations used in biopharmaceutical manufacturing. The quality of ancillary materials, including enzymes, used in biopharmaceutical manufacturing can have an impact on the therapeutic products. Several enzymes are used in this type of cell processing. Examples include trypsin, collagenase, pepsin, and papain. The chapter does not discuss applications of these enzymes but rather focuses on tests to assess their quality as process materials.

USP <89.1> provides analytical procedures to aid in the assessment of quality for collagenase I isolated from Clostridium histolyticum. Collagenase I isolated from Clostridium histolyticum is a key raw material used in the dissociation or destruction of a broad range of tissue types. This chapter is part of a series of general chapters that are under development to address the qualities of the enzymes used as ancillary materials in pharmaceutical manufacturing.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

USP <89.2>: Collagenase II

APPLICABLE SECTOR(S):
Cell therapy, Tissue engineering

STATUS:
Published; Currently Official USP41-NF36; 2017

Description:
USP <89> describes the quality attributes and associated tests with acceptance criteria for enzymatic preparations used in biopharmaceutical manufacturing. The quality of ancillary materials, including enzymes, used in biopharmaceutical manufacturing can have an impact on the therapeutic products. Several enzymes are used in this type of cell processing. Examples include trypsin, collagenase, pepsin, and papain. The chapter does not discuss applications of these enzymes but rather focuses on tests to assess their quality as process materials.

USP <89.2> provides analytical procedures to aid in the assessment of quality for collagenase II isolated from Clostridium histolyticum. Collagenase II isolated from Clostridium histolyticum is a key raw material used in the dissociation or destruction of a broad range of tissue types. This chapter is part of a series of general chapters that are under development to address the qualities of the enzymes used as ancillary materials in pharmaceutical manufacturing.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

USP <90>: Fetal Bovine Serum—Quality Attributes and Functionality Tests

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published; Currently Official USP41-NF36; 2013

Description:
This chapter covers the testing and specifications for identity, functionality, and other tests of fetal bovine serum, which is used as a component of growth media to support the proliferation of cells in culture. This general information chapter provides analysts with (a) procedures to measure the fetal bovine serum quality attributes and (b) functionality assays to assess performance of different types and lots of fetal bovine serum.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- Logistics and compliance criteria
- Preclinical studies
- Clinical trials

USP <92>: Growth Factors and Cytokines Used in Cell Therapy Manufacturing

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published; Currently Official USP41-NF36; 2013

Description:
This chapter provides general considerations and requirements for growth factors and cytokines used in cell manufacturing. Growth factors and cytokines are important for the maintenance, growth, selection, and purification of cultures of cell therapy products. This chapter describes the accepted tests, procedures, and acceptance criteria for growth factors and cytokines that may be involved in the manufacturing of cell therapy products.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <127>: Flow Cytometric Enumeration of CD34+ Cells

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published

Description:
This standard describes a method of cell enumeration for human hematopoietic stem and progenitor cells that possess the CD34 antigen on their surface. The single-platform flow cytometric CD34+ cell enumeration method described in this standard can be used to enumerate CD34+ cells in samples of peripheral blood, leukapheresis products, bone marrow, and cord blood.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <130>: Protein A Quality Attributes

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	Published; Currently Official USP41-NF36; 2013

Description:
This chapter describes quality attributes of protein A ligands that are used in chromatography media for the manufacture of therapeutic monoclonal antibodies such as: Protein A; rProtein A; rProtein A, C-Cys; rProtein A, B4, and C-Cys.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <1024>: Bovine Serum

APPLICABLE SECTOR(S):	STATUS:
Cell therapy, Tissue engineering	Published; Currently Official USP41-NF36; 2013

Description:
This chapter describes issues related to sourcing, production, and characterization of bovine serum to ensure its safe use. A list of relevant regulatory and guidance documents is presented in appendix 1. Serum manufacturers and serum end users (manufacturers of biological products) should consider and apply as needed the controls and procedures outlined in this chapter to ensure the safe use of bovine serum components in research and pharmaceutical manufacturing.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ○ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <1027>: Flow Cytometry

APPLICABLE SECTOR(S):	STATUS:
Cell therapy	Published; Currently Official USP41-NF36; 2013

Description:
This chapter presents the technical aspects of the flow cytometry method, including instrumentation, sample handling and staining, and data analysis. Sources of error are considered in the context of technical features, as well as in the discussion of quality control, quality assurance, and standardization.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ○ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ○ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <1043>: Ancillary Materials for Cell, Gene, and Tissue-Engineered Products

