独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Regulatory Updates and a Perspective on Biopharmaceuticals in Japan

SAKURAI Akira, Ph.D.
Senior Scientist for Biopharmaceutical Quality
Center for Product Evaluation
Pharmaceuticals and Medical Devices Agency (PMDA), Japan

Ice Breaker

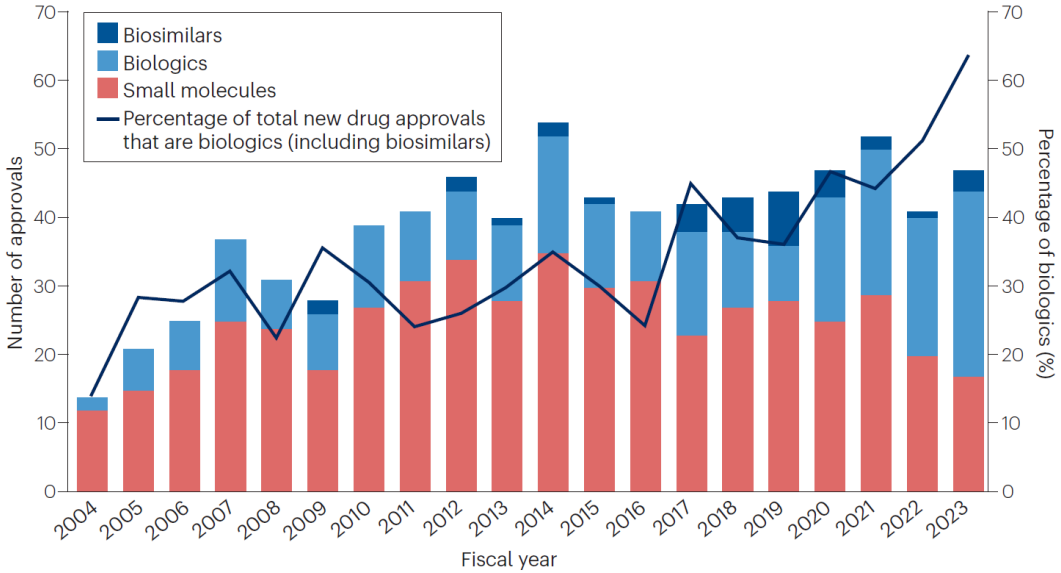
nature reviews drug discovery

FROM THE ANALYST'S COUCH | 02 October 2024 | Correction 28 October 2024

Two decades of new drug approvals in Japan

By Ryosuke Kuribayashi ✉, Aya Hariu, Yasuhiro Kishioka & Akira Sakurai

The Pharmaceuticals and Medical Devices Agency (PMDA) was established in fiscal year (FY) 2004 to evaluate the quality, efficacy and safety of drugs and medical devices for marketing authorization in Japan. Here, we analyse trends in the new drugs reviewed and approved by the PMDA and Ministry of Health, Labour and Welfare (MHLW) in the 20 years from FY2004.



doi: https://doi.org/10.1038/d41573-024-00153-w

Agenda

- Regulatory Update in Japan
  - ✓ Post-approval Change for Moderate risk (trial)
  - ✓ Partial Approval Change with a period of suspension
- Science Board
  - ✓ Microbiome
  - ✓ EV products
  - ✓ *in vivo* gene therapy products with Target Specificity
- Information

Agenda

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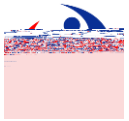
Recent MHLW's Initiatives



(MHLW; Minister of Health Labour and Welfare)

10. Jul, 2023～

Review Committee on Pharmaceutical Regulation for Strengthening Drug Discovery Capabilities and Securing Stable Supply

https://www.mhlw.go.jp/stf/shingi/other-iyaku_128701_00006.html

9. Jun, 2023

Report of the Panel of Experts on Comprehensive Measures to Achieve Rapid and Stable Supply of Pharmaceuticals

https://www.mhlw.go.jp/stf/newpage_33548.html

- Ensure stable supply
- Strengthen drug discovery capabilities
- Resolve the issues of "drug lag/loss"
- Efforts toward appropriate distribution of pharmaceuticals

Review Committee on Pharmaceutical Regulation for Strengthening Drug Discovery Capabilities and Securing Stable Supply

- Summary of considerations
  - Promotion of pharmaceutical development
  - Clinical trials
  - Post-marketing safety measures
  - Dissemination of information
  - Quality

https://www.mhlw.go.jp/content/11121000/001248959.pdf

Review Committee on Pharmaceutical Regulation for Strengthening Drug Discovery Capabilities and Securing Stable Supply

- Quality

  Review the description of manufacturing process in Application Form and post-approval CMC changes, taking into account international consistency

  - Introduce “middle-category” (pilot program)
  - Introduce “annual report” (pilot program)

（２）検討会における議論

事務局作成の資料[19]に基づいて議論が進められたが、その中では、日米欧の変更管理の手続の概要（図９）や、実際の変更カテゴリの日本と欧米間の違いに関する製薬協のアンケート結果などが示された。また、日本製薬工業協会・柏谷構成員からは、製薬業界の意見[20]が発表された。

