20th
Periodic meetings to exchange opinions on approval reviews and safety measures for medical devices and in-vitro diagnostics

September 1st 2022

American Medical Device and IVD Industries Association (AMDD)
Advanced treatments Technology Industries Association (AdvAMeD)
European Business Council (EBC) Medical Devices and IVD Committee

Details of today

- **Introduction**
- **Issues and requests concerning program medical devices**
- **Development of an environment to accelerate the creation of evidence**
- **Efforts for International Harmonization and Reference Countryization**

1. Mutual utilization of various regulations and investigation results
2. Toward further rationalization and international harmonization of the QMS inspection system
3. In order to utilize the examination results in Japan overseas (explanation of cases)

Introduction

I would like to express my appreciation for the flexible and prompt response by the government that there has been no delay in pharmaceutical administration such as approval reviews during the novel coronavirus outbreak since the year before last.

In the " Formulation of a Collaborative Plan for Optimizing Medical Device Regulations and Reviews, " AMDD / AdvAMeD / EBC has taken measures to promote the development and market introduction of innovative medical devices. These measures include continuing discussions on a wide range of improvements and reform items ; DASH for sAMD within the Ministry of Health, Labour and Welfare PMDA strengthening of the Screening Department system, unification of consultation services, establishment of the IDATEN system, etc. strengthening of the system of the Ministry of Health, Labour and Welfare by the DASH for SaMD DASH for the Ministry of Health, Labour and Welfare for the Ministry of Health, Labour and Welfare for the Ministry

■ Expectations for the Increased Value of Pharmaceutical Approval in Japan on a Global Basis

➢ There have been cases in which approval in Japan precedes FDA and CE marks due to the acceleration of PMDA review and the introduction of MDR. As a result, the number of cases in which Japanese approval is referred to in the examination of other countries is increasing. However, practical problems have arisen to allow Japanese approval to be used in other countries. (One of the specific requests is explained in Slide 8 below)

➢ The expansion and deepening of Asian leadership, especially the strengthening of bilateral relations with the People's Republic of China, will greatly benefit not only Japanese companies but also AMDD / AdvAMeD / EBC member companies.

Issues and requests related to program medical devices

Establishment of a review system according to the characteristics of programmed medical devices

- Through the DASH for sAMD, the Ministry of Health, Labour and Welfare (MHLW) and the PMDA (Screening Department) have been strengthened, consultation services have been unified, and the IDATEN system has been improved.
- However, the Company recognizes that there are still issues to be addressed in " establishing a review system based on the characteristics of programmed medical devices. "

- Application of examination requirements for hardware as they are (affecting the handling of partial changes)
- Necessity of premarketing clinical evaluation (inconsistent with development speed)

- The Government of Japan requests the Government of the United States to establish and ensure the operation of a system that reflects its characteristics.

- New review of the change system and operation that should be applied to program medical devices
- Establishment of a system that assumes, for example, the use of RWD (not clinical trial)
- Establishment of a new system to provisionally approve, for example, safety assurance + validity estimation

Cybersecurity

- In addition to the WORKING Group of the Federation of Medical Devices and Manufacturers (PMSB), discussions have been held in various places toward legislation in Japan based on the IMDRF guidance. A notification is scheduled to be issued within this fiscal year and to take effect next summer.
- The Government of Japan requests the Government of the United States to continue discussions with the industry and ensure the establishment and operation of an internationally harmonized system (without any unique requirements of Japan).

Development of an environment to accelerate the creation of evidence

Use of real-world data for pharmaceutical applications

- There have been cases of using registry data in foreign countries for approval applications. When using overseas registry data for approval applications in Japan, there are concerns about differences in the way of thinking between Japan and the United States regarding the reliability of databases and handling of personal information.
- DBs led by academic societies have problems such as patient consent, access restrictions for companies, and restrictions on acquired information, and companies have not made progress in the development of new products, improvement of algorithms, and utilization in pharmaceutical applications.

