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The 451st International Symposium on Therapy

The 451st International Symposium on Therapy was held by the Zoom Webinar on September 16, 2021. Dr. Takahisa Murakami, Director of the International Medical Society of Japan (IMSJ), presided over the meeting.

Trends in pharmaceutical regulations in the development of pharmaceuticals and medical devices

- The Roles of Pharmaceuticals and the Medical Devices Agency (PMDA) -

Introductory Message from the Chair

Takahisa Murakami, PhD
Director, IMSJ

Needless to say, drugs and medical devices are important tools in medical treatment, and safe, highly efficient drugs and medical devices are always expected. In a situation like the spread of COVID-19 infections that occurred recently, the expectations society has are even greater. However, increasing social interest may cause the dissemination of unconfirmed information that results in confusion.

In addition, the first two COVID-19 vaccines approved in Japan were RNA vaccines that have a different development concept from conventional vaccines. In order to accurately evaluate such new technology, the people who evaluate it must be highly capable.

Therefore, a specialized institution that conducts neutral, scientific evaluations is indispensable.

Today, we are welcoming the chairman of the board, Dr. Yasuhiro Fujiwara (MD, PhD, Chief Executive), and the medical management supervisor, Dr. Haruko Yamamoto (MD, PhD) from the Pharmaceuticals and Medical Devices Agency (PMDA), which is an organization that examines pharmaceuticals and medical devices in Japan. They will talk about the PMDA's initiatives for the recent development of new drugs and medical devices.

We would like to take this opportunity to reaffirm the importance of the PMDA's activities.

Lecture I

PMDA's efforts to promote medical innovation in the COVID-19

Yasuhiro Fujiwara, MD, PhD
Chief Executive
Pharmaceuticals and Medical Devices Agency (PMDA)

The Pharmaceuticals and Medical Devices Agency (PMDA) plays three key roles—relief services for persons injured by adverse reactions, product reviews, and safety measures. In recent decades, the progress of medical science and health care in the world has been rapid, and people's expectations of medical treatment have risen accordingly. We aimed to speed up review and safety assurance measures, in order to introduce new drugs and medical devices in a timely manner from a social welfare point of view, while at the same time enabling continuous and rapid monitoring of safety. To provide patients and healthcare professionals with timely access to safer, more effective medical products, the PMDA is engaged in ensuring quality, efficacy, and safety from development to post-market stages.

Since its inception in 2004, the PMDA has steadily attained progress. In April 2008, the number of PMDA staff was less than 450, but the total has now reached nearly 1,000. After having overcome the issues of drug-lag and device-lag, PDMA has introduced other measures, PMDA has improved its standing in the global positioning of regulatory authorities by building up its scientific capabilities to speed up new drug review and safety measures, as exemplified by achieving the world's fastest review speed for new drugs with new active ingredients. With the emergence of innovative products, the quality of our work has to be further improved enough to be capable of making first decision in the world on those products.

As a part of this work, it is important to harmonize international scientific norms and evaluation methods. We believe such an approach will enhance the social implementation of new outcomes of science and technology for the benefit of patients in the human society.

Further, based on regulatory science implementation, we were able to propose and introduce the world's first regulatory category for regenerative medical products (cell, tissue and gene therapies), as well as to introduce a new system of conditional early approval for medicines. In the Center for Regulatory Science which PMDA established in 2018, we also organized the Science Board to bring together researchers who are directly involved in advanced studies leading to the development of innovative medicines. The board summarizes evaluation reports on advances in medical science and technology, including iPS, providing the foundation for horizon scanning of potential medical advances.

The need for such measures has been clearly illustrated by the recent work to develop, test and approve coronavirus vaccines. Furthermore, with the worldwide spread of novel coronavirus infections these days, PMDA has been able to facilitate developing coronavirus related products smoothly, by providing consultations and responding to requests from the early stages of development of drugs and medical devices related to the corona virus infectious disease. Once an application for approval has been submitted, we work on to proceed review process as fast as possible. In addition, as large-scale vaccination program against novel coronavirus infections has started in Japan, number of Adverse Events Following Immunization (AEFI) have been reported more than before. We have been working hard, even day and night, to sort out and to make analysis on suspected AEFI associated with the novel coronavirus vaccines.

The modality of products such as pharmaceuticals has also been diversified, and the expected effects and evaluation methods of these products vary, depending on different natures of origin such as small molecules, macromolecules, cells, genes, etc. In this lecture, I would like to introduce PMDA's activities for faster access to safer and more effective medical products, even in response to the products emerging new modalities of medicine.

Lecture II

Recent trends of clinical development of medical devices and new regulatory frameworks in Japan

Haruko Yamamoto, MD, PhD
Chief Medical Officer
Pharmaceuticals and Medical Devices Agency (PMDA)

With recent advances in science and technology, the speed at which innovative technologies will be adapted and applied to medical devices continues to increase. On the other hand, the fact remains that there are some medical devices whose development is challenging to promote because of small market size, despite their high degree of medical necessity.

In 2014, the Pharmaceutical Affairs Law, the essential legislation for regulation of medical products, was largely revised and renamed. In the revised law named the "Act on Securing Quality, Efficacy, and Safety of Products Including Pharmaceuticals and Medical Devices" (in short, Pharmaceuticals and Medical Devices Act; PMD Act), the independent chapters for medical devices and regenerative medical products were newly installed, while medical devices were put in the same chapters for drugs and no description for regenerative medical products before revision. This revision enabled to develop more effective regulatory frameworks for medical devices for Japanese regulatory authority, apart from other categories of medical products. The Revision of PMD Act in 2019 gave legal basis of several new frameworks for approval of medical devices including the SAKIGAKE designation system", the "conditional early approval system", the "PHOENIX (physical operation items' extrapolative and inclusive approval)", the "IDATEN (improvement design within approval for timely evaluation and notice)", and the "IDATEN for AI". The Pharmaceutical and Medical Device Agency (PMDA), Japanese regulatory agency, plays an important role, in close cooperation with the Ministry of Health, Labour and Welfare (MHLW), in these frameworks.

