

# **Grand Design for Asian Pharmaceutical and Medical Device Regulatory Harmonization**

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Established by the Headquarters for  
Healthcare Policy of Japan

Based on the “Act on Promotion of Healthcare Policy” enacted in May 2014, the Headquarters for Healthcare Policy of Japan established “Basic Principles of the Asia Health and Wellbeing Initiative (AHWIN)” (Hereinafter referred to as the “Basic Principles”) in July 2016. The Asia Health and Wellbeing Initiative is based on mutually advantageous cooperation in Asia that aims to achieve forward movement where healthy lives and economic growth comprise the wheels of the vehicle. The Asia Health and Wellbeing Initiative is supported by many countries, and concrete cooperation and enterprises have already been started. The Basic Principles were also revised in July 2018 after stakeholders became aware of themes and issues that had not been included in the original version. The revised version promotes the development of the necessary industries in Asia with a view to autonomous supply of pharmaceuticals, medical devices, and regenerative medicine products (hereinafter referred to as “pharmaceuticals and medical devices”) in Asia, and it incorporates the aspiration that “In order to contribute to resolving the ‘drug lag’ between Japan and Asia, Japan will promote harmonization efforts to make pharmaceutical approval systems and safety regulations more effective and rational by ensuring interoperability in Asian countries of data used for approval of pharmaceuticals.”

Japan aims to realize “Universal Health Coverage (UHC)” as a contribution in the international health field. In order to realize UHC, it will be essential to disseminate all basic services such as infectious disease control and non-infectious disease control, and to respond to the need for prevention, diagnosis and treatment of diseases associated with changes in lifestyle and aging. However, in Asian countries/regions, access to pharmaceuticals and medical devices, including products utilizing innovative technologies, is insufficient, and this is one of the important issues. International harmonization plays an important role in improving access to pharmaceuticals and medical devices in Asian countries/regions, as Japan has been participating in international harmonization activities and incorporating the results in efforts to eliminate drug lag and device lag in Japan. To improve access to pharmaceuticals and medical devices in Asia, Japanese Government decided to make a Grand Design for regulatory harmonization and related matters.

## **1. Significance of Formulation of Grand Design**

### **(1) Situation Surrounding Asian Countries/Regions**

Asian countries have experienced rapid economic development in recent years. According to the estimation<sup>1</sup> by Asian Development Bank (ADB), the economic growth rate in the Asia Pacific region excluding Japan and Australia is estimated at 6.0% for 2018, and high-level growth is expected to continue in

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<sup>1</sup> Asian Development Outlook, April 2018, Asian Development Bank

the future. According to the United Nations demographic statistics, the Asian population was less than 1.5 billion in 1950 but reached 4.5 billion in 2017 and is estimated to exceed 5.3 billion by 2050<sup>2</sup>. Amid this population growth, the compound annual growth rate (CAGR) of medical expenses in Asia from 2000 to 2016 was roughly 21% in Myanmar, 16% in China, 13% in Indonesia and 10% in other Asian countries/regions, showing marked increases, respectively<sup>3</sup>. In addition, the pharmaceutical market is expanding. For example, in China, the CAGR exceeded 10% between 2010 and 2017<sup>4</sup>. According to the Organization for Economic Co-operation and Development (OECD), the average growth rate of actual pharmaceutical expenditures per average purchasing power in China and Bangladesh was reported to be greater than 8% between 2010 and 2015<sup>5</sup>. The situation is similar for medical devices, where, for example, the Chinese market is estimated to have reached 21.4 billion USD in 2017, with an average annual growth of 9.3% since 2018, and is forecast to grow to 31.4 billion USD by 2021<sup>6</sup>. In the future, demand for pharmaceuticals and medical devices is expected to grow more and more in Asian countries/regions against a background of economic development and population growth.

On the other hand, rapid aging is an inevitable situation worldwide. For example, the 2017 Annual Report on the Aging Society states that the rate of aging in 2015 was 17.6% in developed regions and 6.4% in developing regions, but it is expected to rise to 27.4% and 16.8%, respectively, by 2060. It has been reported that aging will rapidly progress not only in the developed regions but also in the developing regions. Under such circumstances, public health issues in Asian countries/regions are expanding from infectious disease control to non-communicable disease control. In Asian countries/regions, awareness of health has been increasing with the improvement of health and hygiene. Particularly, due to the development of information and communication technology (ICT), there is increasing attention to the latest medical technology and products to appear in various countries. In addition, while Asian countries/regions are highly motivated to introduce innovative pharmaceuticals and medical devices, their interest in cost-effective and high-quality products is increasing in the context of the impact on financial burdens.

