PMDA International Vision

PMDA EPOCH Toward 2020

○ As one of the world's top three medical products regulatory agencies comparable to its American and European counterparts, PMDA aims to:

1. Secure the highest level of Excellence in Performance in the following aspects:
   A. Quality and speed of product reviews, safety measures, and relief services (PMDA's Safety Triangle)
   B. Quality and quantity of regulatory science* research
   C. Quality, quantity, and speed of information transmission to the world
2. Maintain a close Partnership with the Orient for the common benefit through:
   A. Cooperation to improve the level of medical products regulation across Asia
   B. Communication of information and opinions to the world as a member of the Asian community
3. Actively Contribute to International Harmonization of regulations, guidelines, and standards for the benefit of both Japan and the world.

○ To achieve the above goals, PMDA employees will need to be more internationally minded and have effective communication skills, including a good command of English. Furthermore, PMDA must develop and maintain a sound interactive partnership with foreign counterpart agencies.

* Regulatory science is the science that serves to regulate the fruits of technology to ensure that they assume the most desirable form in harmony with humankind and society to benefit the public and society.

The PMDA International Vision

1. Introduction

(1) Current status (Is the Japanese regulatory authority comparable to its counterparts in the EU and the U.S.?)

At the time the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) was founded in 1990, the Japanese regulatory authority for medical products (the Ministry of Health and Welfare [MHW], the predecessor of the current Ministry of Health, Labour and Welfare [MHLW]) was among the world's top three agencies along with those of the EU and U.S. At that time, the development and manufacture of pharmaceuticals was largely concentrated in the EU, the U.S. and Japan, which had sufficiently robust drug markets and regulatory systems to accommodate the activity. The MHW employed a comprehensive system to regulate Japan's pharmaceutical industry, which demonstrated strong product development capabilities, and the country's domestic drug market, which was the second largest in the world.

However, as more countries become involved in the development (e.g., clinical trials) and manufacture of drugs, the number of countries with an effective pharmaceutical regulatory system is increasing. Pharmaceutical markets in emerging countries have been rapidly expanding with economic growth. As the difference between developed and developing countries is diminishing in terms of medical product development, production and regulation, Japan's relative status is declining.

Moreover, in comparison with the amount, quality, and speed with which the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) perform product reviews, safety measures, international harmonization, and other activities, PMDA's performance pales in many respects.

There are, however, areas where PMDA equals or outperforms the two agencies. In a broader context, the potential of Japan as a breeding ground for innovative medical products should not be overlooked. A country with active innovation in medical products needs advanced regulation, or a regulatory agency with the required capability, which in turn facilitates innovation. The potential of Japan is heightened by the following:

i) A highly developed medical service system,

ii) A population that is conscious of personal and public health,

iii) Top-level capabilities for developing innovative drugs and medical devices,

iv) Active international cooperation to improve global public health, as shown in its contribution to WHO, and

v) Location in Asia, a region of great potential for developing, manufacturing, and marketing medical products.

Taking the current situation into account, PMDA aims to improve its performance in the areas where it compares equally with its EU and U.S. counterparts. In other areas, be they the review of drugs in certain therapeutic categories, post-market safety information analysis, or related research, PMDA improves its performance to match that of the top two agencies.

(2) Nature of the Vision

The “PMDA International Vision” (hereinafter “the Vision”) is an image of PMDA over the next 5–10 years in the international arena of pharmaceutical and medical device regulation. PMDA’s future is not just as another Asian regulatory agency, but as one of the world’s leading agencies, comparable to the EMA and FDA.

(3) Relationship between domestic and international activities

The functions of a drug regulatory agency are often dichotomized into those that fulfill domestic needs (domestic activities) and those for international purposes (international activities). The domestic and international activities are often considered to be independent of each other, and yet the latter also clearly serves domestic needs. Foreign regulatory information, for example, is being used to improve national health and security as well as the efficiency of domestic regulation.

The following cases illustrate how PMDA’s international activities benefit Japan’s public health and the efficiency of regulatory activities:

○ Foreign authorities’ regulatory actions and corresponding rationale are promptly communicated through international channels to PMDA, allowing the Agency to swiftly formulate domestic measures, a good example being precautionary safety measures taken for a drug reported to have caused adverse events abroad but not (yet) in Japan.

○ As was evident in the heparin contamination incident in 2008, the production and distribution of drugs has become increasingly globalized. The quality of drugs used in Japan will be better maintained through international cooperation such as joint GMP

inspections with foreign authorities.

○ Harmonization of regulations on clinical development as well as improvement of the clinical trial environment achieved internationally and regionally (e.g., within East Asia) will enhance simultaneous global/regional development of medical products involving Japan, which would speed up delivery of advanced medical products to Japanese patients.

○ PMDA's limited resources will be more effectively used by avoiding reinventing the wheel, through acceptance of foreign clinical data, implementation of joint GCP and GMP inspections, and formulation and use of globally harmonized regulatory guidelines.

Conversely, a regulatory agency's domestic performance raises the effectiveness of its international activities. A joint product review with a regulatory authority overseas is more effective in an area where the quality and speed of PMDA's review are world-class.

