2024.10.07

22nd Regular Meeting on Approval Review and Safety Measures for Medical Devices and In Vitro Diagnostics

--Toward the promotion of globalization and digital transformation—

Today's main topic

I. Promoting innovation and facilitating medical device development and market introduction
II. Improving productivity to contribute to continuous supply
III. Promoting system construction and DX using digital technology
IV. Promoting international harmonization and globalization

As Japan moves away from a cost-cutting economy and aims to become a growth-oriented economy through aggressive investment in areas such as digitalization, it will need to aim for growth while facing changes in the environment surrounding the medical device industry, such as rising prices and a shrinking labor force, and in order to promote "a stable supply of medical devices that support medical care" and "the promotion of innovation that provides new value to the medical field," it is essential that globalization and digital transformation be promoted, and these are the prerequisites for considering the form of regulation.

Looking ahead to the next 5 to 10 years in the medical device industry, we would like to advance discussions and considerations centered on the following four points in order to achieve strong growth as an industry.

1. Promote innovation and promote medical device development and market introduction
2. Improve productivity to contribute to continuous supply
3. Promote regulatory operation with the promotion of DX using digital technology in mind
4. Consider the characteristics of medical devices and make regulations internationally harmonized with an eye toward globalization

1. Promote innovation and promote medical device development and market introduction

"Promoting innovation" is an important element for providing new value to the medical field and for the future development of the medical device industry.

There are issues and proposals (5 items as shown below) that are being discussed in the Pharmaceutical and Medical Device System Subcommittee, but I would like to state our opinions again, including issues that can be addressed without amending the Pharmaceuticals and Medical Devices Act.

(i) Promoting medical device development using RWD
(ii) Considerations for revitalizing clinical trials and clinical research
(iii) Regarding the handling of pioneering medical devices
(iv) Educational advertising aimed at general consumers to improve health literacy
(v) Request for cooperation in device loss surveys and analysis

(i) Promoting medical device development using RWD

【Background】

In developing medical devices using AI, a large amount of medical information is required for learning and verification, and it is desirable to utilize medical information stored individually at each medical institution, as well as information compiled into a database. However, due to the complex requirements for handling personal information, the responses of each medical institution vary, and it is difficult to collect medical information based on ethical guidelines and to conduct verification tests for approval applications, which has prevented rapid development.

Notification 0929 (2) of 2021 states that when existing medical information related to existing medical image data is collected and used for performance evaluation, it is considered to be a clinical trial result in place of a clinical trial, and is expected to promote development. However, consent is often not obtained for the purpose of approval applications, making it difficult to utilize the existing accumulated data.

At the Pharmaceutical and Medical Device System Subcommittee meeting (June 5, 2014), the establishment of new standards regarding the reliability of RWD was proposed as a direction for consideration (draft) for strengthening and enhancing pharmaceutical application responses using RWD, with the following statement being raised: "From the perspective of promoting the use of RWD, reliability standards should be established by ministerial ordinance, similar to the GCP ministerial ordinance."

【Suggestions and Requests】

1. The Ministry of Health, Labour and Welfare has indicated the possibility of pseudonymizing information as a way to utilize existing medical data without obtaining consent. However, even if we try to utilize data in accordance with this view, the handling of data is complicated, as we need to check multiple laws and regulations, such as the Personal Information Protection Act, Ethical Guidelines, and the Pharmaceuticals and Medical Devices Act. As a part of this, we would like your cooperation in creating and revising the guidance for companies.
2. When establishing new standards (ministerial ordinances) regarding the reliability of RWD, we would like you to take into account the above-mentioned issues and consider not to set excessive standards, assuming that a variety of RWD can be used. We would also like the participation of the industry in the consideration.