Due to globalization and diversification of products, the regulatory system for pharmaceuticals and medical devices is complicated and advanced. Regulators worldwide are arriving at a common recognition of the importance of international cooperation. In August 2018, the World Health Organization (WHO) announced Good Practice (draft) for conducting registration procedures in other countries for drugs approved in reliable reference

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<sup>2</sup> World Population Prospects: The 2017 Revision, the United Nations

<sup>3</sup> Estimated from WHO "Global Health Expenditure Database"

<sup>4</sup> Estimated by IQVIA World Review Analyst

<sup>5</sup> OECD/WHO (2018): Health at a Glance: Asia/Pacific 2018: Measuring Progress Towards Universal Health Coverage, OECD publishing, Paris

<sup>6</sup> FY2017 Medical Technology and Service Base Promotion Project's Global Medical Development Country Report: Basic information on healthcare market environment in emerging countries – China Edition, edited by Ministry of Economy, Trade and Industry, March 2018

countries, with an understanding of the importance of avoiding duplication of regulations in each country through cooperation with regulatory authorities. In addition, the International Coalition of Medicines Regulatory Authorities (ICMRA), which is composed of leaders of pharmaceutical regulatory authorities in each country/region, aims to respond to common issues by more effectively utilizing the resources of each regulatory authority through information sharing from a strategic and high-level perspective, beginning at the stage of the regulation's inception<sup>7</sup>.

There is a close relationship between establishing a system for the development of pharmaceuticals and medical devices and improving regulatory standards, including proper use after marketing. For example, the establishment of systems of organization for conducting clinical trials at medical institutions leads to the establishment of a system whereby post-marketing adverse reactions are reported through medical institutions. Moreover, making it possible to conduct high-quality global clinical trials at medical institutions throughout the world is an important driving force in the improvement of drug access in Asian countries/regions. Among the drugs approved in Japan in FY2017, 39.4% were investigated in global clinical trials. Global clinical trials that promote simultaneous global development and lead to efficient development have contributed greatly to the elimination of drug lag and device lag in Japan. On the other hand, of the products approved in the same year, only 6.73% went through joint clinical trials in Asia, and further promotion of global clinical trials in Asian countries/regions is expected.

## **(2) Efforts to Improve Japan's Access to Asia**

### **[1] Past Initiatives**

Japan has long led global regulatory harmonization activities for pharmaceuticals and medical devices with regulatory authorities in Europe and the United States. For example, Japan has participated in the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), which started in 1990, as a founding member, together with Europe and the United States, and has contributed to the preparation of guidelines on pharmaceutical regulations from scientific and technical viewpoints. Japan has also participated in the International Medical Device Regulators Forum (IMDRF) from the time of its establishment, to lead discussions on international harmonization of medical device regulations. In addition, Japan joined the Pharmaceutical Inspection Co-operation Scheme (PIC/S) in 2014 and has played an important role in the international development, implementation, and maintenance of harmonized Good Manufacturing Practice (GMP) and quality systems for inspection authorities in the pharmaceutical field.

At the same time, in the span of approximately 10 years following the establishment of the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan in 2004, drug lag and device lag were eliminated with the enhancement of regulatory science. As a result, PMDA's performance in

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<sup>7</sup> WHO Drug Information Vol. 29, No. 1, 2015

reviewing new drugs is now comparable to that of the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Based on the improvement of the Japanese system and the development of health and medical strategies, the Ministry of Health, Labour and Welfare (MHLW) formulated its International Regulatory Harmonization Strategy in 2015, and the PMDA developed its PMDA International Strategy 2015. Since then, PMDA has disseminated Japanese knowledge on pharmaceutical and medical device regulations to the world, including Asian countries/regions, and has been promoting activities aiming to further contribute to the improvement of health and hygiene throughout global society. In 2016, PMDA newly established the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs to provide persons in charge at regulatory authorities in Asian countries/regions with experience and know-how on the construction of pharmaceutical regulations, and has been continuously developing a foundation for future regulatory harmonization. In 2017, the MHLW and PMDA hosted the Summit of Heads of Medicines Regulatory Agencies and its Symposium in Kyoto for the first time in Japan. Representatives of regulatory authorities from 29 countries and regions, including Japan, the U.S., and Europe, participated in this Summit, which also helped foster trust in Japan and Japanese regulations. By inviting the heads of medicines regulatory agencies to take part in this Summit, Japan secured their understanding of the direction of proceeding with regulatory harmonization from a common Asian perspective.

