The 23rd Congress of the Japanese Society for Regenerative Medicine
Symposium 16 “Standards -A tool to connect academia and industry-
シンポジウム16　標準　～アカデミアと産業界をつなぐためのツール～

International standards for industries related to regenerative medicine

再生医療の周辺産業に関する国際標準

Mar. 21st, 2024
Tetsunori Matsumoto
SHISEIDO

DYNAMIC HARMONY
Incremental/Disruptive

Agenda

- Introduction
- Standards for Industries Related to Regenerative Medicine
  - Transportation
  - Ancillary materials
  - Equipment Systems, Packaging, Labeling Materials
- Utilization of Standards for Industries Related to Regenerative Medicine
  - FDA Voluntary Consensus Standards Recognition Program
  - FIRM Certification System
  - Benefits for International Standards

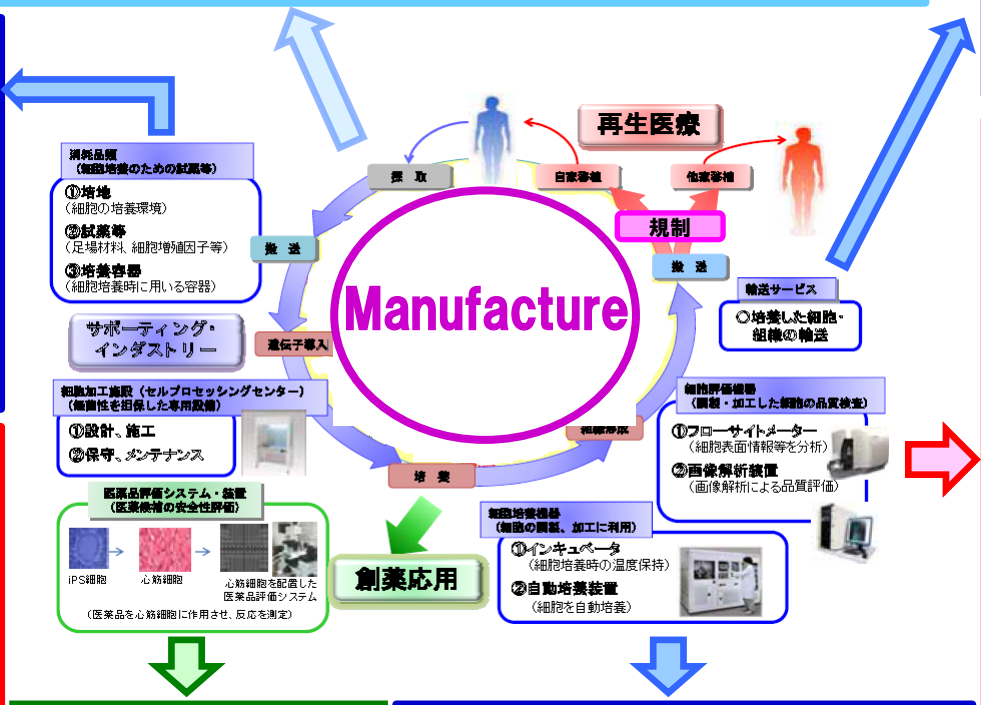
Introduction

Overview of Standards in Regenerative Medicine

Cellular starting materials

Supporting industries
SY-16-5

Supporting industries
SY-16-5



Analytical methods

Related field
(Gene delivery System)

Related field

Supporting industries
SY-16-5

ISO/TC276 Biotechnology

ISO/TC 276:Biotechnology
Chair : Germany, Vice Chair : China

SC1 Analytical Methods Chair:US
- WG1:Gene delivery
- WG2:Cell Characterization
- WG3:Nucleic Acid Characterization

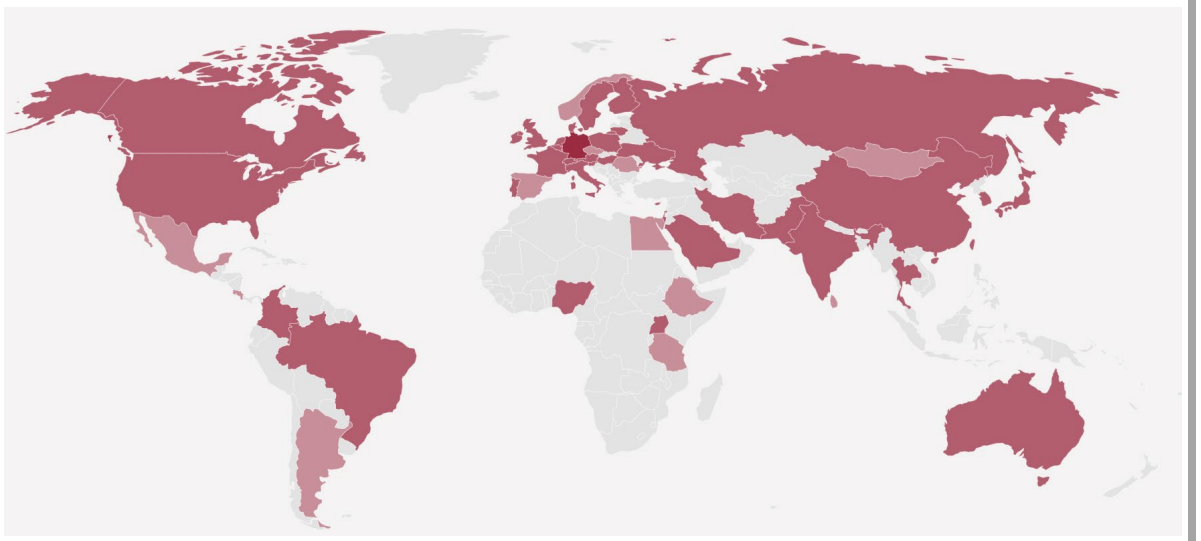
WG2:Biobanks and bioresources
Convenor:Austria