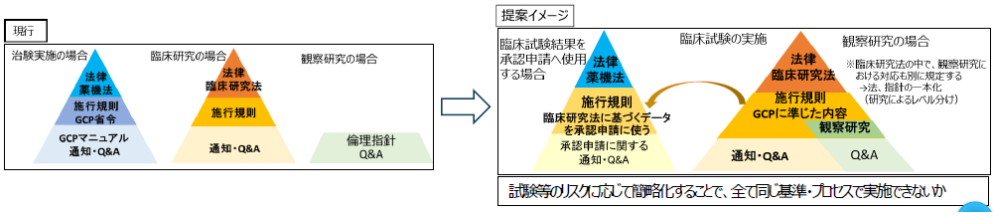
(ii) Considerations for revitalizing clinical trials and clinical research

【Background】

When conducting clinical trials and clinical research, the applicable laws and regulations (GCP/GPSP, Clinical Research Act, Ethical Guidelines for Life Science and Medical Research Involving Human Subjects) differ depending on the purpose of use and type of study, which makes the review system and procedures in the medical field complicated and places a heavy burden on the medical community.

【Suggestions and Requests】

1. With regard to the GCP GPSP Ordinance under the Pharmaceuticals and Medical Devices Act, the Clinical Research Act, and ethical guidelines, we believe that by simplifying regulations regarding the clinical trial implementation system and procedures in medical facilities, while creating a legal system that is easy to utilize depending on the purpose of use of research results and the type of trial, we can reduce the burden on medical facilities and improve the environment, leading to earlier access to medical products.
2. Prior to discussing the legal system, how about starting with a discussion on consolidating the review systems and procedures of each review committee (IRB, CRB, ethical review committee) at medical institutions? In particular, it would be useful to consider studies divided by interventional research and subject risk.



(iii) Regarding the handling of pioneering medical devices

【Background】

The pioneering medical device review system was officially introduced when the revised law came into effect in 2020 after a trial run from 2015. There are four designation requirements for target items: ①revolutionary treatment or diagnostic method, ② severity of the target disease, ③ extremely high efficacy or safety for the target disease, and ④ intention and system for early development and approval application in Japan before the rest of the world. Only one item has been approved since the official introduction.

A similar trial implementation is also set for program medical devices, and three items have been designated each year for the past two years that do not have the above requirement ② regarding the target disease, and a proposal was made to legislate this at the Pharmaceutical and Medical Device System Subcommittee in July.

【Suggestions and Requests】

In addition to program medical devices, there are medical devices that use a variety of technologies and are used in various fields. Since this system is intended to promote "early development in Japan ahead of the rest of the world," removing "② the severity of the target disease" from the designation requirements may lead to the promotion of the development of groundbreaking medical devices with high medical utility.

The interpretation of "ahead of the rest of the world" is different to review schemes in each country, so please discuss it separately.

【Expected effects】

The development of medical devices with high medical utility will be promoted.

(iv) Educational advertising aimed at general consumers to improve health literacy

【Background】

Although the creation of individual guidance has lifted the ban on advertising some items,

medical devices are considered to be at a disadvantage compared to non-medical devices in terms of providing information to general consumers.

In response to the opinion in the proposal that "it is important to allow advertising to general consumers in principle and to contribute to improving the public's health literacy by striving to provide correct information under certain rules," the Ministry of Health, Labour and Welfare proposed that "using a framework such as a research group, academics, medical professionals and other relevant parties will hold discussions and consider methods of advertising to raise awareness of diseases."

According to the Interpretation Notice in 2010, there are no restrictions on advertising to general consumers for products that are "not likely to be used by the general public" in the Appropriate Advertising Standards for Pharmaceuticals, etc. However, there is a strong perception that such products are prohibited in principle, and so they are not advertised much despite the demand.

【Suggestions and Requests】

1. In order to accelerate the transmission of objective and accurate information about medical devices, we would like the research group to consider lifting the ban on advertising for all items in principle, and to proceed with concrete considerations, such as:
   ① Allowing discussions to take place in a separate conference from pharmaceuticals;
   ② Considering separating medical devices from the existing fair advertising standards;
   ③ Considering guidelines for medical device awareness advertising aimed at physicians, based on the premise of providing information to patients and others when selecting appropriate treatments and diagnoses;
   ④ Developing an overall schedule leading up to the lifting of the ban in principle.