The business community is also developing activities that contribute to regulatory harmonization of pharmaceuticals and medical devices. Representatives of the Japanese pharmaceutical and medical device industries also contribute to constructive discussions on regulatory harmonization as members of ICH and IMDRF. For example, the Japan Pharmaceutical Manufacturers Association has led the Asia Partnership Conference of Pharmaceutical Associations (APAC), which consists of 13 Asian pharmaceutical organizations belonging to the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), in promoting collaboration among Asian pharmaceutical industry organizations by holding a meeting every year in Japan since 2012. In the area of regenerative medicine products, the Forum for Innovative Regenerative Medicine (FIRM) held a meeting with Asia Partnership Conference of Regenerative Medicine Associations (APACRM) from 2018 to promote understanding of regenerative medicine products in Asia.

From the viewpoint of improving the clinical trial environment in Asia, academia has also been active. For example, the National Center for Global Health and Medicine (NCGM) is developing a global clinical research network base for Asia-centered global collaboration, through which Japan has brought together human resources from various countries who have a lot of R&D experience in the field, and is contributing to global health through international deployment of Japanese medical care. In addition, the National Cancer Center (NCC) established a consortium with the medical institutions that are the early new drug development bases (Phase 1 Centers) in Asia in

2017, and has been working to accelerate the joint conduct of early-phase clinical studies and efficiently develop early new drugs based on the characteristics of Asia.

## **[2] Acceptance by Asian Regulatory Authorities**

Since the Summit of Heads of Medicines Regulatory Agencies held in Kyoto in October 2017, the regulatory authorities in Asian countries/regions have been very interested in making new drugs, etc. reviewed by PMDA subject to the reference country system (Simplified or Expedited Review), together with Western countries. In addition, efforts to harmonize Japanese regulations, centering on the PMDA's Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs, are welcomed by regulatory authorities in Asian countries/regions as collaborative initiatives. For example, at the ASEAN-Japan Health Ministers' Meeting on Universal Health Coverage and Population Ageing in 2017, a written agreement to use the PMDA's Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs to improve the capabilities of ASEAN countries was compiled.

## **(3) Necessity of Further Efforts**

In Asian countries/regions, the environment surrounding pharmaceuticals and medical devices has greatly changed as economic development and the population increase. Improvement of access to pharmaceuticals and medical devices in individual Asian countries/regions contributes to the improvement of the health of the people in Asian countries/regions, and it is desirable to aggressively work toward this from the viewpoint of promoting UHC. From the viewpoint of patients who will benefit from pharmaceuticals and medical devices, a borderless market for pharmaceuticals and medical devices is being established in Asia, ushering in an era in which remarkable pharmaceuticals and medical devices that have been approved in Japan can be accepted by Asian countries/regions and promptly provided to patients.

With innovative product development making progress in many parts of the world and rapidly providing new products to other countries, it has become difficult for a sole regulatory authority to handle all regulatory matters related to the quality, efficacy, and safety of pharmaceuticals and medical devices. Under these circumstances, regulatory harmonization plays a major role in ensuring access to pharmaceuticals and medical devices. In particular, many countries in Asia have much in common with Japan in terms of cultural and social infrastructure, and Japan's regulatory experience and measures are considered to be sufficiently relevant to their situation to use as a reference.

On the other hand, access to pharmaceuticals and medical devices has complex aspects involving various factors such as research and development, regulation, and securing of intellectual property. To address these problems, business community, academia, and government need to cooperate in a concerted effort.