WG4:Bioprocessing
Convenor:Japan

WG5:Data processing and integration
Convenor:Germany

WG6:Nucleic acid- and protein-based devices
Convenor:China

Japan mirror committee
85 members from industry, academia and government



Participating member :38 Countries

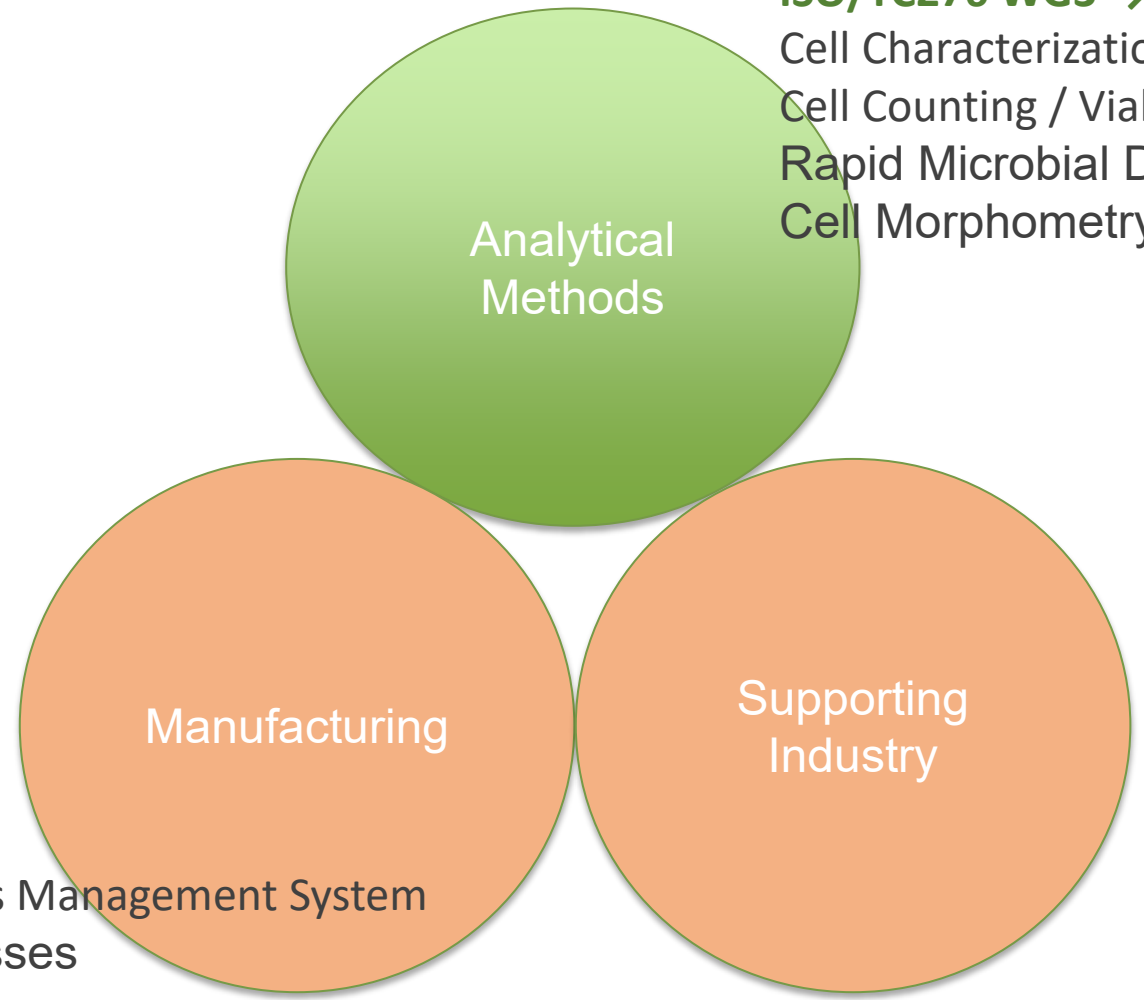
Australia, Austria, Belgium, Brazil, Canada, China, Colombia, Cyprus, Denmark, Finland, France, Germany, Hungary, India, Islamic Republic of Iran, Ireland, Israel, Italy, Japan, Republic of Korea, Lithuania, Luxembourg, Netherlands, Nigeria, Pakistan, Poland, Portugal, Russian Federation, Saudi Arabia, Singapore, Slovenia, Sweden, Switzerland, Uganda, Ukraine, United Kingdom, United States

Observing member :15Countries

Argentina, Costa Rica, Czech Republic, Egypt, Ethiopia, Hong Kong, Kenya, Malta, Mexico, Mongolia, Norway, Romania, Spain, United Republic of Tanzania, Thailand

Standards for Industries Related to Regenerative Medicine
再生医療周辺産業の国際標準

ISO/TC276 WG3 → ISO/TC276/SC1
Cell Characterization
Cell Counting / Viability
Rapid Microbial Detection
Cell Morphometry



ISO/TC276/WG4
JIS
Cell Manufacturing Process Management System
Cryopreservation Processes

ISO/TC276 WG4
Ancillary Materials
Transportation
Equipment Systems
Packaging
CoA of Ancillary Materials
Labeling Materials

Value Chain for Regenerative Medicine and Standards

Material Cell (WG 2/4)

Biobanking

ISO 20387:2018:General requirements for **biobanking**

Supply facility of Cellular starting materials

under consideration

Supporting Industry (WG 4)

Ancillary material

ISO 20399:2022

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

Packaging

ISO 20404:2023

General requirements for the **design of packaging** to contain cells for therapeutic use

Gene Delivery (WG 3)