2. We would like the definition of "items that are not likely to be used by the general public" that can be advertised to be clarified as soon as possible.

【Expected effects】

Providing objective and accurate information about medical devices to the general consumer can lead to improved health literacy and patient-centered medical care.

(v) Request for cooperation in device loss surveys and analysis

【Background】

Although there are voices saying that there is device loss in medical devices, the actual situation is unclear. Therefore, as a first investigation, AMDD is conducting a desktop survey based on publicly available information on the Internet to find out how many of the items approved by the US FDA (PMA original, De Novo) between January 2018 and March 2022 have also been approved in Japan.

【Prompt survey report】

The survey's preliminary results show that of the 202 files approved in the US, 72% were not approved in Japan. 79% of the items applied for by companies without a Japanese subsidiary, and 51% of the items applied for by companies with a Japanese subsidiary, were not approved in Japan. Looking at the breakdown of the four areas with the most unapproved items (cardiac and vascular, gastroenterological and urological, orthopedics, and neurology), it was suggested that similar medical devices may exist in Japan for 81% of the total 81 files. We plan to further investigate the impact of this unapproval on the medical field and the reasons for its non-approval.

【Suggestions and Requests】

We would appreciate your cooperation in providing a detailed analysis of whether the current situation, and the future of Japan's medical field, can be said to be problem-free and whether any necessary measures need to be taken, as well as in providing an interpretation and countermeasures.

2. Improve productivity to contribute to continuous supply

Due to the impact of work style reforms, the predicted decline in the working population, and the impact of rising prices of materials, etc., there is an even greater need to improve productivity in processes such as manufacturing, logistics, and sales.

Regarding the review of regulations in line with the Digital Principles, a notice was issued on June 17th of this year, which was a major step forward. As a more detailed application of this thinking, and taking other perspectives into account, we would like to see more flexible application of regulations with regard to the following items.

(i) Reconsider how to handle sales and rental business related to warehouse operators
(ii) Handling of separated storage warehouses in line with digital principles
(iii) Improving the installation of program medical devices
(iv) Request for grace period for legal labeling of direct containers, etc.
(v) Regarding the change management system

(i) Reconsider how to handle sales and rental business related to warehouse operators

【Background】

When a medical equipment distributor or lender (hereinafter referred to as "distributor") uses a warehouse operator to store and manage medical equipment owned by the distributor or lender, distributor must obtain a license to operate a medical equipment distributor or lender bujiness using operater's warehouse as its business office.

Under the previous QA, warehouse operators were required to have a license to sell and rent medical equipment, and in reality, warehouse operators were able to manage medical equipment (management and operation of property owned by companies other than the warehouse operator) without any problems.

It is often recognized that opinions on this matter differ depending on the licensing authority, such as prefectures, public health centers, and their counterparts. Some warehouse operators organize the opinions of each licensing authority and work with their entrusting distributors to ensure that business policies are not impeded.
In addition, for those who have entrusted the storage, management, sale, and rental of products with the permission of the warehouse operator, this is a major change in their internal structure, which has caused confusion and burdens such as new personnel deployment.

In the current social situation where the "Logistics 2024 Problem" has been raised, the burden of using warehouses for efficient logistics is being placed on both distributors and warehouse operators.

【Suggestions and Requests】

As there are many different types of medical devices and their distribution methods are equally diverse, we would like you to consider a system that enables a storage and management system that allows for efficient and reliable distribution.

For example, we would like you to clarify that a system that allows for appropriate responses to diversity will be allowed, such as by organizing and considering the circumstances of each medical equipment product group in accordance with the actual situation, and allowing warehouse operators to store and manage the medical equipment regardless of ownership if it is possible to reliably store and manage the product.

【Expected effects】
By improving this handling process, the efficiency of medical equipment warehouse management and business activities will be improved.