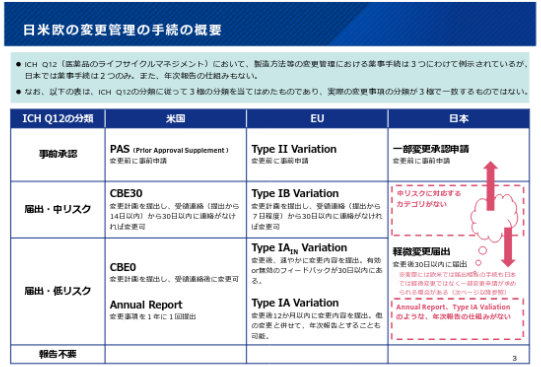


図９　日米欧の変更管理の手続の概要

https://www.mhlw.go.jp/content/11121000/001248959.pdf

Background: Post-Approval Change Reporting Categories

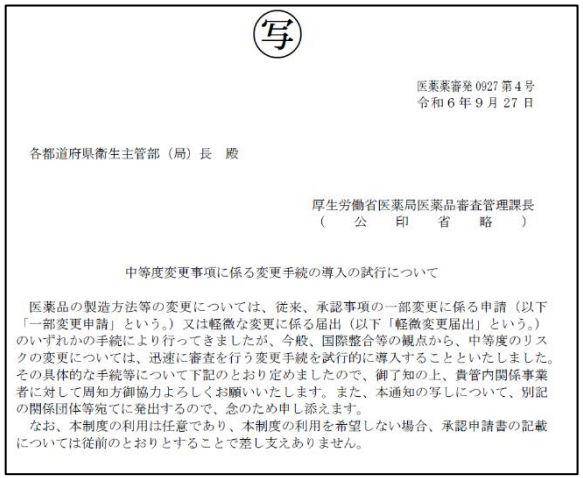
ICH Q12 Classification	Japan	US	EU
Prior Approval	PCA (Partial Change Application)	PAS (Prior Approval Supplement)	Type II Variation
Notification Moderate		CBE-30	Type IB Variation
Notification Low	MCN (Minor Change Notification)	CBE-0	Type IA_{IN} Variation
		Annual Report	Type IA Variation
Not Reported	Not Approved Matters		

Background: Post-Approval Change Reporting Categories

ICH Q12 Classification	Japan	US	EU
Prior Approval	PCA (Partial Change Application)	PAS (Prior Approval Supplement)	Type II Variation
Notification Moderate	**Trial Start!!**	CBE-30	Type IB Variation
Notification Low	MCN (Minor Change Notification) Preparing	CBE-0 Annual Report	Type IA_{IN} Variation Type IA Variation
Not Reported	Not Approved Matters		

Partial Change Application 40 (Trial version)

PCA-40 Trial Notification



写

医薬薬審発 0927 第 4 号
令和 6 年 9 月 27 日

各都道府県衛生主管部（局）長　殿

厚生労働省医薬局医薬品審査管理課長
（　公　印　省　略　）

中等度変更事項に係る変更手続の導入の試行について

医薬品の製造方法等の変更については、従来、承認事項の一部変更に係る申請（以下「一部変更申請」という。）又は軽微な変更に係る届出（以下「軽微変更届出」という。）のいずれかの手続により行ってきましたが、今般、国際整合等の観点から、中等度のリスクの変更については、迅速に審査を行う変更手続を試行的に導入することといたしました。その具体的な手続等について下記のとおり定めましたので、御了知の上、貴管内関係事業者に対して周知方御協力よろしくお願いいたします。また、本通知の写しについて、別記の関係団体等宛てに発出するので、念のため申し添えます。

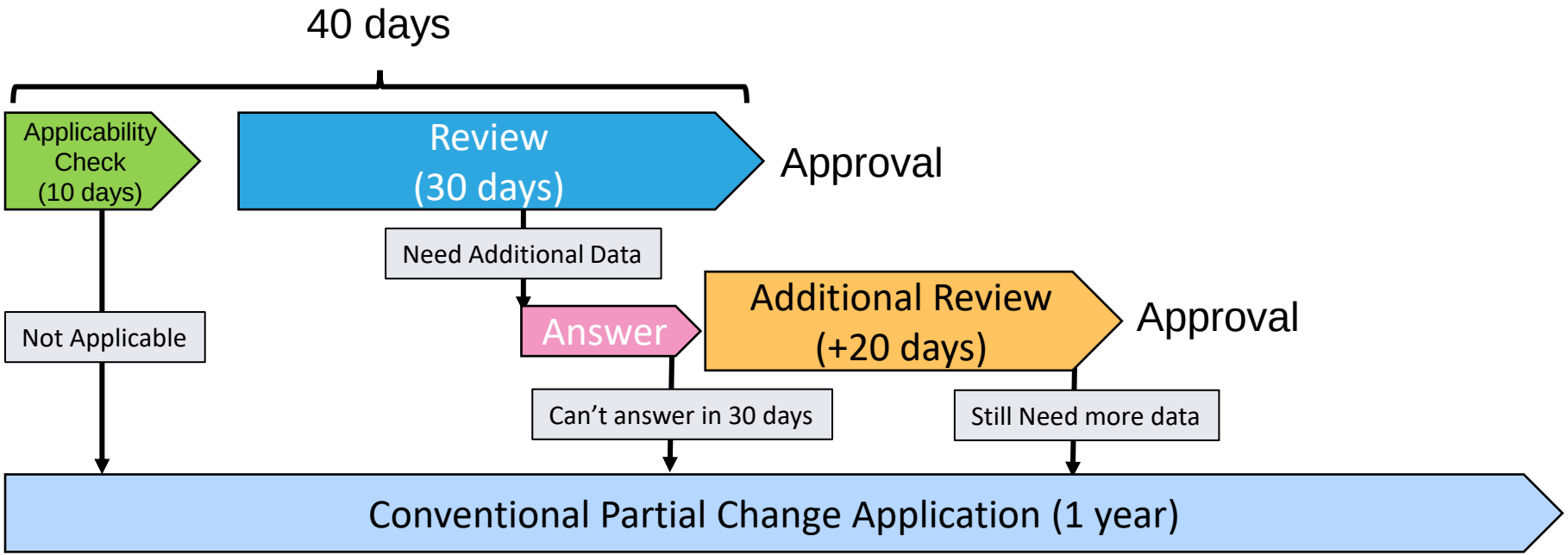
なお、本制度の利用は任意であり、本制度の利用を希望しない場合、承認申請書の記載については従前のとおりとすることで差し支えありません。

PAC-40 is the variation of conventional PAC,
but the administrative processing time is 40 days.
(Conventional: 1 years)

Scope

- The changes which commit as “Moderate change” on the Shonin-sho (established condition).
- The changes which PMDA agreed as “Moderate change” on an official consultation.