Vocabulary

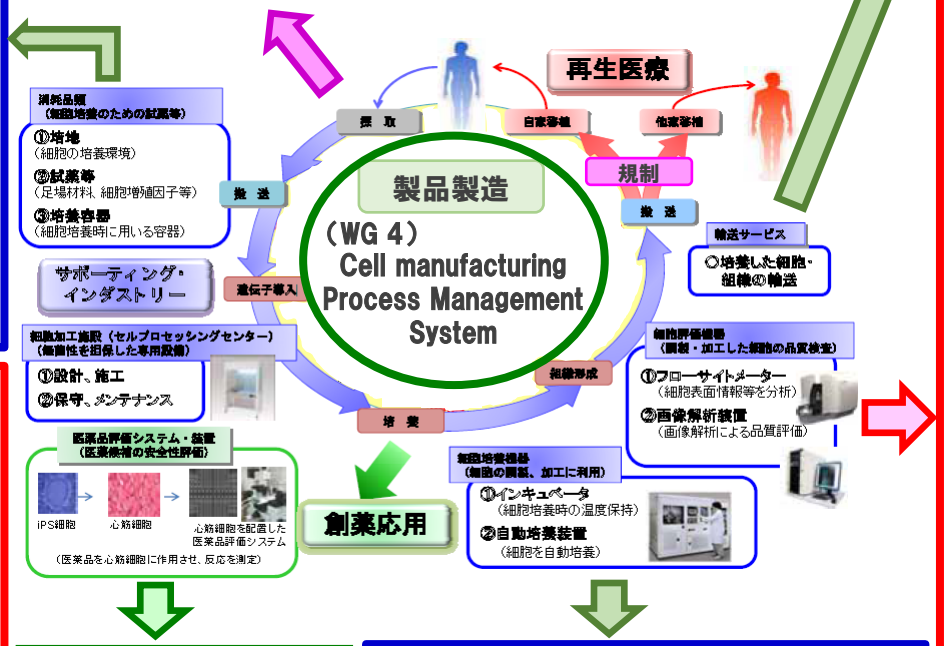
ISO/WD 16921-1:Gene Delivery Systems — Part 1: Vocabulary

Viral Vector

ISO/WD 16921-2:Gene Delivery Systems — Part 2: Guide for Methods for the Qualification of Viral Vectors

mRNA-Lipid Nanoparticles

ISO/PWI 16921-3:Gene Delivery Systems — Part 3: Guide for Methods for the Measurements of mRNA-Lipid Nanoparticles



Drug discovery support

under consideration

Manufacturing equipment (WG 4)

Equipment system

ISO/TS 23565:2021

General requirements and considerations for **equipment systems** used in the manufacturing of cells for therapeutic use

Supporting Industry (WG 4)

transportation

ISO 21973:2020:General requirements for **transportation** of cells for therapeutic use

Analytical method (WG 3)

testing and characterization

ISO 23033:2021:General requirements and considerations for the **testing and characterization** of cellular therapeutic products

Cell counting - General guidance

ISO 20391-1:2018:**Cell counting** -- Part 1: **General guidance** on cell counting methods

Cell counting - Experimental design

ISO 20391-2:2019:**Experimental design and statistical analysis** to quantify counting method performance

Rapid microbial detection

ISO 24190:2023:Risk based approach for method selection and validation of methods for **rapid microbial detection** in bioprocesses

Cell viability

ISO/CD 8934:General considerations and requirements for **cell viability** analytical methods — Part 1: Mammalian cells

Cell morphology

ISO/DIS 24479:Minimum requirements for cellular morphological analysis

Standards for Industries Related to Regenerative Medicine

Standards for Industries Related to Regenerative Medicine

ISO/TC 276

Biotechnology

34 Published ISO standards *

23 ISO standards under development *

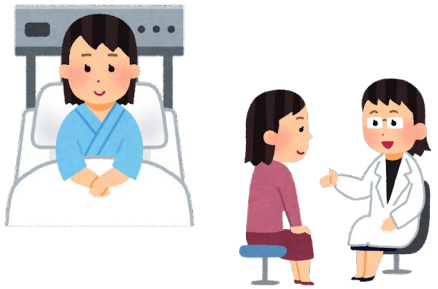
WG4	ISO 20399 :2022	Ancillary materials present during the production of cellular therapeutic products and gene therapy products
	ISO 21973 :2020	General requirements for transportation of cells for therapeutic use
	ISO/TS 23565:2021	General requirements and considerations for equipment systems used in the manufacturing of cells for therapeutic use
	ISO 20404 :2023	General requirements for the design of packaging to contain cells for therapeutic use
Under Development		Guidelines for Certificate of Analysis of Ancillary Materials Used in Cell and Gene Therapy Product Manufacturing
		Labeling Materials