Based on the above, harmonization of regulations for pharmaceuticals and

medical devices in Asian countries/regions, human resource development by regulatory authorities, and establishment of related “hard” and “soft” approach development systems are urgent issues. To create the ecosystem necessary for the improved access that will make a “society of health and longevity” a reality for Asian countries/regions, the competent ministries and agencies will need to work together with business community, academia, and government in a manner that is open to civil society.

## **2.Efforts to Improve Patient Access to Pharmaceuticals and Medical Devices**

### **(1) Basic Approach**

The basic approach to be taken by Japan in efforts to improve patient access to pharmaceuticals and medical devices is as follows.

#### **[Shared principles and values]**

For pharmaceuticals and medical devices, the goal is to realize rational medical care that provides optimal medical care to patients, based on the latest scientific knowledge. Moreover, since each Asian country/region has limited human and physical resources, what is being proposed is to promote healthcare that has been evaluated not only in terms of its medical value based on the efficacy and safety of pharmaceuticals and medical devices, but also from the viewpoint of improving the labor productivity and economic performance of the entire society through medical care. In the promotion of healthcare and medical care, regulations based on scientific evidence, i.e. regulatory science<sup>8</sup>, can serve as a common language. In Asian countries/regions, there is insufficient understanding of the regulatory science that is the basis of regulations on pharmaceuticals and medical devices, and efforts will also need to be made to promote the understanding and utilization of regulatory science.

#### **[Close cooperation that respects the position of regulatory authorities in other Asian countries/regions]**

The regulatory authorities of each country/region are responsible for contributing to the health of the people by making effective pharmaceuticals and medical devices swiftly available to the public while ensuring the safety of these products. Cooperation between Japanese and Asian regulatory authorities is essential for regulatory harmonization of pharmaceuticals and medical devices and establishment of the development system. Japan’s regulatory authorities have forged ties with their counterparts in other Asian countries/regions in a spirit of mutual respect and equal partnership, and will build upon those ties to promote further cooperation. During that process, the utmost priority will be given to developing the human resources needed in each country/region. In particular, it is important to utilize the

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<sup>8</sup> Science that aims to make the fruits of science and technology useful to humans and society by making accurate predictions, evaluations, and judgments based on evidence and coordinating the incorporation of the fruits of science and technology into society to achieve the most desirable state of harmonization with humans (4th Science and Technology Basic Plan)

human-resource development programs being carried out by Japan's Pharmaceuticals and Medical Devices Agency (PMDA) at the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs, for example, to deepen the understanding of Japanese regulations as a means to lay the foundation for regulatory harmonization in Asia.

### **[Coordination and cooperation with the business community's activities]**

Regulatory harmonization requires understanding and cooperation not only on the part of those imposing regulations, but also on the part of the business community that is subjected to the regulations. In addition, it will be difficult for the countries of Asia to improve their regulations without upgrading of skills, not only on the part of regulatory authorities but also within the business communities. This will necessitate constant communication between Japan and the business communities of partner countries. Hence, the business community and regulatory authorities need to work together by coordinating their respective activities. For example, the Asia Partnership Conference of Pharmaceutical Associations (APAC) promoted by the Japan Pharmaceutical Manufacturers Association was held with the participation of regulatory authorities from Japan and other Asian countries/regions, and this is a desirable form of collaboration and cooperation between business community and regulatory authorities.

### **[“Hard” and “soft” approaches to infrastructure development]**

Conventional initiatives for things like regulatory harmonization have focused primarily on the aspect of “soft” elements. However, to enable Asian countries/regions to make cutting-edge pharmaceuticals and medical devices available to the public quickly, it is also necessary to develop the infrastructure, especially for the clinical trial phase onward, through “hard” approaches, including the establishment of clinical trial sites. This “hard” approach will also lead to the practical training of specialized personnel to put this infrastructure into action. These “hard” and “soft” approaches need to be taken in a balanced manner.

## **(2) Measures Package**

The matters that could be addressed by Japan in order to improve patient access to pharmaceuticals and medical devices are as follows:

### **[1] Establish Systems and Frameworks**

#### **[Platform organization in Asian countries/region]**

Japan could take the lead in organizing an “Asian network meeting,” comprised of the heads of national regulatory authorities in Asia, which could serve as a platform for regulatory harmonization and other activities. This could be expected to serve as a forum for heads of regulatory authorities to demonstrate initiative in tackling difficult problems through close cooperation and coordination.

