Japanese Society for Artificial Organs

Challenges in Research and Development, Productization, and Clinical Application of Advanced Medical Devices in Japan

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Introduction

Although advanced medical devices are currently playing important roles in medical services, there are various hurdles to overcome before such medical devices reach the stage of productization and clinical application. In particular, high-risk therapeutic devices rarely achieve practical application domestically, even if they are developed in Japan. Underlying this phenomenon is the current situation that the environment smoothly linking the research and development venue to the stage of productization and clinical application is not yet sufficiently established.

Characteristics of Medical Devices and International Competitiveness of Japan

Advanced medical devices require concentration and fusion of various technologies including material manufacturing, chemistry, machinery, electronics, information technology and biotechnology; multimodal technologies are used in most cases. From the viewpoints of potency and efficacy, advanced medical devices also have a great variety of actions and functions in physical, chemical and biological terms. As a result, the number of medical device items is about 300,000, overwhelmingly greater than that of drugs (about 17,000).[1] When in practical use, no special techniques are necessary for most drugs, but medical devices require professional expertise and handling, sometimes even a procedure or operation for embedding and removal. In addition, a number of specialist personnel including clinical engineers and radiological technicians are involved in the department in charge at a medical institution, although such specialist personnel are limited. Because of these difficulties, the annual number of registered clinical trials is remarkably smaller for medical devices than for drugs (15–20 trials vs. 110–130 trials).[1]

On the other hand, the balance of trade for Japanese medical devices shows that the annual export account is 475.1 billion yen, whereas the annual import account is 1,075 billion yen, indicating an import surplus of approximately 600 billion yen.[2] Although Japan exports a number of diagnostic devices, most therapeutic devices used in this country are imported; therapeutic devices thus account for most of the import surplus. Japan is importing medical devices mainly from the US (53.5%), followed by European countries such as Ireland and Germany. In the meantime, the ratio of research and development cost to sales volume in medical devices is 12.9% in the US and 6.9% in Europe on average, whereas it is 5.8% in Japan. Thus, it is apparent that greater funding is needed for research and development in countries from which Japan is importing medical devices.[3]

Public Consciousness of "Medical Services" and the Stance of Companies Involved in Research and Development of Medical Devices

Japan has been receiving extremely high appraisals,

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ranking first in the world, in the comprehensive evaluation of health performance by the World Health Organization (WHO).[4] Japan also holds the world record for average life expectancy of women alone and women and men as a whole. In addition, the maternal mortality rate is the lowest globally, and the Japanese perinatal mortality is also in the lowest range. Therefore, Japan is a country where women can conceive and give birth to a baby in maximum safety, from an international perspective. On the other hand, the proportion of national medical expenses to gross domestic product (GDP) in Japan is 8.1%, ranking 25th among 39 counties of the Organization for Economic Co-operation and Development (OECD), and at the bottom among the 7 major industrialized countries (G7).[5] The number of physicians is 2.15 per 1,000 population, which is in the lowest range, ranking 23rd among 31 OECD countries. In Japan, people visit hospitals at a 2-fold higher frequency per capita than in Western countries, and society is facing an unprecedented rate of aging with an aging rate of more than 20%. Under these conditions, the number of physicians is overwhelmingly insufficient, hospitals are over-extended, and healthcare collapse is ongoing. However, there is still a tendency for healthcare bashing in society, and people are still lacking in healthcare cost-consciousness.

The negative national consciousness for overall healthcare casts a shadow on the attitude of companies involved in the development of medical devices. Manufacturers in Japan have high quality, and a number of companies hope to make their own technologies useful in the fields of healthcare and welfare. However, particularly with high-risk therapeutic devices, some companies may eventually withdraw even when development of devices has proceeded to the stage of productization. As reasons for such withdrawal, cited are the issues of product liability and the lack of a formulated law corresponding to the US Biomaterials Access Assurance Act. However, their true intent is to avoid the risk of suffering severe damage from harmful rumors. The attitude of the media and harmful rumors that demonize medical institutions and medical devices even without accurate understanding of the situation represent the greatest concern for companies engaged in manufacturing medical devices. This is also the case for material manufacturers that provide parts and materials, and they consider supplying the field of healthcare to be filled with risks and uncertainty.[6] In addition, when the degree of innovation in state-of-the-art devices is higher, the marketability and profit forecasting are less clear, and it is more difficult to maintain perspectives concerning applications for clinical trials and approval or inclusion in the insurance coverage list. These are major obstacles to companies.