Industries Related to Regenerative Medicine

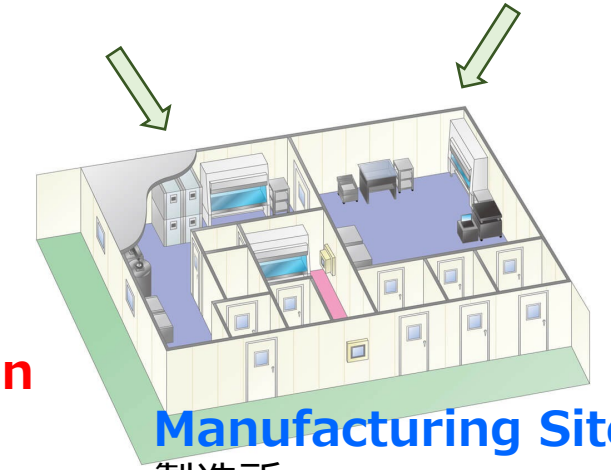
Ancillary Materials
CoA
原料

Equipment

Starting Materials
Cell / Tissue
原料（細胞/組織）



Transportation
輸送



Manufacturing Site
製造所
細胞培養加工施設

Transportation
輸送

Medical Institution
医療機関
再生医療等提供機関

Medical Institution
Cell Bank

Packaging

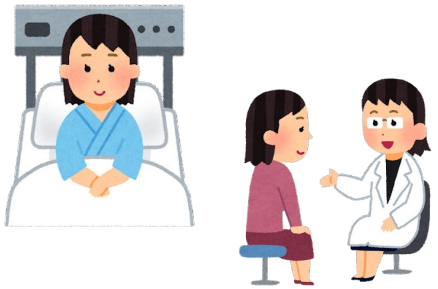
Labeling Materials

Standard for Transportations

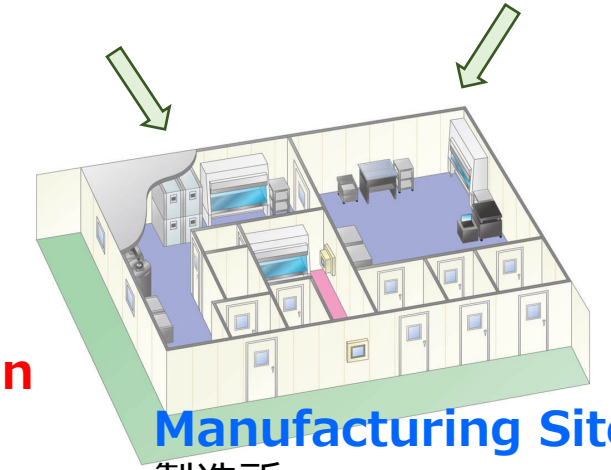
Ancillary Materials
原料

Equipment

Starting Materials
Cell / Tissue
原料（細胞/組織）



Transportation
輸送



Manufacturing Site
製造所
細胞培養加工施設

Transportation
輸送

Medical Institution
医療機関
再生医療等提供機関

Medical Institution
Cell Bank

Packaging

Labeling Materials

ISO 21973:2020
バイオテクノロジー－治療用細胞の輸送に関する一般要求事項
Biotechnology -- General requirements for transportation of cells for therapeutic use

Cell / Tissue Collection
細胞/組織採取

Patients
患者

Transportation
輸送

Manufacturing Site
製造所
細胞培養加工施設

輸送

医療機関
再生医療等提供機関

Transportation
輸送

Transportation
輸送

Donor
ドナー

細胞バンク

輸送時の要求事項　様々
輸送容器の能力
　温度、時間、振動、・・・

ISO 21973:2020
バイオテクノロジー－治療用細胞の輸送に関する一般要求事項
Biotechnology -- General requirements for transportation of cells for therapeutic use

Abstract

This document specifies general requirements and reviews the points to consider for the transportation of cells for therapeutic use, including storage during transportation.

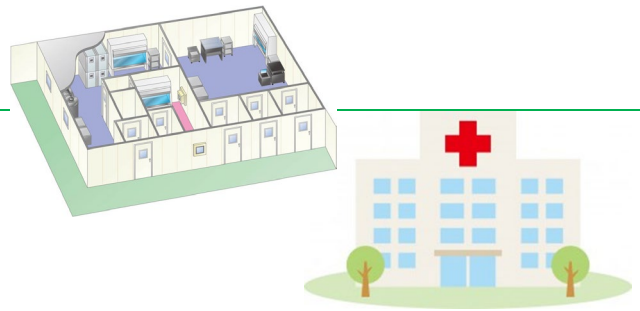
Transportation starts from the transfer of the packaged cells by the sender to the transportation service provider and ends when the package is delivered to the receiver at its destination.

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.

https://www.iso.org/standard/72326.html



ISO 21973:2020
バイオテクノロジー－治療用細胞の輸送に関する一般要求事項
Biotechnology -- General requirements for transportation of cells for therapeutic use

原料（細胞/組織）

Transportation
輸送

製造所
細胞培養加工施設

Transportation
輸送

医療機関
再生医療等提供機関

Appropriate transportation
・Planning/Implementation Validation
・Traceability
・Documentation

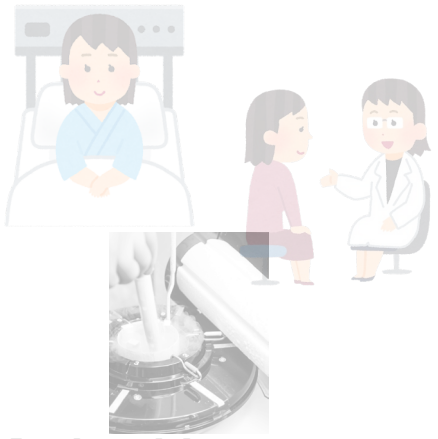
Client ⟺ Transportation Service Provider
Communication

ISO 20399:2022 製造補助材料（原料）
Ancillary materials present during the production of cellular therapeutic products and gene therapy products

Ancillary Materials
原料

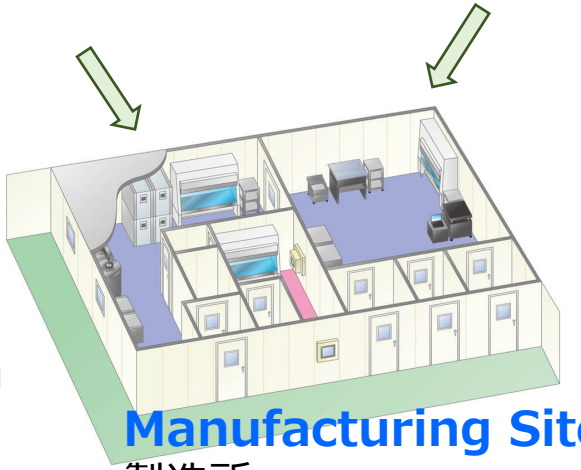
Equipment

Starting Materials
Cell / Tissue
原料（細胞/組織）



Medical Institution
Cell Bank

Transportation
輸送



Manufacturing Site
製造所
細胞培養加工施設

Packaging

Labeling Materials

Transportation
輸送

Medical Institution
医療機関
再生医療等提供機関

ISO 20399:2022
Biotechnology
Ancillary materials present during the production of cellular therapeutic products and gene therapy products