Partial Change Application 40 (Trial version)

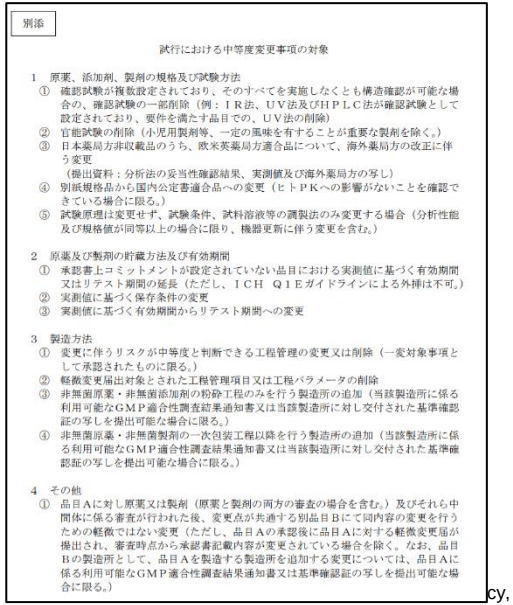


Criteria

The Criteria of PCA-40 is based on EP Guideline.

Guidelines on the details of the various categories of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products and on the documentation to be submitted pursuant to those procedures

https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52013XC0802(04)&from=EN



別添

試行における中等度変更事項の対象

1　原薬、添加剤、製剤の規格及び試験方法
① 確認試験が複数設定されており、そのすべてを実施しなくとも構造確認が可能な場合の、確認試験の一部削除（例：ＩＲ法、ＵＶ法及びＨＰＬＣ法が確認試験として設定されており、要件を満たす品目での、ＵＶ法の削除）
② 官能試験の削除（小児用製剤等、一定の風味を有することが重要な製剤を除く。）
③ 日本薬局方非収載品のうち、欧米英薬局方適合品について、海外薬局方の改正に伴う変更
（提出資料：分析法の妥当性確認結果、実測値及び海外薬局方の写し）
④ 別紙規格品から国内公定書適合品への変更（ヒトＰＫへの影響がないことを確認できている場合に限る。）
⑤ 試験原理は変更せず、試験条件、試料溶液等の調製法のみ変更する場合（分析性能及び規格値が同等以上の場合に限り、機器更新に伴う変更を含む。）

2　原薬及び製剤の貯蔵方法及び有効期間
① 承認書上コミットメントが設定されていない品目における実測値に基づく有効期間又はリテスト期間の延長（ただし、ＩＣＨ　Ｑ１Ｅガイドラインによる外挿は不可。）
② 実測値に基づく保存条件の変更
③ 実測値に基づく有効期間からリテスト期間への変更

3　製造方法
① 変更に伴うリスクが中等度と判断できる工程管理の変更又は削除（一変対象事項として承認されたものに限る。）
② 軽微変更届出対象とされた工程管理項目又は工程パラメータの削除
③ 非無菌原薬・非無菌添加剤の粉砕工程のみを行う製造所の追加（当該製造所に係る利用可能なＧＭＰ適合性調査結果通知書又は当該製造所に対し交付された基準確認証の写しを提出可能な場合に限る。）
④ 非無菌原薬・非無菌製剤の一次包装工程以降を行う製造所の追加（当該製造所に係る利用可能なＧＭＰ適合性調査結果通知書又は当該製造所に対し交付された基準確認証の写しを提出可能な場合に限る。）

4　その他
① 品目Ａに対し原薬又は製剤（原薬と製剤の両方の審査の場合を含む。）及びそれら中間体に係る審査が行われた後、変更点が共通する別品目Ｂにて同内容の変更を行うための軽微ではない変更（ただし、品目Ａの承認後に品目Ａに対する軽微変更届が提出され、審査時点から承認書記載内容が変更されている場合を除く。なお、品目Ｂの製造所として、品目Ａを製造する製造所を追加する変更については、品目Ａに係る利用可能なＧＭＰ適合性調査結果通知書又は基準確認証の写しを提出可能な場合に限る。）

In general, these criteria are mainly for chemical products.

For biologicals (Examples)

- Change in storage conditions for biologicals, when the stability studies have not been performed in accordance with an approved stability protocol.
- Change in parameter for manufacturing process, when the impact against quality is clarified as moderate.

Vague. Need Consultation!

Partial Change Approval with a Period of Suspension

Ministerial Order on the Standard of Manufacturing Control and Quality Control for Pharmaceuticals and Quasi-Pharmaceuticals (GMP Ministerial order)

Manufacturers, etc. for products of pharmaceuticals or quasi-pharmaceuticals must implement manufacturing control and quality control for such products at their manufacturing sites as provided in Article 96 of Enforcement Regulation of the Act on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices (Order of the Ministry of Health and Welfare No. 1 of 1961; hereinafter referred to as the "Enforcement Regulation")

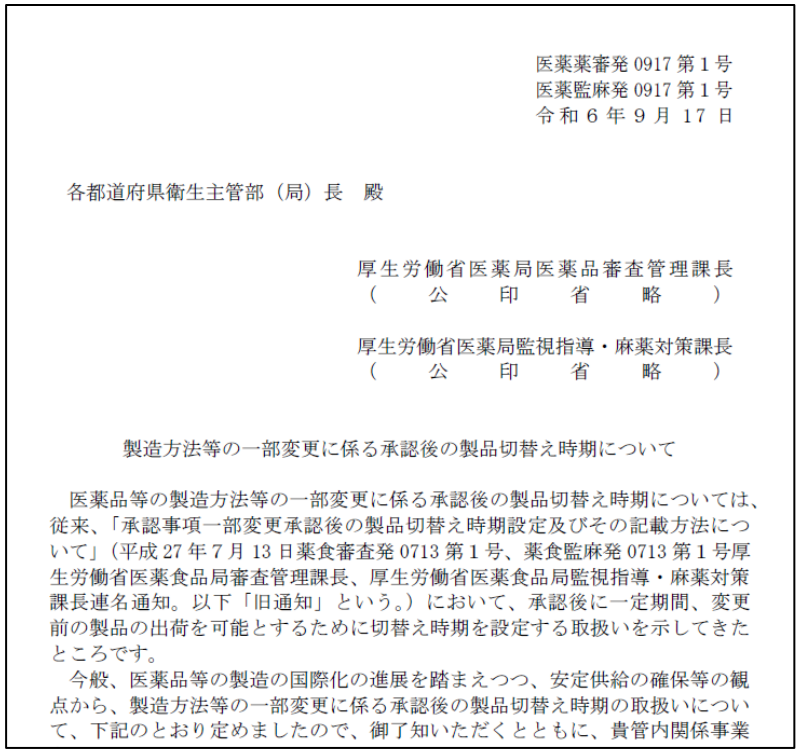
Old regulation

Shonin-sho
(Established condition)

Applicant could claim a period of suspension of recent established condition for shipping products produced by former approved manufacturing process.