Device Lag

According to the internet survey by the American Medical Devices and Diagnostics Manufacturers' Association (AMDD),[7] 87% of Japanese people consider advanced medical technologies to be important, and 80% want to use the newest advanced technologies available globally, with 66% of them not minding if healthcare costs increase to some extent because of the use of such technologies. On the other hand, there is a device lag in Japan, a so-called time lag vis-à-vis the availability of medical devices, i.e. devices tend to be introduced later in Japan than in Western countries. However, the review period for approval has been shortened in Japan, and there is now no difference in priority review items between Japan and the US. Therefore, it is presumed that the ability to review advanced medical devices in Japan is similar to that in the US, such that the problem would be a deficient quantity of reviews in Japan.[8] The Pharmaceuticals and Medical Devices Agency of the Ministry of Health, Labour and Welfare has formulated an action program to accelerate the process of reviewing medical devices, and aims to shorten the period required for approval of new medical devices by 19 months over five years. Another aspect of device lag in terms of the number of approved medical devices, is that only about half of the types of medical devices available overseas are available in Japan.[1] For about half of such devices not available in Japan, application for approval in this country has not been made because of factors other than procedures for device approval, such as market circumstances and business costs. The commonly long period of time from the end of the review until inclusion in the insurance coverage list is another bottleneck in the medical devices business.

On the other hand, a survey of public attitudes toward medical devices carried out by the National

Cerebral and Cardiovascular Center revealed that more than 90% of people were aware of an increased need for medical devices, and that about 80% wanted an increase in the self-sufficiency rate of medical devices.[9] Thus, it is important to promote the development of advanced medical devices by Japanese companies that have excellent technological foundations, and to facilitate the productization of domestic therapeutic devices in particular, aiming at breaking away from import dependence. These efforts are anticipated to create an environment of clinical application of medical devices free from the issue of device lag.

Various Policies to Promote the Development and Productization of Advanced Medical Devices

The Cabinet Office, the Ministry of Education, Culture, Sports, Science and Technology, the Ministry of Health, Labour and Welfare (MHLW), and the Ministry of Economy, Trade and Industry (METI) formulated the Five-Year Strategy for Creation of Innovative Drugs and Medical Devices in April 2007.[10] This is a set of policies aimed at the promotion of precedent development of medical devices in Japan or the world, i.e. simultaneous development in which Japan is participating, in order to provide Japanese people with drugs and medical devices meeting the highest international standards and to assure that the drug and medical device industry will play the role of leading growth in Japan. On the other hand, the Council on Fiscal and Economic Policy decided to create "super-specific districts" to overcome factors that interfere with the development of innovative technologies, as an action of the Basic Policies 2008 for economic and fiscal reform.[11] As the first district of this type, "the specific district for development of advanced medicine" was started in 2009 to select and support projects of a consortium that is centered on an advanced medicine research base. In addition, as a mainstay project based on the New Growth Strategy issued in 2010 by the Japanese government, medical innovation was given a foundation for strong joint efforts of the public and private sectors to promote medical research and development toward the practical application of new technologies. Through such founding of national strategies defining a significant direction, various problems that had shown no sign of settlement are now gradually being resolved in the areas of research and development and practical application of medical devices.

Support Project for Formulating Guidelines for Development Evaluation of Next-generation Medical Devices

As a specific effort concerning the development of advanced medical devices, we can cite the support project for formulating guidelines for the development evaluation of next-generation medical devices, which was a joint project begun in 2005 by the MHLW and the METI. This project was intended to consider and set up, in advance, evaluation criteria for efficient and rapid investigation and review of various innovative medical devices under development when they enter the stage of non-clinical or clinical trials or the approval process. In the area of artificial organs, the next generation artificial heart as an implantable active device was adopted as a subject of discussion, and guidelines for both development and review of such devices were formulated in 2007 after 2 years of discussion.[12–14] In Japan, two types of domestically produced implantable artificial hearts were approved at the end of 2010, through the process of non-clinical and clinical trials and review and approval according to these guidelines. Thus, in the Japanese system of clinical trials devoid of the mechanism of investigational device exemption (IDE), the burden on companies sponsoring trials evaluating expensive medical devices such as artificial hearts has come to be substantially reduced. Both types of implantable artificial hearts were included in the insurance coverage list in April 2011, and ongoing aggressive clinical application of these devices has saved the lives of many patients.

Conclusion

The healthcare system is part of the basic infrastructure of a nation, and also serves as an important industrial base, including medical devices. Japan has abundant human and technical resources, and is capable of developing world-leading advanced medical devices by concentrating and fully applying its expertise and knowledge. Development of such advanced medical devices, particularly therapeutic devices, confers benefits for many patients not only in Japan but

worldwide. It is desirable that the environment of research and development and clinical application be improved, and that people understand medical services and devices and support their development.

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