Abstract

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

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

EXAMPLE
Reagents, anticoagulants, cytokines, growth factors, enzymes, antibodies, serum, buffered solutions, culture media, ····

TECHNICAL SPECIFICATION ISO/TS 20399-1~3

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

Part 1:
General requirements

Part 2:
Best practice guidance for ancillary material suppliers

Part 3:
Best practice guidance for ancillary material users 2019/08

INTERNATIONAL STANDARD ISO20399

Biotechnology — Ancillary materials present during the production of cellular therapeutic products and gene therapy products 2022/12

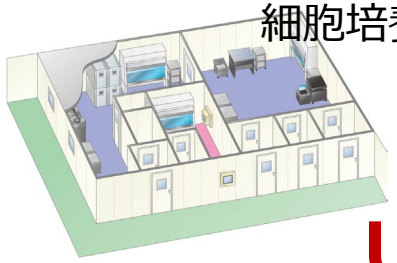
ISO 20399:2022
Biotechnology
Ancillary materials present during the production of cellular therapeutic products and gene therapy products

Ancillary Materials Manufacture

Supplier

Transportation

Manufacturing Site
製造所
細胞培養加工施設



User

Master File

Safety
動物由来原料

安定性

規格及び試験方法

CoA

Information to be provided

Communication

User Requirement

Supplier Qualification

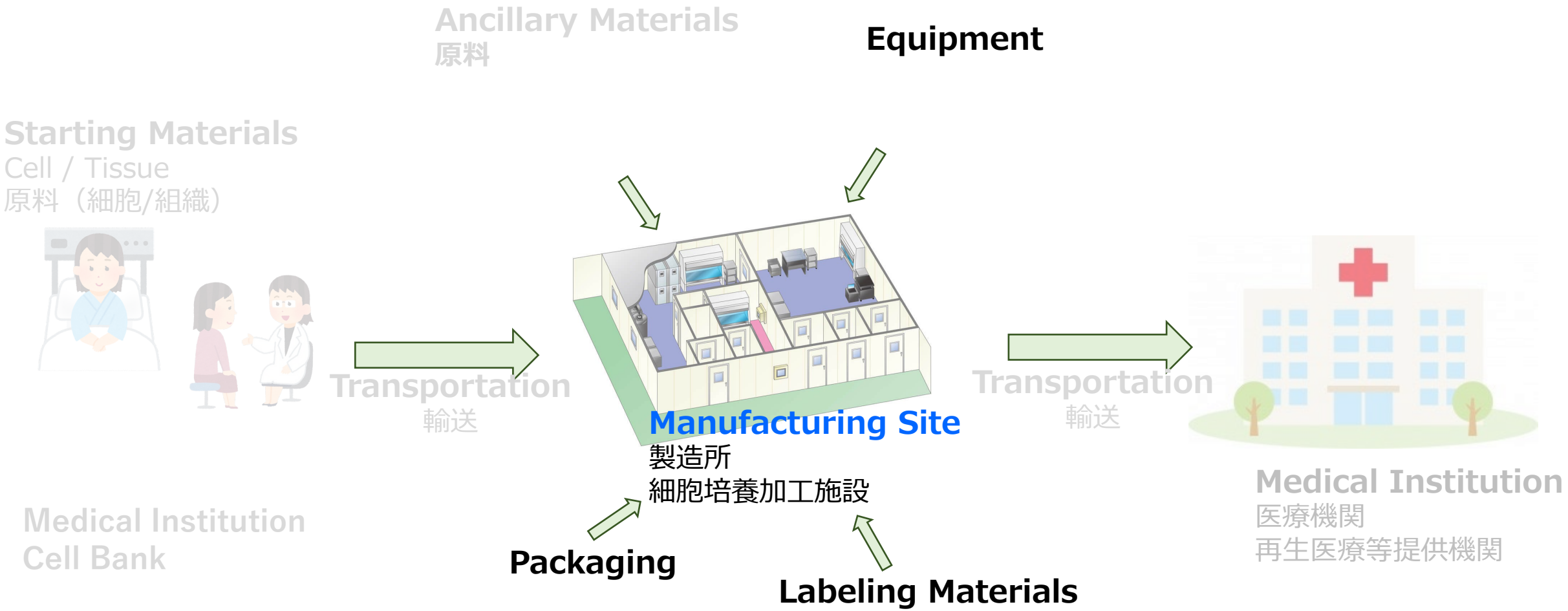
Qualification for intended purpose

Audit

Confirmation of CoA

Fitness for purpose

ISO 20399:2022 製造補助材料（原料）
Ancillary materials present during the production of cellular therapeutic products and gene therapy products



ISO/TS 23565:2021
General requirements and considerations for equipment systems used in the manufacturing of cells for therapeutic use

Abstract

This document specifies minimum requirements and general considerations for **equipment, consisting of hardware, software and consumables**, used in the manufacturing of cells for therapeutic use. This includes equipment for processing cells for therapeutic use starting **from cell isolation/selection, expansion, washing and volume reduction, from cell finish through to cryopreservation for the storage of cells** for therapeutic use.

This document gives guidance on the **design, use and maintenance** of equipment and equipment systems to **both suppliers and users** from aspects including the target parties, i.e. supplier or user, and phase of involved task, i.e. design, use or maintenance.