The period is specific date within 6 month.

Partial Change Approval with a Period of Suspension (New Version)



医薬薬審発 0917 第 1 号
医薬監麻発 0917 第 1 号
令 和 6 年 9 月 17 日

各都道府県衛生主管部（局）長　殿

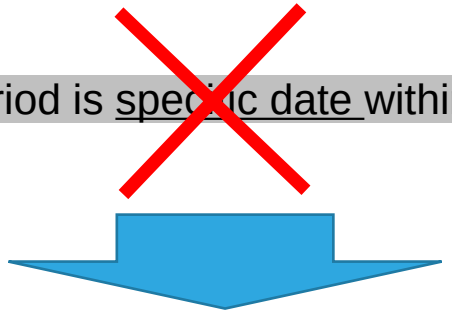
厚生労働省医薬局医薬品審査管理課長
（　　公　　印　　省　　略　　）

厚生労働省医薬局監視指導・麻薬対策課長
（　　公　　印　　省　　略　　）

製造方法等の一部変更に係る承認後の製品切替え時期について

医薬品等の製造方法等の一部変更に係る承認後の製品切替え時期については、従来、「承認事項一部変更承認後の製品切替え時期設定及びその記載方法について」（平成 27 年 7 月 13 日薬食審査発 0713 第 1 号、薬食監麻発 0713 第 1 号厚生労働省医薬食品局審査管理課長、厚生労働省医薬食品局監視指導・麻薬対策課長連名通知。以下「旧通知」という。）において、承認後に一定期間、変更前の製品の出荷を可能とするために切替え時期を設定する取扱いを示してきたところです。

今般、医薬品等の製造の国際化の進展を踏まえつつ、安定供給の確保等の観点から、製造方法等の一部変更に係る承認後の製品切替え時期の取扱いについて、下記のとおり定めましたので、御了知いただくとともに、貴管内関係事業



The period is ~~specific date~~ within 6 month.

Industries can keep old products shipping until the old products run out .

- Only the old products produced or were producing before the partial change approval.

Flexibility is extremely UP!

Agenda

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  - ✓ Post-approval Change for Moderate risk (trial)
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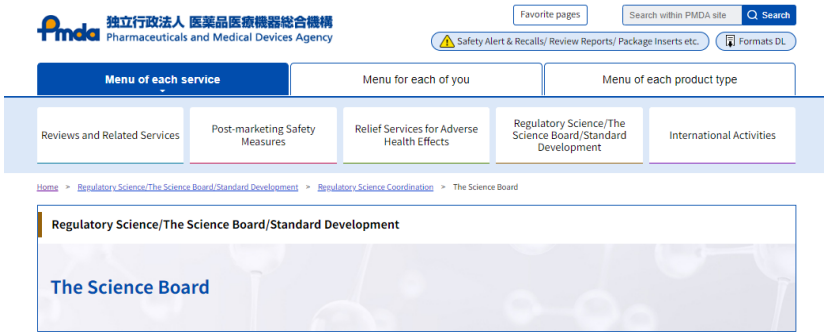
The Science Board, PMDA

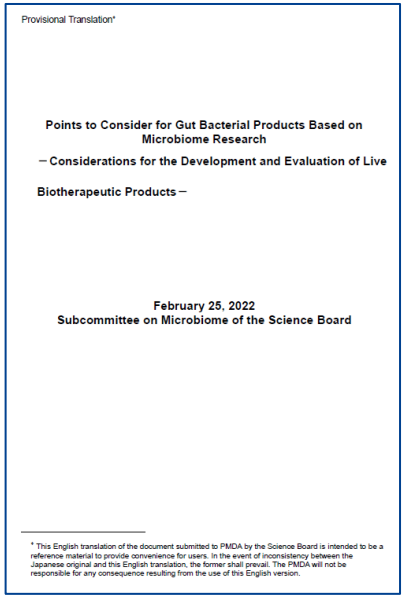
The purposes of the Science Board are, advancing regulatory science and evaluate products with advanced science and technology in appropriate manner by enhancing cooperation and communication with academia and medical institutions, based on PMDA's philosophy to deliver safe and effective drugs, medical devices and regenerative medical products to the people and further promotion of medical innovations.



https://www.pmda.go.jp/english/rs-sb-std/sb/science-committee/0010.html

Microbiome

- Report from PMDA Science Board (25 Feb, 2022)



Provisional Translation*

Points to Consider for Gut Bacterial Products Based on Microbiome Research

—Considerations for the Development and Evaluation of Live Biotherapeutic Products—

February 25, 2022
Subcommittee on Microbiome of the Science Board

* This English translation of the document submitted to PMDA by the Science Board is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail. The PMDA will not be responsible for any consequence resulting from the use of this English version.