To accelerate emerging global trends of developing Software as a Medical Device (SaMD), MHLW has started "DASH for SaMD (Degital transformation action strategies in healthcare for

SaMD)" since 2021. PMDA, in collaboration with MHLW, set up a new review office that specializes in SaMD in April 2021.

Many medical device industries hesitate to pay the cost before obtaining market clearance and insurance coverage because of lack of intensives in small patient population. Several regulatory agencies including PMDA has started considering the use of Real World Data (RWD) such as registry data on regulatory decision making. PMDA has developed and finalized several guidelines to promote RWD utilization, and started a series of consultation services for registry owners, database providers and developers of medical products in 2019, in order to provide scientific advice on feasibility of registry utilization and on registry data reliability.

PMDA will continue to make efforts to expedite patient access to more effective and safe medical devices by collaborating with the manufactures and academia, and by introducing less burdensome and user-friendly regulatory frameworks.

Discourse

Introduction of the speaker of discourse

Takahisa Murakami, PhD
Director, IMSJ

Today we have invited Mr. Mikio Kawa, the President of the Social Welfare Corporation of the Japan Association of Physically and Mentally Challenged Children (Shimada Ryoiku Medical Center for Challenged Children), who has been active in the field of social welfare since joining the Ministry of Health and Welfare (as it was known at that time) in 1975. He possessed a high level of insight into the welfare of people with disabilities before entering the ministry. After entering the ministry, he served as chief of the Planning Division of the Social Assistance Bureau, counselor in charge of social security, and Councillor, cabinet secretariat. After retiring in 2007, he became a professor at Kanagawa University of Human Services, and has been in his current position since 2017. He will talk about the key points of social welfare.

Discourse: The social security system and human services

Mikio Kawa
President
Social Welfare Corporation, Japan Association of Physically and Mentally Challenged Children
Shimada Ryoiku Medical Center for Challenged Children

[Two types of benefits of social security]

According to statistics on the costs of social security in 2019 released by National Institute of Population and Social Security Research at the end of August, Japan's "social security benefits cost" in 2019 was 124 trillion yen (23% of the gross domestic product).

When considering social security, it is customary to classify them into pensions, medical care, and welfare according to their purposes, and then discuss their ratio and composition. However, it is important to pay attention to the nature of the benefits, and to consider them separately as either "cash benefits" (e.g. pension benefits, etc.) or "service benefits" (e.g. medical service fees, nursing care fees, etc.).

When talking about social security in developed countries, in the field of media and politics, and in the subject of economics, many experts discuss only the "cash benefits", such as pensions and benefits that protect people's livelihoods.

However, there are also social security systems such as medical insurance and long-term care insurance which are there to supply human service benefits continuously and stably. Medical services and long-term care services are provided to facility users in the form of human services at hospitals and social welfare facilities. In these systems, the costs of those using the facilities are covered by the general public's payments such as through taxes and insurance premiums, and people can use these human services if they bear a part of the cost.

Since the benefits themselves are human services, they should be called "service benefits" (including drug costs) systems. In these "service benefits" systems, the general public's share of the expenses is actually paid to hospitals and social welfare facilities in the form of "remuneration", where most of the amount will be spent on personnel expenses for staff members.

Hence, "money" is replaced with "service benefits".

[A review of service benefits]

Ten years ago, when I analyzed and calculated 100 trillion yen of social security benefits costs

(FY2009), I found that "cash benefits" accounted for 60 trillion yen (60%) and "service benefits" accounted for 40 trillion yen (40%). Breaking down the financial resources, tax financial resources were 40% and insurance premium financial resources were 60%. As much as 40% of social security benefits costs were "service benefits".

According to recent materials, social security benefits costs (FY2019) were 124 trillion yen, "cash benefits" were 62 trillion yen (50%), and "service benefits" were 62 trillion yen (50%). Service benefits actually accounted for 50% of the costs. (Regarding financial resources, tax financial resources were 40% and insurance premium financial resources were 60%)

Here are three reasons for discussing the two categories, which are cash benefits and service benefits.

(1) Cash benefits are derived from a standpoint of "human rights", and service benefits are derived from a standpoint of "necessity".

(2) Cash benefits are paid mechanically, and service benefits are paid "face-to-face".

(3) Cash benefits are described in terms of "how much they cost" and service benefits are evaluated in terms of their "quality".

[Service benefits supply system theory]

In order that the social security "service benefits" are properly and fairly practiced nationwide, there should be a service supply system nationwide in which there are some people who live there and who can provide human services with a certain level of quality. In order that these human services may be provided stably and continuously, it is necessary that qualified people are engaged in performing these service benefits as their profession, and that they are present [living] in the vicinity of the users.

Moreover, as long as people are required to bear the costs of "service benefits", "publicness" is a requisite for these human services. The human services themselves are "private" things that protect and support the lives of users; however, they have a public nature because they provide safety and security to everyone in local communities. In that sense, the system of providing human service benefits itself should be considered a public asset.

No matter how much money is allocated, providing human services beyond the qualities of service providers or beyond the capabilities of service institutions is impossible.

Great human services cannot be created from enormous or excessive workloads. Although this service provision system theory might seem to be a function of "money", ultimately it is a matter of the "existence of professionals". Thus, we have to promote such awareness until it is a common understanding in society.