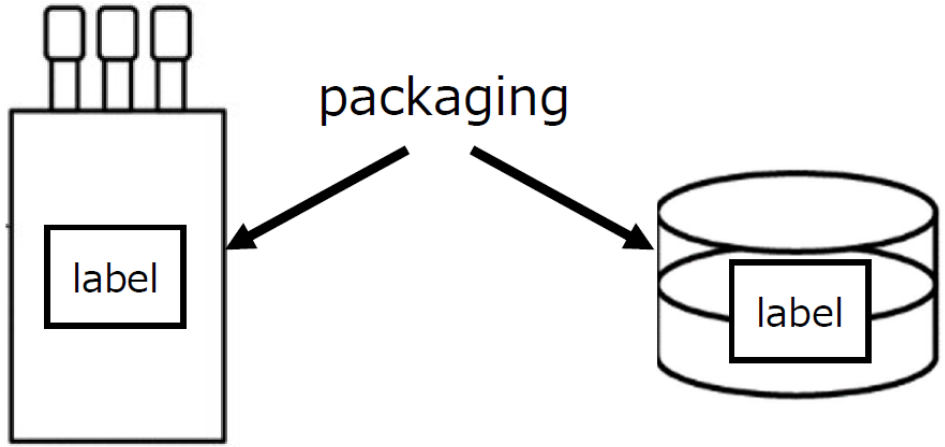
ISO 20404:2023
Biotechnology
General requirements for the design of packaging to contain cells for therapeutic use

Abstract
This document specifies general requirements and considerations for the design of **packaging used to contain cells for therapeutic use**.

This document is applicable to packaging intended to contain the **final products** of cells for therapeutic use, as well as their **starting and intermediate materials**.

This document does not apply to:
a) receptacles used for processing cells in manufacturing processes, e.g. cell culture flask or bag;
b) shipping containers containing packages for transportation;
c) services that utilize packages, e.g. storage services.

Standard for Labeling Materials



Under Development!

Storage Conditions

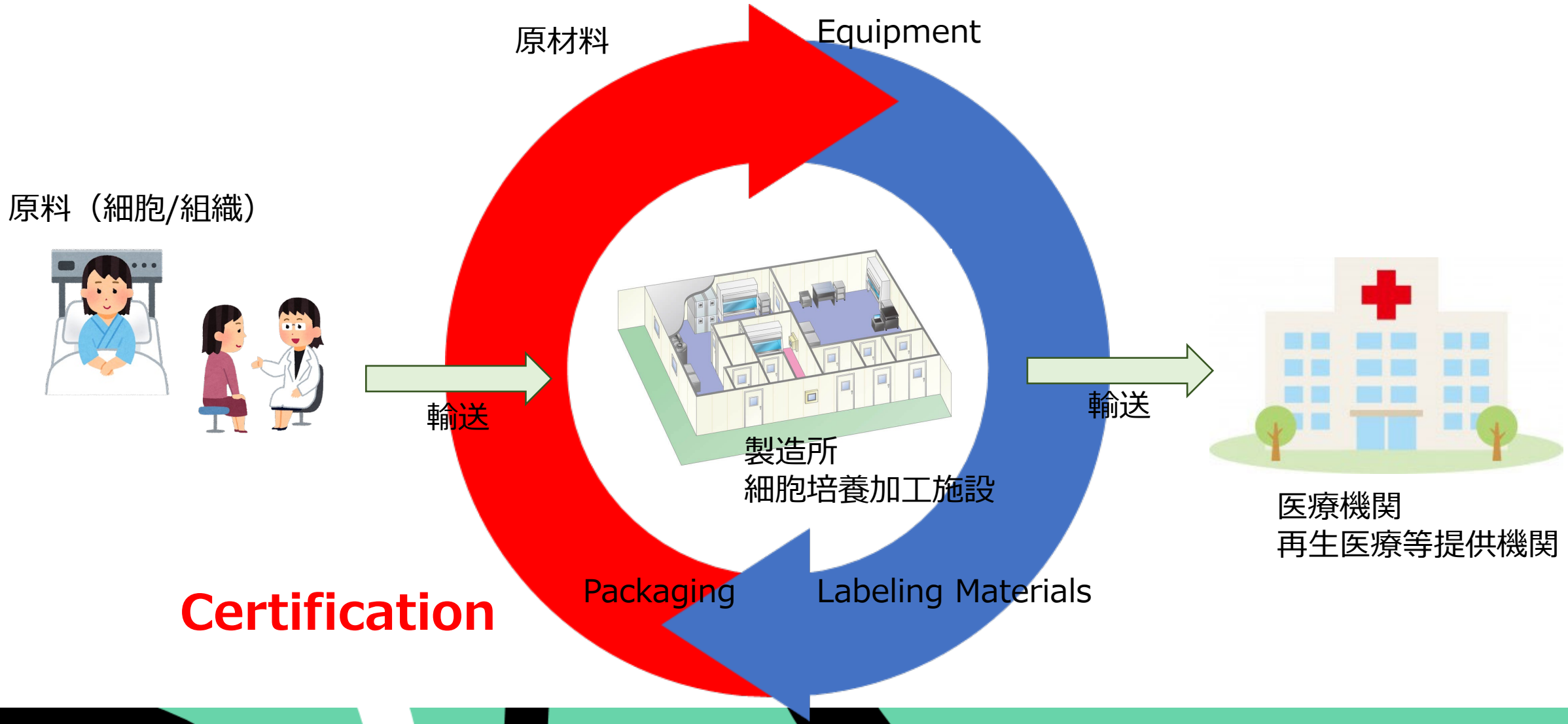
Storage conditions are significantly different, is not used for small molecule drugs.

Product Mix-Ups

For autologous cell products, it is essential to prevent mix-ups.