Promotion of utilization of secondary data acquired by medical data including AI

- It is necessary to discuss the interpretation of the operation of the Personal Information Protection Law (anonymization / kana processing of data), Next Generation Medical Infrastructure Act, Information Security Guidance and Ethics Guidelines.

Standardization (integration) of regulations related to clinical research (GCP, clinical research method, ethical guidelines)

- I look forward to the commencement of discussions on the current status (complexity) of the three regulations concerning clinical research in order to improve the environment for promoting development.

Efforts for International Harmonization and Reference Countryization

1 Mutual use of various regulations and investigation results

- MDSRP(Medical Device Single Review Program) Promotion of Discussions
  - It is expected to be applied to high-class products in the future.
- Continuous international harmonization of regulations (such as ISO, QMS, GCP) is essential for rapid adoption of medical devices.
  - ISO10993-1 revision and the revision of the Basic Concept of Biological Safety Assessment (Notification No. 030 1 20 of the Pharmaceutical and Food Safety Bureau) are aligned.
  - The Government of Japan requests the Government of the United States to continue careful consideration including the operational aspects so that the biological safety evaluation data conducted in the United States and Europe can be used for the application in Japan.
- Mutual acceptance among Japan, the United States, and Europe of the results of GCP compliance inspections based on global clinical trials, etc.
  - GOJ requests USG to consider the possibility of an MRA (Mutual Recognition Agreement) between Japan and the US and between Japan and the EU.
- Scope and reporting methods of foreign case reports and research reports
  - Based on international consistency with overseas reporting systems, I expect discussions on a system that can provide information more quickly and contributes to medical practice in Japan.

International Coordination of Regulatory Operation to Eliminate Development Lag
Requests for mutual utilization of regulations for further acceleration of examination in the future

Efforts for International Harmonization and Reference Countryization

2. Toward further rationalization and international coordination of the QMS inspection system

Full-scale introduction of MDSAP in fiscal 2022 and expectations for the future

- Depending on the business model of manufacturing medical devices in Japan, exporting medical devices overseas, and importing medical devices from overseas, there are differences in each marketing authorization holder's views on MDSAP. MDSAP is one of the options, but in order to encourage more companies to participate in it in the future, it is essential to publicize its advantages.

QMS Opinion Exchange Meeting

- This is a meaningful and valuable opportunity for frank exchange of opinions with the government.
- Health, Labour and Welfare Scientific Research QMS Group " QMS Systems in Light of International Harmonization " took up topics such as " Issues of the current QMS inspection system " and " Issues compared with other countries ' QMS inspection systems " as topics related to the " QMS Inspection System in Light of International Harmonization " which were discussed in the QMS Group. Positive discussions took place. (June 2022)

Review of a QMS compliance inspection system based on international harmonization

- Expectations for the results of activities by the Health, Labour and Welfare Science Research QMS Group (2021-2022) and with industry Please continue discussions after the meeting.
- In the future, I expect that the concept itself from QMS investigation for each product group to QMS investigation for each company, for example will be reviewed and considered.

From QMS inspections for individual products to QMS inspections for individual companies