(ii) Handling of separated storage warehouses in line with digital principles

【Background】
A notification issued in June this year outlined the approach to permanent presence in each business type in line with the Digital Principles, and it is expected that this will lead to more flexible operation.

There are many types of medical equipment, and they are used in a variety of places.
For example, for equipment that requires a lot of transportation, or for equipment used during emergency surgery or treatment, warehouses are set up all over the country to store the equipment in order to meet the needs of the medical field and to supply the equipment quickly, efficiently, and continuously.
However, if the equipment is located far from the sales base, it does not meet the requirements for a separated storage warehouse (within the same prefecture, etc.), so a new sales business is required, but it may not be possible to secure a sales office manager.

Particularly in depopulated areas, it will be difficult to secure human resources due to the decline in the working population, and there is also the possibility of isolation in the event of a disaster such as an earthquake, so measures are necessary.

【Suggestions】
We would like to consider flexible operation of separate warehouses in line with the digital principles.
(For example, if product management is possible using digital technology, separated storage warehouses could be approved regardless of distance.)

【Expected effects】

Improving logistics load and ensuring rapid access to medical equipment, especially in remote and depopulated areas

(iii) Improving the installation of program medical devices

【Background】

Although medical device programs (such as cloud-based) intended for image diagnosis, etc. are not designated as medical devices requiring installation management, they must be configured to access the server where the images are stored and to link with other devices, and this installation work (installation management) requires expertise.

Since medical device programs are standalone medical devices, they are delivered directly to the purchaser and are generally installed by the purchaser. However, in the above case, the purchaser (medical institution) will need to request the distributor, etc. to install the program after delivery.

【Suggestions】

For items that require "installation management" in the medical device program, rather than being designated by a generic name based on JMDA, we would like to make it possible to implement this by specifying that it is "installation management" in the remarks or usage instructions field when applying for approval (certification).

【Expected effects】

Medical institutions will no longer need to make separate installation requests after purchase.

The device will be properly installed at the medical facility, and records of this will be kept by the distributor.

(iv) Request for grace period for legal labeling of direct containers, etc.

【Background】

When a manufacturer changes its name or relocates its offices, it is currently necessary to change the legal labeling on the date of the change (relocation date).

In many cases, the name and address are fixed items printed on the packaging in advance, and the labeling of many products will need to be changed to coincide with the date of the change, but this makes production planning difficult and results in a large amount of old packaging being disposed of. It is particularly difficult to manage the transportation period for items that are packaged overseas and shipped domestically by sea.

Information on precautions and other matters has already been digitized, hence, making it possible to access necessary information, including manufacturer information, in a timely manner.

【Suggestions】
We would like to ask you to consider easing the restrictions, such as providing a grace period for legally required labeling changes, on the condition that medical professionals and others are provided with information about name or address changes in advance.

【Expected effects】
Allowing the shipment and distribution of products with the old labeling for a certain period of time will reduce the risk of distribution becoming unstable and ensure a stable supply.

This will reduce discarded packaging material and promote the SDGs.

(v) Regarding the change management system

【Background】
There are a great number of medical device items, and many changes are required after launch. In addition, managing these changes requires a huge amount of work.
The types of changes include;

① Diligent improvements to improve medical devices
② Changes to materials, etc. to ensure stable supply
③ Changes to names, etc. due to mergers and acquisitions of corporations and manufacturers, reorganizations, etc.

and many other considerations have been conducted over the years regarding a change management system.

Holders of special approval for foreign-manufactured medical devices, etc. are required to submit a change notification for each item when there is a change in name (corporate name/representative name), address, officer conducting business, manufacturing facility, etc. (Article 37-38 of the Enforcement Order), and since they also normally hold a foreign manufacturing registration, they submit the same change notification.
On the other hand, with a regular manufacturing and sales (MAH) approval, a change in the name of the corporate representative is not subject to change.
However, with special approval for foreign-manufactured medical devices, etc., duplicate

change procedures occur.