Table of Content

https://www.pmda.go.jp/files/000249812.pdf (in English)

FMT; Fecal Microbiota Transplantation
LBPs; Live Biotherapeutic Products

Extracellular Vesicles (EVs) incl. Exosomes

- Report from PMDA Science Board (17 Jan, 2023)

エクソソームを含む細胞外小胞(EV)を利用した治療用製剤に関する報告書

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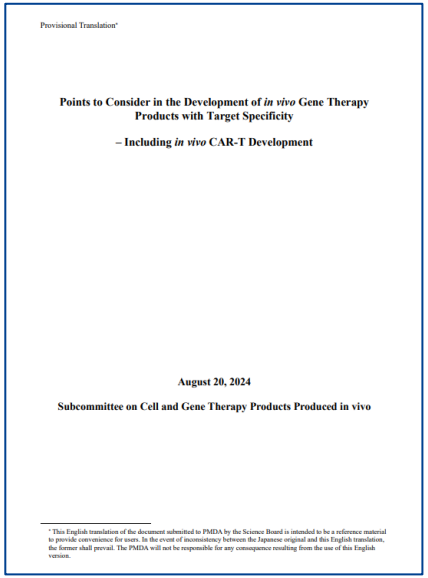
https://www.pmda.go.jp/files/000268368.pdf (in English)

in vivo Gene Therapy Products with Target Specificity

- Report from PMDA Science Board (20 August, 2024)



Provisional Translation*

Points to Consider in the Development of *in vivo* Gene Therapy Products with Target Specificity

– Including *in vivo* CAR-T Development

August 20, 2024

Subcommittee on Cell and Gene Therapy Products Produced in vivo

* This English translation of the document submitted to PMDA by the Science Board is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail. The PMDA will not be responsible for any consequence resulting from the use of this English version.

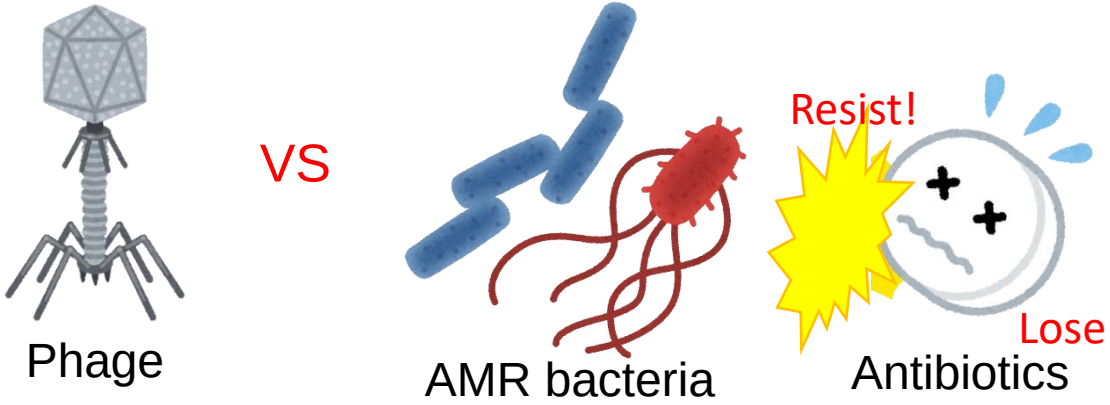
Table of Content

https://www.pmda.go.jp/files/000270120.pdf (in English)

Next theme

Phage therapy products for AMR (antimicrobial resistance) infection.

The details are confidential.



Agenda

- Regulatory Update in Japan
  - ✓ Post-approval Change for Moderate risk (trial)
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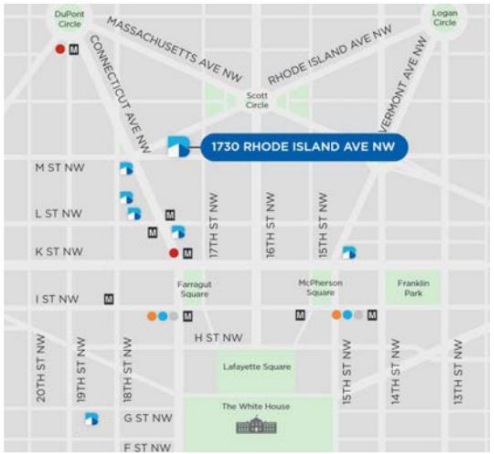
- **Information**

PMDA established PMDA Washington D.C. Office as its first U.S. base

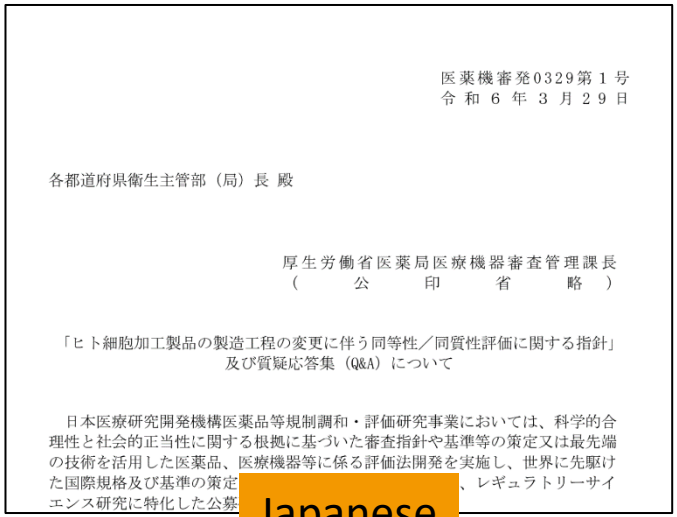
(Reference: Location of the PMDA Washington, D.C. office)

Address: 1730 Rhode Island Avenue, NW, Suite 403, Washington,D.C., USA



PMDA has enhanced to spread the information of Japanese regulation in English!