APPLICABLE SECTOR(S):
Cell therapy, Gene therapy, Tissue engineering

STATUS:
Published; Currently Official USP41-NF36; 2013

Description:
This chapter provides guidance on the development of appropriate material qualification programs for cell, gene, and tissue-engineered products. Because cell, gene, and tissue-engineered products are not usually amenable to extensive purification, filtration, and terminal sterilization procedures, reagents and material qualification are critically important to ensuring product quality.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ○ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <1046>: Cell and Gene Therapies Products

APPLICABLE SECTOR(S):	**STATUS:**
Cell therapy, Gene therapy, Tissue engineering	Published; Currently Official USP41-NF36; 2013

Description:
This general chapter of USP <35> provides a comprehensive overview of considerations for the development of cellular- and tissue-based products. It includes issues related to the manufacturing, sourcing of components, and characterization of cellular or tissue-based products to ensure their safety and efficacy. A list of relevant regulatory and guidance documents is presented in the Appendix.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

USP <1047>: Gene Therapy Products

APPLICABLE SECTOR(S):	**STATUS:**
Gene therapy	Published; Currently Official USP41-NF36; 2013

Description:
This chapter summarizes the issues and best current practices in the manufacturing, testing, and administration of gene therapy products. A list of regulatory and guidance documents applicable to gene therapy is presented in the appendix, together with a list of terms commonly used in the gene therapy field. This chapter attempts to specify when traditional methodologies or standards can be adapted.

How to Access this Standard:
The complete United States Pharmacopeia-National Formulary (USP-NF) is available for purchase from USP.

STANDARD FUNCTIONAL AREA(S):

- ✓ Bioprocessing and production, including equipment or raw/ancillary materials or ingredient specifications
- ✓ Analytical and testing methodologies
- ✓ Product quality and characterization (e.g., identity, potency, or performance characteristics)
- ✓ Logistics and compliance criteria
- ○ Preclinical studies
- ○ Clinical trials

APPENDIX B. ABOUT NEXIGHT GROUP AND THE STANDARDS COORDINATING BODY

In September 2017, the U.S. Food and Drug Administration (FDA) engaged Nexight Group and The Standards Coordinating Body for Gene, Cell, and Regenerative Medicines and Cell-Based Drug Discovery (SCB) to coordinate with experts, increase community participation in the identification and prioritization of needed standards, and support the advancement of the most promising standards for regenerative medicine and advanced therapies.

Nexight Group is a small business based in Silver Spring, Maryland, with extensive experience engaging diverse experts in discussions about gaps and needed solutions to advance scientific fields, establishing new collaborative organizations, developing roadmaps and strategic plans, establishing new business processes, and supporting technical education and outreach efforts. In collaboration with the Georgia Institute of Technology and the Georgia Research Alliance, Nexight Group led the coordination and development of *Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells: A Technology Roadmap to 2025*, a roadmap that aims to facilitate widespread access to life-changing cell therapies, engineered tissues, medical devices, and drug discovery and testing platforms through collaborative research and development.

The Standards Coordinating Body (SCB) is a non-profit organization with a mission to coordinate the accelerated advancement and improved awareness of standards and best practices that address the rapidly evolving needs of the global regenerative medicine advanced therapy community. To accomplish its mission, SCB operates through public-private partnerships with government agencies, regulatory bodies, and other government organizations involved in establishing consensus standards for regenerative medicine and other advanced therapy products. With members from industry, professional societies, and government and academic entities, SCB occupies a unique niche within the regenerative medicine ecosystem and has no vested interests in a particular scientific, commercial, clinical, or policy approach. SCB is focused on facilitating the use and development of standards in response to demonstrated need expressed by a range of stakeholders.

APPENDIX C. ACRONYMS AND ABBREVIATIONS

Acronym / Abbreviation	Definition
AATB	American Association of Tissue Banks
AAV	adeno-associated virus
AAVRSWG	Adeno-Associated Virus Reference Standard Working Group
AM	ancillary material
AMV	Analytical Method Validation
ANSI	American National Standards Institute
API	active pharmaceutical ingredient
ARM	adenovirus reference material
ASHI	American Society of Histocompatibility & Immunogenetics
ATCC	American Type Culture Collection
ATMP	advanced therapy medicine product
BCR-ABL	breakpoint cluster region-Abelson murine leukemia viral oncogene homolog 1
BM	bone marrow
BSI	British Standards Institution
CAR	chimeric antigen receptor
CB	cord blood
CBMP	cell-based medicinal product
CCD	charge coupled device
cDNA	complementary DNA
CFC	colony forming cell
CFU	colony forming unit
cGMPs	current good manufacturing practices
CLR	Classification Results File Format
CLSI	Clinical & Laboratory Standards Institute
CQA	critical quality attribute
CTP	cellular therapy product
DA	deacetylation
DBM	demineralized bone matrix
dECM	decellularized extracellular matrix
dPBS	Dulbecco's phosphate-buffered saline
dPCR	digital polymerase chain reaction