【Suggestions】

1. As for changes in raw materials and components that fall under item ② above, as we have already proposed, we would like to ask you to expand the scope of minor change notifications that are permitted under certain conditions.
2. As for the change corresponding to item ③ above, as we have already proposed, we would like to ask you to introduce the "incidental change/change in addition" as soon as possible in order to streamline administrative procedures.
3. Regarding changes to holders of special foreign approval, if a foreign manufacturer is registered and a change has been made to that registration, we would like there to be no need to carry out change procedures for items.

III. Promoting system construction and DX using digital technology

The Basic Policy on Economic and Fiscal Management and Reform 2024 also gives considerable attention to promoting digitalization, including the promotion of digital government and digital transformation in medical and nursing care.
Digitizing information can lead to transformation in processes and services that can greatly improve productivity, and hopes are high for this potential.
Additionally, the five pillars of the economic measures announced at the end of last year include "improving the efficiency of administrative and public services through digital technology" in order to "overcome population decline and achieve social change that harnesses change as a force."
However, digitalization and systemization require a lot of man-hours and costs, so progress has not been very strong. We believe it is important to create an overall picture with a long-term, multifaceted perspective, and then plan and implement each step.

(i) Proposal for promoting UDI utilization and medical device DB
(ii) Proposal for starting consideration of pharmaceutical Affairs DX

(i) Proposal for promoting UDI utilization and medical device DB

【Background】

1. **Regarding UDI labeling (specific code labeling)**

   Two years have passed since the law came into force in December 2022, but the extent to which the purpose of the legislation has been achieved is unclear. Medical institutions that use UDI labeling are calling for the expansion of regulations to include labeling on the product itself and individual packaging, which were excluded from the scope of the recent legislation. However, the number of medical institutions that use UDI labeling is still not large. In order to get more medical institutions to use UDI labeling, we believe that some kind of response is necessary other than expanding the scope of regulations.

   ⇒We assume that the lack of individual packaging labeling is not the reason for its lack of use.

2. **Regarding the UDI database (medical device database)**

   The current utilization of the database has not reached the expected level, and issues remain with regard to its comprehensiveness and registration quality. In addition, the database itself has been in design for a long time, and in order to expand its utilization, it seems time to reconsider its specifications and operation.

【Suggestions and Expected effects】

1. The survey on the progress of information technology should not only look at the response of manufacturers and distributors, but also at the status of UDI utilization in medical institutions, etc., in order to clarify sufficient conditions for achieving the original purpose.
2. Regarding the database, which is the two wheels of labeling, we would like the government to take the lead in considering using registered data, for example for managing items covered by insurance. Using a database in line with product lifecycle management is likely to naturally lead to improved registration quality and comprehensiveness.

   Furthermore, having medical institutions use UDI and incorporating it into medical digital transformation in the future will lead to secondary use of medical information and improve the significance of data entry on the company side.
3. To achieve the original goal, relevant stakeholders will work together to prepare a master plan for UDI utilization that can be shared among them, and then proceed in a planned manner.

(ii) Proposal for starting consideration of pharmaceutical Affairs DX

【Background】

As administrative procedures become more commonplace online, applications for business licenses other than sales and rental, as well as most applications and notifications handled by PMDA, can now be submitted online in PDF format.

There are many medical device items, and common information related to each item, such as information on the manufacturer, components, etc. Even a single change requires changes to all related items, which places a heavy burden on both applicants and PMDA in terms of administrative procedures. For this reason, over the past few years, we have been calling for the creation of a system that would allow for comprehensive changes.

The sales and rental businesses are operating throughout Japan, but because they are handled by public health centers as local government affairs, the documents to be submitted and the requirements for change procedures vary from prefecture to prefecture, requiring a considerable amount of time and effort, so almost every year they have requested standardization and the establishment of a database system.

【Suggestions】
In order to reduce the administrative burden and improve the efficiency of change management for applicants, shouldn't we aim to build a database that digitizes basic information about items, for example by linking it to the product database mentioned on the previous page?