Efforts for International Harmonization and Reference Countryization

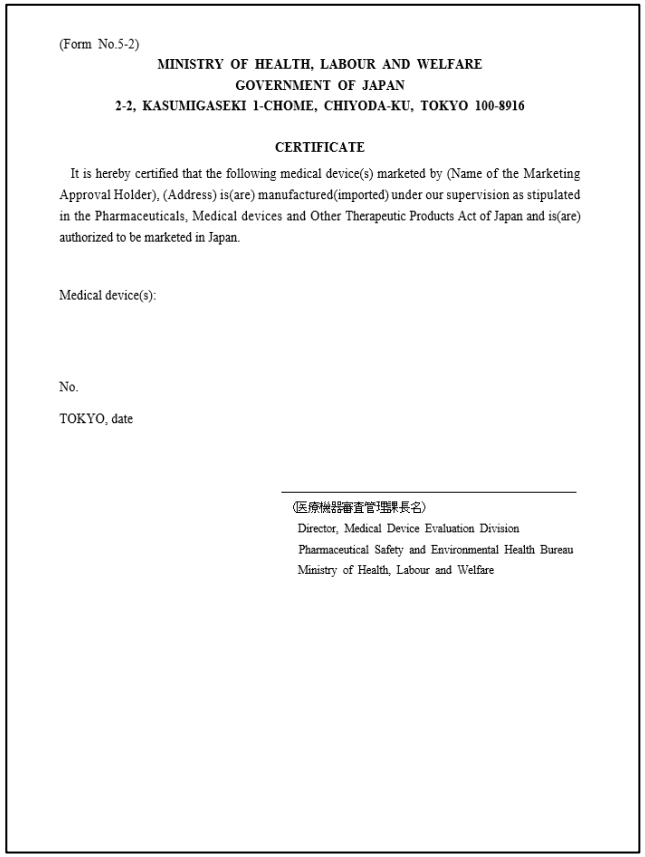
3. In order to utilize the examination results in Japan overseas (explanation of cases)

- It is requested that the brand name (in English) at the import destination be entered in the remarks column of the marketing approval / certification.
  - The procedures for obtaining a certificate to a foreign government for medical devices that have obtained manufacturing / marketing approval / certification for imported products are complex and rapid.
    - ✓ Since the English product name cannot be confirmed on the manufacturing / marketing approval / certification document, the manufacturing / marketing approval / certification details certificate (Form 5-2)) issued by OMETA (Overseas Medical Device Technical Cooperation Association) When it is manufactured in a country other than Japan imported products are required to submit a notification of medical devices to be exported. However, it is necessary to submit a notification of medical devices to be exported.
    - ✓ Since it is not possible to obtain a certificate to a foreign government only with a Japanese approval / certification document, it is necessary to include the English brand name on the approval document. In the case of cosmetics it is possible to specify brand name at the importer in the " remarks " column.)
- Reference information : Handling of Marketing Approval Certificates in Japan in Foreign Countries
  - A foreign government certificate in English that is issued by the Ministry of Health, Labour and Welfare as the issuing authority in a country to which the simplified examination is applied is treated in the same manner as Free Sales Certificate (FSC) or FDA Certificate to Foreign Government (CFG) of CE.
  - In Singapore and Thailand, certificates addressed to foreign governments of two of the five major countries are required .

Overseas request for new operation due to simplified examination for approval in Japan

Examples of various certifications described on page 8

Certificate of contents of marketing approval / certification (MHLW Form 5-2)



(Form No.5-2)

MINISTRY OF HEALTH, LABOUR AND WELFARE
GOVERNMENT OF JAPAN
2-2, KASUMIGASEKI 1-CHOME, CHIYODA-KU, TOKYO 100-8916

CERTIFICATE

It is hereby certified that the following medical device(s) marketed by (Name of the Marketing Approval Holder), (Address) is(are) manufactured(imported) under our supervision as stipulated in the Pharmaceuticals, Medical devices and Other Therapeutic Products Act of Japan and is(are) authorized to be marketed in Japan.