\*The Asian network meeting is expected to lead regulatory harmonization in Asian countries/regions and to perform the function of establishing and managing milestones substantially.

### **[Promotion and coordination of business community's activities]**

The government will continue to promote the activities of the business community by cooperating with its efforts to respond to shared problems in Asian countries/regions. In addition, the holding of bilateral symposia will establish an environment where the Japanese business community can directly communicate with regulatory authorities in Asian countries/regions. These activities are expected to create an environment of public and private collaboration that encompasses Asian countries/regions, and to promote cooperation.

### **[Understanding needs and identifying priorities]**

There have been improvements in the hygienic environment, medical standards and regulatory standards in Asian countries/regions. Although sharing of Japan's medical technology and the knowledge and experience gained through the public health insurance system has been promoted by dispatching experts to and accepting trainees from emerging countries (e.g. International Project for the Development and Promotion of Medical Technology (Ministry of Health, Labour and Welfare)), there are limits to the degree to which this can reflect needs in individual countries, since it is an open recruitment project in which business operators propose the target countries and themes. In the future, the need for pharmaceuticals and medical devices in each Asian country/region will be investigated and identified in detail in cooperation with the Japan External Trade Organization (JETRO), Medical Excellence Japan (MEJ), and overseas authorities where necessary.

The scheme for how best to respond to those needs will also be considered. Specifically, based on information and survey results on Asian countries/regions compiled by the competent ministries, agencies, and related organizations, a framework for identifying priority issues will be established, with the business community at its core. The results will form the basis for a practical approach to regulatory harmonization.

### **[Strengthening of systems of organization in Japan]**

In order to promote activities conducted hand in hand with the competent ministries and agencies, the International Pharmaceutical Partnership Promotion Council will be utilized for cross-agency coordination. In addition, from the viewpoint of further promoting collaboration with Asian countries/regions, PMDA will assign dedicated persons-in-charge in each priority country to strengthen the system of organization for promoting international harmonization.

In addition, PMDA's Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs sometimes dispatches employees overseas to hold seminars, and face-to-face interactions with many employees have been shown to be very effective. While considering utilizing and coordinating with the framework of the Japan International Cooperation Agency (JICA), PMDA is also considering personnel exchanges as part of this response,

such as dispatching regulatory personnel overseas for a certain period of time and inviting their foreign counterparts to Japan at the request of the other government.

When engaging in activities based on this Grand Design, efforts will be made, not only to cooperate with international organizations such as the WHO Regional Offices, but also to disseminate information to civil society, with constant attention to transparency and accountability.

## **[2] Establish Clinical Trial Systems**

### **[Establishment of clinical trial sites]**

Highly innovative pharmaceuticals and medical devices often spread to other sites, mainly study sites, after marketing. Therefore, the establishment of sites that can conduct clinical trials of highly innovative pharmaceuticals and medical devices may not only accumulate clinical trial evidence useful for the country concerned but also lead to improved access to post-marketing pharmaceuticals and medical devices. In light of this, we will cooperate with the development of clinical trial sites to ensure international technical standards in Asian countries/regions.

To this end, we will examine what the government can do in terms of financing for “hard” aspect maintenance in Asian countries/regions. For example, this may take the form of financing by the Asian Development Bank (ADB) or the World Bank, or utilization of the Economic Research Institute for ASEAN and East Asia (ERIA). It may also be possible to make this function organically through linkage with JICA's projects.

### **[Development of human resources related to implementation of clinical trials]**

Healthcare professionals are not the only personnel required in order to conduct clinical trials; there is also a need for biostatisticians, clinical research associates (CRAs), and clinical research coordinators (CRCs). In order to accumulate higher quality clinical evidence, these human resources need to be developed reliably, and it is desirable to do so in collaboration with academia (e.g. the Japanese Society of Clinical Pharmacology and Therapeutics). How to link these academic activities with the activities of the PMDA's Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs will be also discussed.

Some medical devices and regenerative medicine products need to be provided to Asian countries/regions along with the procedures of their clinical use. From this standpoint, projects requiring technology transfers need to be the highest priority in site capability improvement. This will also lead to the establishment of a foundation for utilization of the latest medical devices. As will be discussed below, improvement of access to innovative products requires improvement of the post-marketing safety measures system, and improvement of clinical trial sites also leads to improvement of skills for adverse reaction reporting from medical institutions.