Utilization of Standards for Industries Related to Regenerative Medicine

Utilization of Standards for Industries Related to Regenerative Medicine



Encouragement of the use of appropriate standards in the development of RM products
FDAによる国際標準活用の推奨


U.S. FOOD & DRUG ADMINISTRATION

Home / Vaccines, Blood & Biologics / Standards Development for Regenerative Medicine Therapies

Standards Development for Regenerative Medicine Therapies

CBER Voluntary Consensus Standards Recognition Program for Regenerative Medicine Therapies

Last updated on November 28, 2023

Recognition Number	SDO	Designation ID	Year	Title	Recognition Status	Standard Recognition Summary (SRS)
011	ISO	23033	2021	General requirements and considerations for the testing and characterization of cellular therapeutic products	Complete Recognition	Rec 011
019	ISO	21973	2020	General requirements for transportation of cells for therapeutic use	Complete Recognition	Rec 019
021	ASTM	F3259	2017	Standard Guide for Micro-computed Tomography of Tissue Engineered Scaffolds	Complete Recognition	Rec 021
023	ASTM	F3106	2022	Standard guide for in vitro Osteoblast Differentiation Assays	Complete Recognition	Rec 023
025	ISO	20399	2022	Biotechnology - Ancillary materials present during the production of cellular therapeutic products and gene therapy products	Complete Recognition	Rec 025

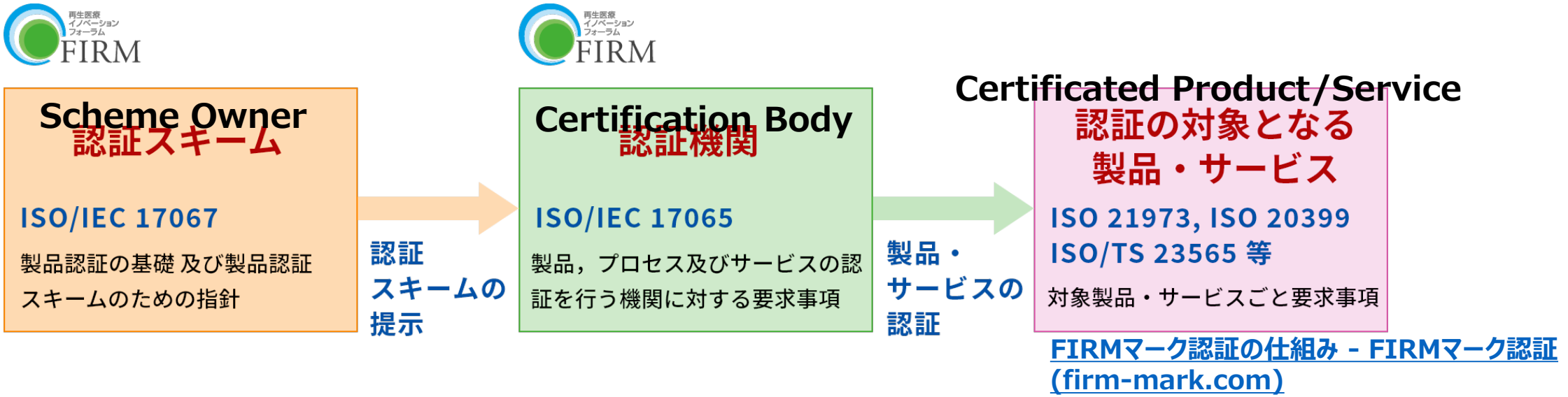
https://www.fda.gov/vaccines-blood-biologics/standards-development-regenerative-medicine-therapies

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/voluntary-consensus-standards-recognition-program-regenerative-medicine-therapies

FIRM Certification System

FIRMマーク認証

再生医療周辺産業の製品・サービスに対する認証制度



FIRMマーク認証の仕組み - FIRMマーク認証 (firm-mark.com)

Certification based on the requirements stated in ISO standards (applicable standards).

Products and Services that are certified to use the FIRM mark.