New Guideline :Guideline for Comparability of Cell therapy



医薬機審発0329第１号
令和６年３月29日

各都道府県衛生主管部（局）長 殿

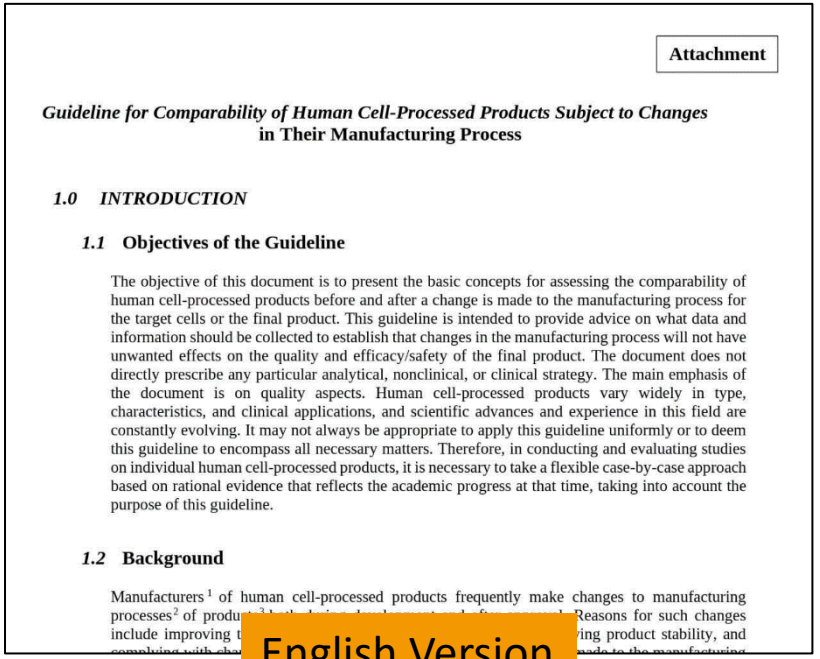
厚生労働省医薬局医療機器審査管理課長
（ 公 印 省 略 ）

「ヒト細胞加工製品の製造工程の変更に伴う同等性／同質性評価に関する指針」
及び質疑応答集（Q&A）について

日本医療研究開発機構医薬品等規制調和・評価研究事業においては、科学的合理性と社会的正当性に関する根拠に基づいた審査指針や基準等の策定又は最先端の技術を活用した医薬品、医療機器等に係る評価法開発を実施し、世界に先駆けた国際規格及び基準の策定
、レギュラトリーサイエンス研究に特化した公募

Japanese

https://www.pmda.go.jp/files/000267916.pdf



Attachment

Guideline for Comparability of Human Cell-Processed Products Subject to Changes in Their Manufacturing Process

1.0 INTRODUCTION

1.1 **Objectives of the Guideline**

The objective of this document is to present the basic concepts for assessing the comparability of human cell-processed products before and after a change is made to the manufacturing process for the target cells or the final product. This guideline is intended to provide advice on what data and information should be collected to establish that changes in the manufacturing process will not have unwanted effects on the quality and efficacy/safety of the final product. The document does not directly prescribe any particular analytical, nonclinical, or clinical strategy. The main emphasis of the document is on quality aspects. Human cell-processed products vary widely in type, characteristics, and clinical applications, and scientific advances and experience in this field are constantly evolving. It may not always be appropriate to apply this guideline uniformly or to deem this guideline to encompass all necessary matters. Therefore, in conducting and evaluating studies on individual human cell-processed products, it is necessary to take a flexible case-by-case approach based on rational evidence that reflects the academic progress at that time, taking into account the purpose of this guideline.

1.2 **Background**

Manufacturers[1] of human cell-processed products frequently make changes to manufacturing processes[2] of produ
Reasons for such changes include improving t
ing product stability, and

English Version

https://www.pmda.go.jp/files/000271048.pdf

PMDA website (English version) has been updating!

◆ Biosimilars

https://www.pmda.go.jp/english/review-services/reviews/0005.html

◆ Regenerative medicine

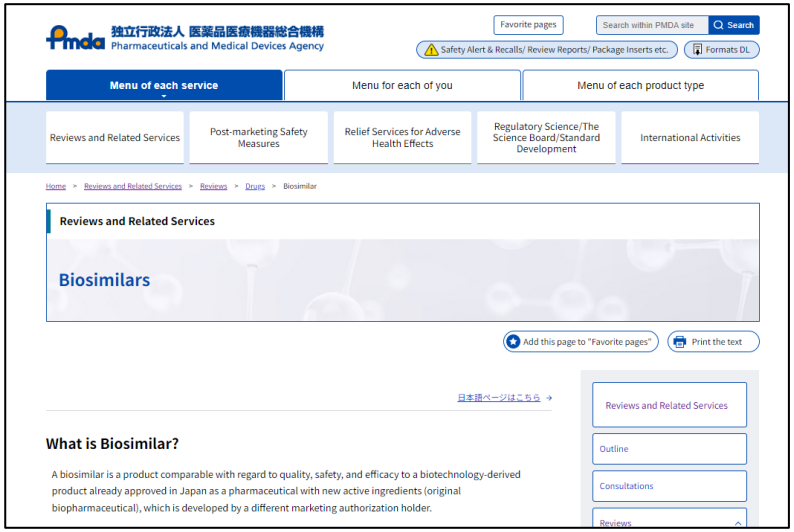
https://www.pmda.go.jp/english/review-services/reviews/0003.html

◆ GMO regulation (Cartagena Act)

https://www.pmda.go.jp/english/review-services/reviews/cartagena-act/0001.html

English Guidelines as well !

Biosimilars Web Site



Guideline and notification on ensuring quality, safety, and efficacy for Biosimilars

- Questions and Answers (Q&A) on Guideline for Ensuring the Quality, Safety, and Efficacy of Biosimilars[200KB]
  January 25, 2024
  PSB/PED Administrative Notice
- Guideline for Ensuring Quality, Safety, and Efficacy of Biosimilars[150KB]
  February 4, 2020
  PSEHD/PED Notification No. 0204-1

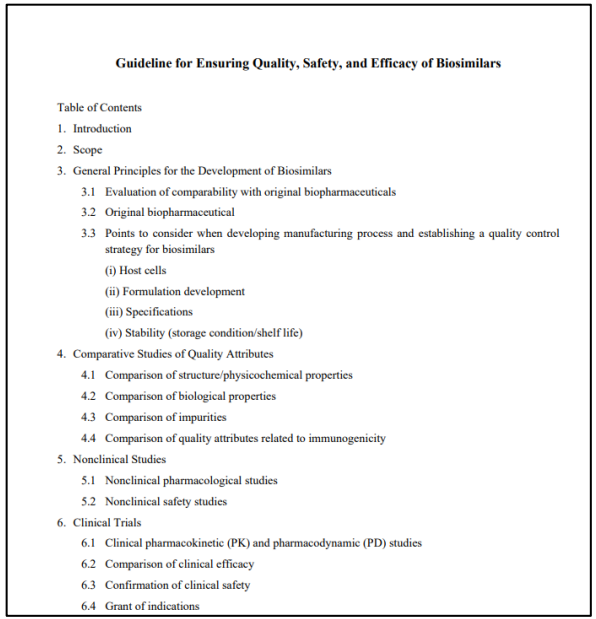
Learning Videos: Review

- Review of Biosimilars - PMDA-ATC Learning Video - YouTube
  You will be transferred to an external website (YouTube : Pmda Channel) by clicking the image.