The establishment of these clinical trial implementation systems will first

need to be considered independently by the Asian countries/regions themselves. Japan will establish a system to support the establishment of systems in each country while respecting the Asian countries/regions' own discussion and ownership on the basis of previous experience. In this case, discussion of human resource development in developing countries through JICA projects will also be considered.

Furthermore, it is important to be collaborate between WHO and Asian countries/regions on programs for capacity improvement and human resource development. Within this framework, contributions from Japan by responding to requests for dispatch of specialists will be promoted.

### **[3] Promote Regulatory Harmonization [Incorporation of international standards]**

The incorporation of international standards agreed to by ICH, IMDRF, and PIC/S in Asian countries/regions is being promoted. With various innovations arising, the movement to develop international standards is gaining momentum. In countries where the incorporation of international standards is not sufficient, there is concern that the gap with other countries' regulations may widen. There is a need for improvement of guidance and standards that are not in sync with international standards. In order to respond to these issues, PMDA will promote the incorporation of international standards and improvement of guidance by Asian countries/regions through training provided by the PMDA's Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs and sharing of Japan's experience through bilateral symposia.

In recent years, WHO has promoted "Reliance"<sup>9</sup>-related activities. Japan will work with WHO to promote the spread of this concept to Asian countries/regions. This will promote the utilization of Japanese approval results and inspection results, leading to the formation of a borderless Asian market.

### **[Increase capacity of Asian regulatory authorities (Human resource development)]**

In addition to improving regulations, persons in charge in regulatory agencies will also be called upon to improve their own capabilities in the areas of review, quality control surveys, reliability surveys, and post-marketing safety measures. In particular, Asian countries/regions have many global manufacturing sites for pharmaceuticals, and the countries of the world are looking to them to improve their quality control capabilities. The PMDA's Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs conducts highly acclaimed mock GMP inspections using actual manufacturing sites. In order to provide more effective training on biopharmaceuticals, etc., the use of simulation manufacturing sites owned

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<sup>9</sup> Reliance in this context means that, when a regulatory authority of one country region conducts approval reviews or inspections, they consider, attach importance to, and utilize in their regulatory activities, the outcomes of assessments made by their counterparts in other countries/regions.

by academia will also be promoted.

In the area of GMP, the PIC/S General Meeting is scheduled to be held at Toyama in November 2019. This will provide an opportunity for fostering a shared awareness of the need to improve the level of quality control in Asia as a whole with the persons concerned at Asian regulatory authorities.

One other idea will be to use the framework of JICA to provide the necessary training while dispatching Japanese experts for onsite cooperation in Asia, in response to requests from the government of the other country.

#### **[Sharing of safety information in each country]**

Japan is also providing support for the improvement of safety measure capabilities and information sharing in Asian countries/regions. Increased access to innovative products needs to be accompanied by post-marketing safety measures. With the aim of improving the capabilities of the regulatory authorities and strengthening functions for reporting from the front lines of medicine, approaches that bring the business community into cooperation with academia and government will be considered in deliberations with other countries. Information will be shared by promoting reporting to the Uppsala Monitoring Center, WHO's safety information database.

In addition, real-world data (RWD) is becoming increasingly important in safety measures. In Japan, a system by the name of MID-NET has been established to convert electronic medical information such as electronic medical charts and receipts held by cooperating medical institutions in Japan into databases and analyze them. Because it makes it possible to analyze more data with greater assurance of quality, RWD is significant from the standpoint of detecting safety signals. We can play a leading role in building a framework for utilization of RWD in Asia, including from the standpoint of ensuring the quality of the database and establishing rules for collection and management of information.

#### **[4] Priorities in Individual Fields**

##### **[Pharmaceuticals]**

Recent years have seen an increasing number of pharmaceutical development projects that utilize multiregional clinical trials, participated in primarily by Japanese, US, and European entities. Given that a large percentage of the world's population lives in Asia, the region's contribution to such multiregional projects would accelerate pharmaceutical development. Pharmaceuticals particularly in need of active development are those for diseases common in Asia, such as hepatitis, stomach cancer, and infectious disease, along with those for dementia and other diseases expected to become more prevalent with the aging of the region's population. To advance the development of these products, the necessary foundations are required to be laid, especially by harmonizing regulatory requirements for pharmaceutical development and creating clinical trial networks based on specific areas of diseases for the purpose of increasing joint clinical trials in

Asia and thereby improving access at a faster pace.