FIRM Certification System

FIRMマーク認証

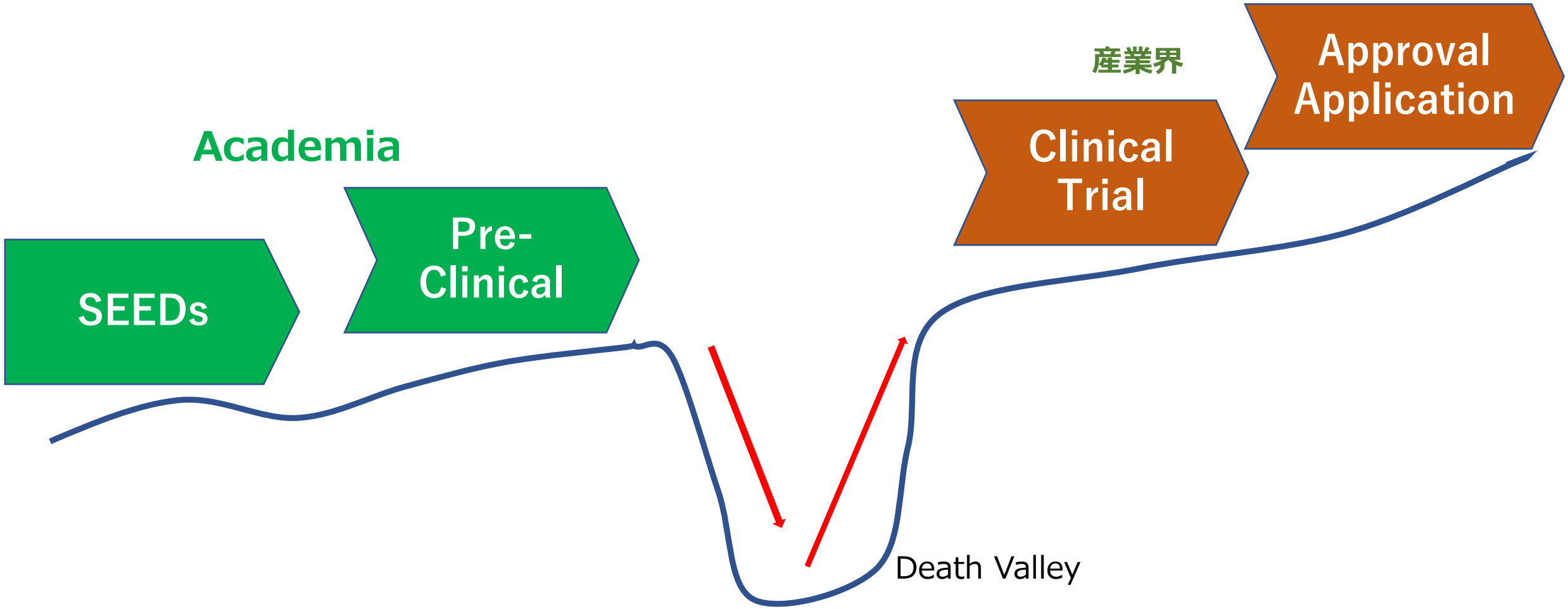
再生医療周辺産業の製品・サービスに対する認証制度

Certification Scheme	Applied Standards
Transportation Service* Shipping Container*	ISO 21973:2020 General requirements for transportation of cells for therapeutic use
Ancillary Materials*	ISO 20399:2022 Ancillary materials present during the production of cellular therapeutic products and gene therapy products
Equipment Systems	ISO/TS 23565:2021 General requirements and considerations for equipment systems used in the manufacturing of cells for therapeutic use
Packaging	ISO 20404:2023 General requirements for the design of packaging to contain cells for therapeutic use

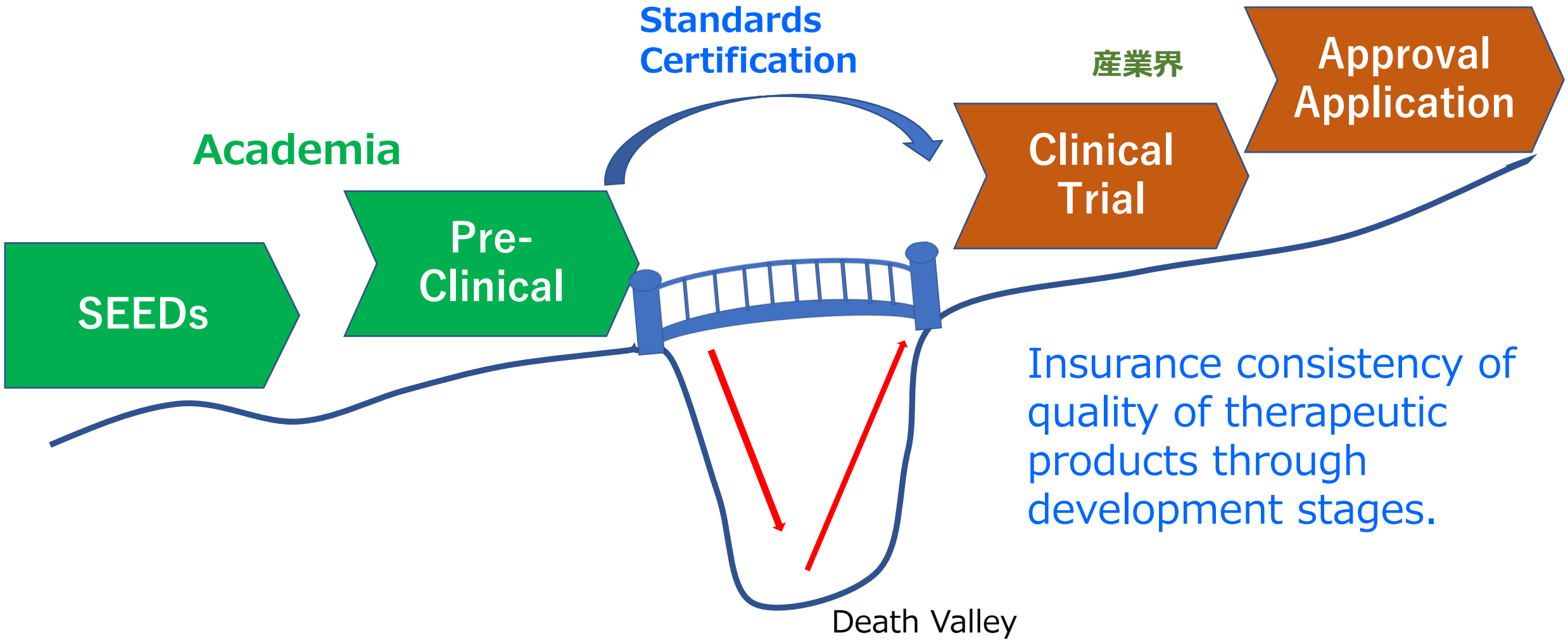
◆ * pilot operation

◆FIRM certification allows to choose the appropriate products meet specific requirements.

Standards as -a Tool to Connect Academia and Industry-



Standards as -a Tool to Connect Academia and Industry-



まとめ

◆International standards for industries related to regenerative medicine are being developed in ISO/TC276 WG4.
ISO/TC276 WG4において、再生医療周辺産業の国際標準が開発されている

◆The usage of these standards is optional, but they make activities efficient.
これらの標準の使用はmustではないが、取引を効率的にする可能性がある

◆Standards are increasingly being utilized in the development of regenerative medicinal products.
＊FDA Standards Recognition Program, FIRM Certification System
再生医療製品の開発において、標準の活用が進みつつある

◆Standards and Certification Systems using standards could serve as a bridge to smoothly cross the valley of death.
標準と認証システムは死の谷を越える架け橋となる可能性がある

DYNAMIC
HARMONY

SHISEIDO