In conclusion, PMDA's domestic and international measures complement each other and simultaneously enhance its international status and improve its domestic regulation. PMDA's domestic and international operations should be carried out seamlessly with the understanding that they are inseparable in nature.

2. Discussion on items of the Vision

(1) <u>To Secure Excellence in Performance</u>

To be among the world's top agencies along with its American and European counterparts, PMDA, in cooperation with MHLW, aims to attain the highest level of performance to protect Japan's public health as well as its international and regional contribution. Although PMDA's performance should be evaluated as a whole, the items cited under 1.A. to C. of the Vision are the major yardsticks.

Regulatory science cited in 1.B. deserves special emphasis. Its enhancement is also prioritized in the agenda of the Japanese government. Regulatory science is expected to improve the evaluation of efficacy, safety and quality of drugs and medical devices, and to contribute to developing review guidelines and standards that ensure scientific soundness and social appropriateness of regulatory decisions. PMDA is determined to promote its research functions and to maintain a work force well versed in regulatory science. (International Strategy 1 & 5)

(2) To Maintain a Partnership with the Orient

Asia is becoming increasingly important as a venue of pharmaceutical development and manufacture (especially that of drug substances). As more and more of the drugs manufactured in the region are being imported to Japan, their quality directly affects the country's public health. Also, drugs developed in Asia for Asian populations and regionally common diseases are expected to better suit the Japanese due to ethnic similarities and thus better meet their needs. These factors justify PMDA's efforts to strengthen its partnerships with Asian countries to improve the drug quality and the clinical development environment.

The significance of Asia should be discussed beyond the direct benefits. The population and hence the market size for drugs and medical devices in Asia is rapidly growing, as is the region's importance in pharmaceutical development and manufacture. In view of its great potential, co-prosperity with Asia is the obvious path for Japan in the medium to long term. Under this strategy, PMDA should strengthen its partnerships with Asian countries and contribute to improving the region's general standards related to medical products, in order to attain and share in the prosperity of Asia.

Also, it is noteworthy that the world's three leading agencies should be located in America, Europe, and Asia, the three major geopolitical masses on the globe. By playing a significant role in Asia through its contribution, PMDA will exert substantial influence globally, because of the geopolitical importance of Asia. This entails having status as well as responsibility commensurate to that of the EC/EMA and FDA.

Reflecting the above considerations, PMDA shares information with the Asian authorities, provides advice on regulatory issues, and assists in their capacity building, in order to improve the regulatory system in Asian countries for the development and manufacture of medical products. Through this process, PMDA seeks and promotes common benefits for Japan and Asia as a whole. There are many issues of common interest, such as developing therapeutics for diseases prevalent in Asia. (International Strategy 1)

In spite of Asia's great potential, PMDA's limited resources leave the Agency with few realistic strategic options but to concentrate on partnering with the countries in East Asia (China and South Korea) and Southeast Asia (such as Indonesia) for the time being.

(3) Contribution to International Regulatory Harmonization

PMDA intends to positively promote global regulatory harmonization, and to never be only passively involved. As one of the world's top three regulatory agencies, and for the sake

of Asia (and Japan as its member), PMDA will actively propose new topics and play a leading role in their harmonization through chairing related meetings and other activities. Among the many harmonization issues, PMDA prioritizes those with tangible benefits for the Japanese public. (International Strategy 2)

Although the items of the Vision have been explained individually, they are not mutually independent, but are interrelated. For example, in order to maintain its performance in protecting public health at the world's leading level, PMDA must first take part in developing international standards and then implement them when finalized. Also, PMDA's excellence in performance should attract Asian regulatory agencies for partnership.

3. Preconditions for the Vision

To fulfill any of the items of the Vision, it is essential for PMDA staff to acquire an international mindset and English communication skills so that they can discuss various issues directly with their counterparts in the EU, the U.S. and other countries. Globalization of drug- and medical device-related matters increases the necessity, and the opportunity, for interagency activities such as (a) cooperative product review and safety information analysis (b) reception of reviewers/experts from foreign regulatory agencies, and (c) participation in international meetings including those conducted through telecommunications. The Vision will be realized only when each PMDA member can pursue such activities without any language barriers.

PMDA, on the other hand, must construct an excellent bi-directional relationship with its counterparts around the world, as communication between its individual members and their foreign counterparts is premised on the relationship. (International Strategy 1, 3, & 4)

Reference

PMDA International Strategic Plan

Three Targets to Be Achieved During the Second Mid-Term Plan Period

1. Strengthening of cooperation and building of collaborative relations with the United States (US), the European Union (EU), Asian countries, and relevant international organizations
2. Proactive participation in international harmonization activities and further contributions to such activities
3. Improvement and strengthening of information provision to overseas countries

International Strategy

1. Strengthening of cooperation with the US, the EU, Asian countries, and relevant international organizations
2. Strengthening of activities for international harmonization
3. Promotion of personnel exchanges
4. Fostering of internationally minded human resources with communication skills
5. Improvement and strengthening of international publicity and information provision