With respect to generic drugs, other Asian countries/regions have high expectations for the quality products made in Japan. As such, these drugs represent a field in which great benefits can be gained from internationally harmonized guidelines. Toward that end, we encourage active participation in projects aimed at developing internationally standardized guidelines. Based on the outcome, efforts can then be made to disseminate those guidelines to other Asian countries/regions.

As for over-the-counter (OTC) drugs, the high quality and other benefits of the products made in Japan are attracting considerable interest as Asian countries/regions become increasingly health conscious, and demand for Japanese OTC drugs is expected to rise further. In that context, Self-CARER<sup>10</sup> could be utilized to facilitate more vigorous exchanges of views with the aim of raising health awareness and improving access in Asia.

A pharmacopoeia is a fundamental element in setting a country/region's quality standards for pharmaceuticals. As such, standardizing and harmonizing pharmacopoeias would eliminate duplicate testing. In view of that, Japan could carry out initiatives and exchanges of opinion in order to encourage both harmonization with the Japanese Pharmacopoeia and the use of it as a reference for the pharmacopoeias of other Asian countries/regions. Considering that traditional herbal medicines are widely used throughout Asia, it is particularly important to cooperate in setting standards for the safety of crude drugs.

#### **[Medical devices and in vitro diagnostics]**

Given the different medical environments and diversity of medical devices in Asia, it would be difficult to adopt a single, uniform approach to Asia as a whole. It will therefore be essential to take a systematic approach by first surveying the needs of each country/region, then designing policies based on the findings on a field-by-field basis.

ASEAN member states and others are currently working to increase consistency among national regulations for medical devices. By supporting this process, Japan can help them establish regulations that are in line with the international efforts to harmonize medical device regulations.

A report published by the Japanese Ministry of Health, Labour and Welfare's Health Science Council on December 25, 2018 also merits attention. Compiled by the Council's subcommittee on pharmaceutical and medical device regulations as a summary of the revisions to the Pharmaceuticals and Medical Devices Act and relevant systems, this report indicates the direction of initiatives to develop innovative medical devices efficiently.

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<sup>10</sup> Self-medication Collaborative Asian Regulator Expert Roundtable Regulatory authorities in the Asia-Pacific region are participating in regulatory harmonization activities for OTC drugs.

### **[Regenerative medicine products]**

In recent years, the development of regenerative medicine products in Asia has been progressing rapidly. As the markets and the regulatory regimes for these products are expanding, the field of regenerative medicine products is at an important stage for developing globally acceptable regulatory regimes in Asian countries/regions. Having established a conditional and time-limited approval system, Japan leads the world in the area of regulating regenerative medicine products. By promoting the comparison of the Japanese system with systems in Asian countries/regions, Japan could encourage the establishment of regulations in Asian countries/regions, including quality control, in accordance with characteristics peculiar to regenerative medicine products, such as heterogeneity and strict transportation conditions. Efforts will also be made to introduce safety evaluation tests and other tools throughout Asia, based on regulatory science.

Simultaneously implementing the measures described above could be expected to create a multilateral environment conducive to acceptance of Japan's approval/inspection results and regulatory system by Asian countries/regions.

### **3.Looking Ahead**

This Grand Design organizes the current concept. Given the constantly changing international environment, however, additional responses may present themselves, and those can be incorporated and pursued as well.

Asian countries/regions vary in terms of their levels of medical services, maturity of healthcare systems, and processes for decision making. Accordingly, it would be helpful to adjust to the actual situation in the other country by adopting a "vehicular" model

Where by seamlessly combining all of these forces into a "four-wheel-drive vehicle"

where business community-academia-government collaboration serves as the engine; dialog and cooperation provide steering; and the business communities of the two countries push the initiative forward from behind,

Japan could proactively help other Asian countries/regions to improve access to pharmaceuticals and medical devices in an effective and organic manner.

We hope to contribute to healthy longevity in Asia through this new Japanese initiative.