https://www.pmda.go.jp/english/review-services/reviews/0005.html

Guideline for Ensuring Quality, Safety, and Efficacy of Biosimilars (English)

Guideline



Guideline for Ensuring Quality, Safety, and Efficacy of Biosimilars

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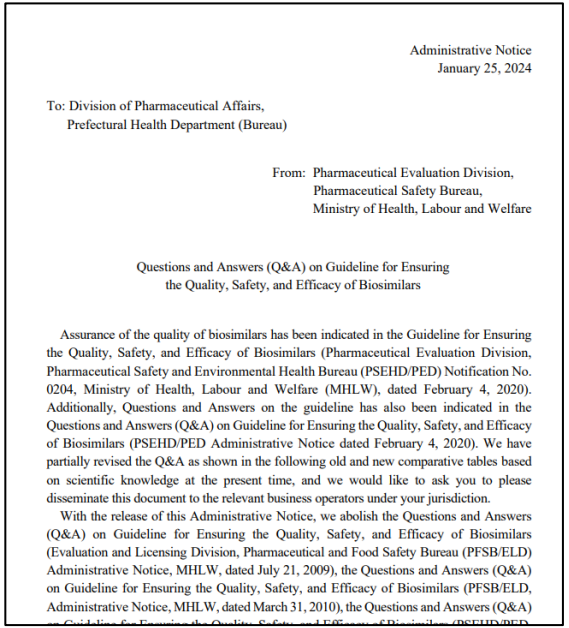
https://www.pmda.go.jp/files/000267479.pdf

Q and A



Administrative Notice
January 25, 2024

To: Division of Pharmaceutical Affairs,
Prefectural Health Department (Bureau)

From: Pharmaceutical Evaluation Division,
Pharmaceutical Safety Bureau,
Ministry of Health, Labour and Welfare

Questions and Answers (Q&A) on Guideline for Ensuring
the Quality, Safety, and Efficacy of Biosimilars

Assurance of the quality of biosimilars has been indicated in the Guideline for Ensuring the Quality, Safety, and Efficacy of Biosimilars (Pharmaceutical Evaluation Division, Pharmaceutical Safety and Environmental Health Bureau (PSEHD/PED) Notification No. 0204, Ministry of Health, Labour and Welfare (MHLW), dated February 4, 2020). Additionally, Questions and Answers on the guideline has also been indicated in the Questions and Answers (Q&A) on Guideline for Ensuring the Quality, Safety, and Efficacy of Biosimilars (PSEHD/PED Administrative Notice dated February 4, 2020). We have partially revised the Q&A as shown in the following old and new comparative tables based on scientific knowledge at the present time, and we would like to ask you to please disseminate this document to the relevant business operators under your jurisdiction.

With the release of this Administrative Notice, we abolish the Questions and Answers (Q&A) on Guideline for Ensuring the Quality, Safety, and Efficacy of Biosimilars (Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau (PFSB/ELD) Administrative Notice, MHLW, dated July 21, 2009), the Questions and Answers (Q&A) on Guideline for Ensuring the Quality, Safety, and Efficacy of Biosimilars (PFSB/ELD, Administrative Notice, MHLW, dated March 31, 2010), the Questions and Answers (Q&A)

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Standard for Biological Raw Materials

Provisional Translation (as of May 2024)*

STANDARDS FOR BIOLOGICAL RAW MATERIALS

Enacted on May 20, 2003 (MHLW Notification No. 210)
Enacted on March 30, 2004 (MHLW Notification No. 157)
Enacted on July 5, 2004 (MHLW Notification No. 262)
Enacted on March 31, 2005 (MHLW Notification No. 177)
Enacted on September 28, 2007 (MHLW Notification No. 310)
Enacted on July 1, 2009 (MHLW Notification No. 343)
Enacted on September 26, 2014 (MHLW Notification No. 375)
Enacted on February 28, 2018 (MHLW Notification No. 37)

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III. General Rules for Human-Derived Raw Materials

1. Standards for Human Cell/Tissue-based Raw Materials

(1) The human-derived cell or tissue serving as raw materials, etc. constituting drugs, etc. (excluding blood products) (hereinafter, "human cell/tissue-based raw materials, etc.") must be collected in facilities with sufficient personnel and equipment for necessary sanitation management.

(2) For collection of human cell/tissue-based raw materials, etc., the following measures must be taken:

A. Necessary measures must be taken to prevent contamination with microbial pathogen and other pathogenic agents when collection of human cell/tissue-based raw materials, etc.

B. The collected human cell/tissue-based raw materials, etc. shall be confirmed to be free from contamination with microbial pathogen and other pathogenic agents by appropriate examinations in light of the latest knowledge about infections, if it necessary.

(3) The donor must meet all the following conditions and be sufficiently eligible to donate human cell/tissue-based raw materials, etc. In the case where the donor is the same as the recipient of the drugs, etc., the donor screening may not be always required.

A. Infection of the donor with any pathogens including bacteria, fungi, viruses, etc. is denied by interview, medical examinations, tests, etc. before the human cell/tissue-based raw materials, etc. are collected, according to their intended uses.

B. The test items and test methods used at A. should be appropriate in light of the latest knowledge about infection, etc.

C. The tests or management shall be performed in consideration of the window period: for example, based on the test items and test methods, etc. used at A, re-tests are performed in appropriate timing.

D. In addition to the conditions A-C, the donor eligibility must be determined by conducting interview, medical examinations, tests, etc. for important diseases, and the consideration of experience of blood transfusion or transplantation therapy, etc.