Acronym / Abbreviation	Definition
DNA	deoxyribonucleic acid
DT	diffusion tensor
EDQM	European Directorate for the Quality of Medicines and Healthcare
EFI	European Federation for Immunogenetics
ERF	Equivalent Reference Fluorophore
EU	European Union
FACT	Foundation for the Accreditation of Cellular Therapy
FCS	flow cytometry standard
FDA	U.S. Food and Drug Administration
FOV	field of view
gDNA	genomic DNA
GMP	good manufacturing practice
hBM-MSCs	human mesenchymal stromal cells derived from bone marrow
HCT/P	human cell, tissue, and cellular and tissue-based product
HIV	human immunodeficiency virus
HLA-DRB1	human leukocyte antigen class II histocompatibility antigen D related beta chain
HNPCC	hereditary nonpolyposis colorectal cancer
HPC	hematopoietic progenitor cells
HSC	hematopoietic stem cell
HSCT	hematopoietic stem cell transplantation
HSV-1	Herpes Simplex Virus 1
HSV-2	Herpes Simplex Virus 2
HTLV-1	human T-lymphotropic virus
ICCBBA	International Council for Commonality in Blood Banking Automation
ICEFormat	Image Cytometry Experiment Format
ICH	International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use
ICT	Information and Communications Technology
IFATS	International Federation of Adipose Therapeutics
IRB	Institutional Review Board
ISA	International Society of Automation
ISAC	International Society for Advancement of Cytometry
ISBER	International Society for Biological and Environmental Repositories
ISCT	International Society for Cellular Therapy
ISO	International Organization for Standardization

Acronym / Abbreviation	Definition
ISSCR	International Society for Stem Cell Research
ITR	inverted terminal repeat
IVD	in vitro diagnostic device
JAK2	Janus kinase 2
LSAPC	light scattering airborne particle counters
MALL	maximum allowable leakage limit
MESF	Mean Equivalent Soluble Fluorophores
microCT	micro-computed tomography
MIFlowCyt	Minimum Information about a Flow Cytometry Experiment
MLH1	DNA mismatch repair protein MutL homolog 1
MLPA	multiplex ligation-dependent probe amplification
mM	Millimolar
MRI	magnetic resonance imaging
MSC	mesenchymal stromal cells
MSH2	DNA mismatch repair protein MutL homolog 2
NIBIB	National Institute of Biomedical Imaging and Bioengineering
NIBSC	National Institute for Biological Standards and Control
NIH	National Institutes of Health
NIST	National Institute of Standards and Technology
NMR	nuclear magnetic resonance
NTTAA	National Technology Transfer and Advancement Act
OEM	original equipment manufacturer
PAS	publicly available specification
PDA	Parenteral Drug Association
PB	peripheral blood
PBS	phosphate buffered saline
PCR	polymerase chain reaction
PLGA	poly-lactic-co-glycolic acid
PMDA	Pharmaceuticals and Medical Devices Agency, Japan
PRP	platelet-rich plasma
PSC	pluripotent stem cell
QCRU	quality control reagents unit
qPCR	quantitative Polymerase Chain Reaction
rAAV	recombinant adeno-associated virus
rAAV2	recombinant adeno-associated virus serotype 2

Acronym / Abbreviation	Definition
rAAV8	recombinant adeno-associated virus serotype 8
rhBMP-2	recombinant human bone morphogenetic protein-2
RhD	Rh blood group, D antigen
RIM	Random Illumination Microscopy
RMTM	rapid microbial test method
RNA	ribonucleic acid
RQ-PCR	real-time polymerase chain reaction
RSS	reference standard stock
SCB	Standards Coordinating Body for Gene, Cell, and Regenerative Medicines and Cell-Based Drug Discovery
sCMOS	scientific complementary metal oxide semiconductor
SDO	standards developing organization
SEC-MALS	size exclusion chromatography with multi-angle light scattering detection
sGAG	sulfated glycosaminoglycans
SOP	standard operating procedures
SRY	sex-determining region Y
SSO-PCR	sequence-specific oligonucleotide polymerase chain reaction
SSP-PCR	single specific primer polymerase chain reaction
STR	short tandem repeat
SUS	single-use system
SVF	stromal vascular fraction
TAE	total analytical error
TEMP	tissue-engineered medical product
TSE	transmissible spongiform encephalopathy
USP	United States Pharmacopeia
VDI	Association of German Engineers
WHO	World Health Organization
WJ	Wharton's jelly