In order to reduce overlapping work among prefectures, we would like you to consider building a database system for information management and change management for sales and rental offices across prefectures, making it possible to make changes all at once, such as changing the responsible officer.

It is anticipated that there will be high hurdles to overcome in areas such as securing budgets, but we would like to work closely with the Digital Agency to move forward with this project, including collaborating with other databases and considering long-term plans for each step.

IV. Promoting international harmonization and globalization

Japan's stable regulations and review system are a major advantage compared to other

countries. In order to make the most of this advantage, we need to spread the idea of "Reliance," which is attracting attention in various countries, increase the number of countries that refer to Japan in reviews and QMS inspections, and make effective use of this system, which will increase Japan's influence. In addition, considering future domestic market trends, overseas expansion is inevitable, and international harmonization of various regulatory requirements is essential. In particular, we believe that we should strongly promote the following points.

(i) Considering the state of the QMS conformity inspection system in light of international harmonization
(ii) Promoting the use of reference country systems

(i) Considering the state of the QMS conformity inspection system in light of international harmonization

【Background】

As the supply chains involved in medical device manufacturing become increasingly globalized and complex, and as domestic medical devices are expected to expand overseas, it will be important to further harmonize Japan's QMS inspection systems with other countries in order to further promote reliance on Japan's QMS inspection reports.

In major overseas countries/regions (MDSAP member countries, Europe, etc.), comprehensive surveys are being conducted that focus on quality management systems centered on (legal) manufacturers, and we believe that a "QMS inspection system at the manufacturing/distributor/manufacturer level" is the ideal.

Because QMS inspections are conducted on an application item basis (except in cases where inspections have been conducted on the same product group and at the same manufacturing plant), duplicate inspections are occurring at the same manufacturing plant.

In order to consider the above as a long-term issue, and to consider immediate operational improvements to the QMS inspection system as a short-term issue, a working group was established and activities have begun with the participation of the Ministry of Health, Labour and Welfare and PMDA.

【Once again/Furthermore】

Long-term issue:
Assuming international harmonization, we would like to consider a more efficient and effective QMS inspection system by clarifying the relationship between the organization that operates the QMS and each business type, the unit of inspection, and the nature of inspections by PMDA and certification bodies, with the aim of establishing a QMS inspection system at the marketing authorization holder/manufacturer level.
We would appreciate your cooperation when we begin concrete consideration of this issue.

Short-term issues:
We have identified four issues to address as immediate operational improvements and have begun considering them.
1) Further consolidation of product groups,
2) Rationalization of documents required for QMS conformity survey applications,
3) Handling of issuance of standard conformity certificates,
4) Handling of QMS conformity surveys for discontinued products.

(ii) Promoting the use of reference country systems

【Background】
As a result of the efforts made so far, Japan has become a reference country for many countries, especially in Asia, when applying for medical device approvals.
The status of use of reference country systems in applications to these countries is unclear, and regulatory authorities have the impression that efforts to promote the use of the systems by industry are insufficient.
On the other hand, some companies that have applied to the country in question have said that they are not aware of the reference country system, or that they are aware of it but do not feel that it is beneficial to use the system.

【Suggestions】
The Japan Medical Device Manufacturers Association conducted a survey of member companies of its member organizations regarding the use of the reference country system. Going forward, the association plans to use the survey results to understand the current status of use and to summarize whether there are any issues with the use or awareness of the system. In addition to reporting the results, the association would like to ask for your cooperation if any improvements are identified to promote the use of the system.

When a new system is concluded, we would like the government to not only announce it as

"speeding up medical device reviews in Country X," but also to clearly state its contents (changes from previous procedures and the benefits of the revisions).

【Expected effects】
By sharing information on the use of reference country systems between industry and government, it will be possible to concretely discuss the direction of future system development.

By improving the system and raising awareness, the use of the reference country system can be increased to the expected level.

By increasing its use, global companies can also raise the priority when considering introducing products into Japan.

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