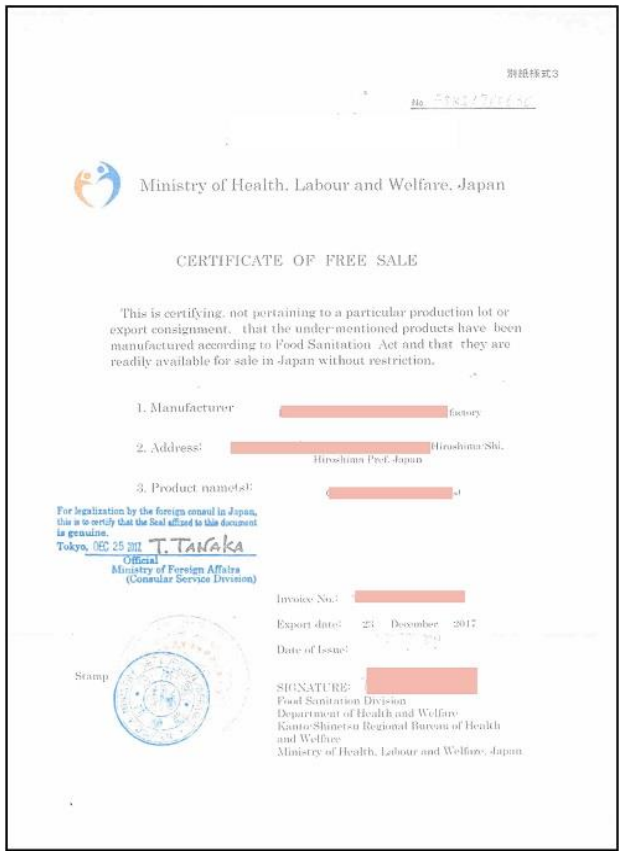
Medical device(s):

No.

TOKYO, date

(医療機器審査管理課長名)
Director, Medical Device Evaluation Division
Pharmaceutical Safety and Environmental Health Bureau
Ministry of Health, Labour and Welfare

Certificate to Foreign Government (MHLW)



Ministry of Health, Labour and Welfare, Japan

CERTIFICATE OF FREE SALE

This is certifying, not pertaining to a particular production lot or export consignment, that the under-mentioned products have been manufactured according to Food Sanitation Act and that they are readily available for sale in Japan without restriction.

1. Manufacturer [redacted] factory
2. Address: [redacted] Hiroshima-Shi, Hiroshima Pref. Japan
3. Product name(s): [redacted]

For legalization by the foreign consul in Japan, this is to certify that the Seal affixed to this document is genuine.
Tokyo, DEC 25 2012 T. TANAKA
Official
Ministry of Foreign Affairs
(Consular Service Division)

Invoice No.: [redacted]
Export date: 25 December 2012
Date of Issue:

Stamp

SIGNATURE: [redacted]
Food Sanitation Division
Department of Health and Welfare
Kanto-Shinetsu Regional Bureau of Health and Welfare
Ministry of Health, Labour and Welfare, Japan

Certificate to Foreign Government(FDA)

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Building 66
Silver Spring, Maryland 20993

Certificate No. [redacted]

CERTIFICATE TO FOREIGN GOVERNMENT

In order to allow the importation of United States products into foreign countries, the U.S. Food and Drug Administration (FDA) certifies the following information concerning the product(s) to be exported listed below:

Name of Product(s) | Name of Manufacturer/Distributor Address

[redacted]

The product(s) described above (and the manufacturing/distribution site(s) which produces/distributes it) is subject to the jurisdiction of the FDA under the Federal Food, Drug, and Cosmetic Act.

It is certified that the above product(s) may be marketed in, and legally exported from, the United States of America at this time. The manufacturing plant(s) in which the product(s) is produced is subject to periodic inspections. The last such inspection showed that the plant(s), at that time, appeared to be in substantial compliance with current good manufacturing practice requirements for the product(s) listed above.

Theresa McDonald
Chief, Regulatory Policy and Systems Branch
Division of Risk Management Operations
Office of Compliance
Center for Devices and Radiological Health

This certificate expires 24 months from the date notarized.

COUNTY OF MONTGOMERY
STATE OF MARYLAND

Subscribed and sworn to before me this 19 day of NOV month 2009 year.

CATHRYN N. MORRIS
NOTARY PUBLIC STATE OF MARYLAND
County of Montgomery
My Commission Expires January 4, 2013