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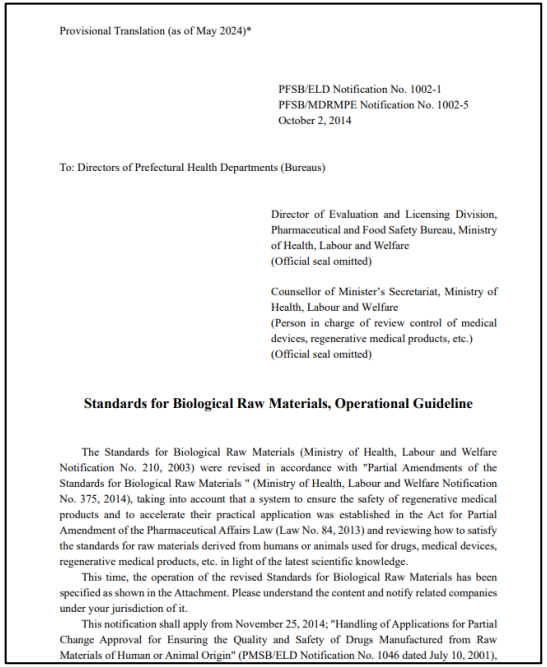
Standard for Biological Raw Materials, Operation Guidance



Provisional Translation (as of May 2024)*

PFSB/ELD Notification No. 1002-1
PFSB/MDRMPE Notification No. 1002-5
October 2, 2014

To: Directors of Prefectural Health Departments (Bureaus)

Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare
(Official seal omitted)

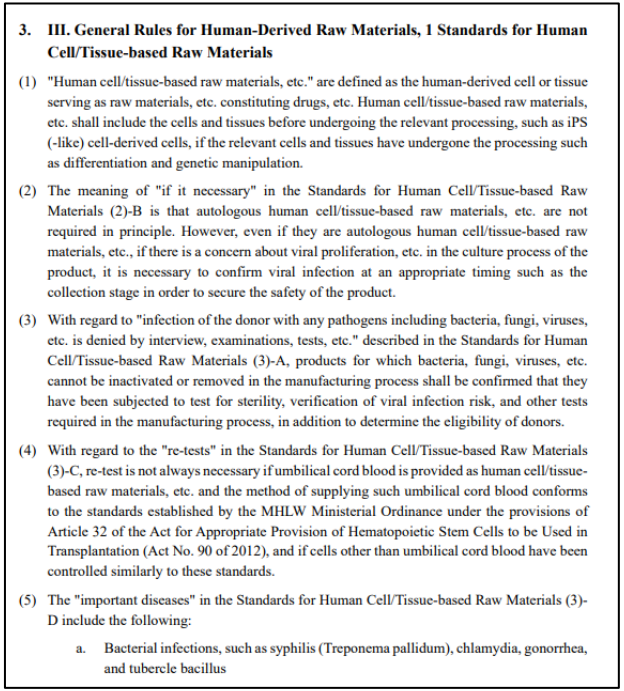
Counsellor of Minister's Secretariat, Ministry of Health, Labour and Welfare
(Person in charge of review control of medical devices, regenerative medical products, etc.)
(Official seal omitted)

Standards for Biological Raw Materials, Operational Guideline

The Standards for Biological Raw Materials (Ministry of Health, Labour and Welfare Notification No. 210, 2003) were revised in accordance with "Partial Amendments of the Standards for Biological Raw Materials " (Ministry of Health, Labour and Welfare Notification No. 375, 2014), taking into account that a system to ensure the safety of regenerative medical products and to accelerate their practical application was established in the Act for Partial Amendment of the Pharmaceutical Affairs Law (Law No. 84, 2013) and reviewing how to satisfy the standards for raw materials derived from humans or animals used for drugs, medical devices, regenerative medical products, etc. in light of the latest scientific knowledge.

This time, the operation of the revised Standards for Biological Raw Materials has been specified as shown in the Attachment. Please understand the content and notify related companies under your jurisdiction of it.

This notification shall apply from November 25, 2014; "Handling of Applications for Partial Change Approval for Ensuring the Quality and Safety of Drugs Manufactured from Raw Materials of Human or Animal Origin" (PMSB/ELD Notification No. 1046 dated July 10, 2001),



3. III. General Rules for Human-Derived Raw Materials, 1 Standards for Human Cell/Tissue-based Raw Materials

(1) "Human cell/tissue-based raw materials, etc." are defined as the human-derived cell or tissue serving as raw materials, etc. constituting drugs, etc. Human cell/tissue-based raw materials, etc. shall include the cells and tissues before undergoing the relevant processing, such as iPS (-like) cell-derived cells, if the relevant cells and tissues have undergone the processing such as differentiation and genetic manipulation.

(2) The meaning of "if it necessary" in the Standards for Human Cell/Tissue-based Raw Materials (2)-B is that autologous human cell/tissue-based raw materials, etc. are not required in principle. However, even if they are autologous human cell/tissue-based raw materials, etc., if there is a concern about viral proliferation, etc. in the culture process of the product, it is necessary to confirm viral infection at an appropriate timing such as the collection stage in order to secure the safety of the product.

(3) With regard to "infection of the donor with any pathogens including bacteria, fungi, viruses, etc. is denied by interview, examinations, tests, etc." described in the Standards for Human Cell/Tissue-based Raw Materials (3)-A, products for which bacteria, fungi, viruses, etc. cannot be inactivated or removed in the manufacturing process shall be confirmed that they have been subjected to test for sterility, verification of viral infection risk, and other tests required in the manufacturing process, in addition to determine the eligibility of donors.

(4) With regard to the "re-tests" in the Standards for Human Cell/Tissue-based Raw Materials (3)-C, re-test is not always necessary if umbilical cord blood is provided as human cell/tissue-based raw materials, etc. and the method of supplying such umbilical cord blood conforms to the standards established by the MHLW Ministerial Ordinance under the provisions of Article 32 of the Act for Appropriate Provision of Hematopoietic Stem Cells to be Used in Transplantation (Act No. 90 of 2012), and if cells other than umbilical cord blood have been controlled similarly to these standards.

(5) The "important diseases" in the Standards for Human Cell/Tissue-based Raw Materials (3)-D include the following:

a. Bacterial infections, such as syphilis (Treponema pallidum), chlamydia, gonorrhea, and tubercle bacillus

https://www.pmda.go.jp/files/000268475.pdf

Thank you for your attention!