Brave new world: how to navigate the new Japanese medical device regulatory landscape

For more than 50 years, medical devices in Japan were regulated the same way as drugs. But all this changed at the end of last year when a new legislation came into force, enabling devices to finally have a separate regulatory route which would hopefully expedite their entry to market. Masanori Otake* discusses the three most significant changes how devices are regulated and advises on how to navigate the new landscape

On 25 November 2014, the Pharmaceuticals and Medical Devices Act (PMD Act) was enforced. The new act – officially known as the Act for Ensuring Quality, Effectiveness and Safety of Pharmaceutical Products and Medical Devices – amends and replaces the Pharmaceutical Affairs Law (PAL), which had been used for regulating medicines and devices alike since 1960. The aim of the amendment was not only to introduce new rules for reinforcing the safety measures for devices and drugs, but it also established – for the first time – a separate regulatory framework for medical devices.

The details of the amendment are wide ranging and comprehensive, and they are individually discussed. For example, to reinforce safety measures, submission of package inserts for Class IV devices became obligatory; in addition, the content description on the package inserts and the operation rules for all medical devices were reviewed. Rationalization of the application document content for approvals and certifications, as well as the procedures required for changes and additions, are now being reviewed in terms of their detailed operational regulations.

Even in the short period between the writing of this article in December 2014 and it being published, new operation rules would have been released and more updates made. This article will highlight some changes which could have significant implications for medtech companies, as well as potential remaining issues.

Masanori Otake: The new rules have achieved more fruitful, mutual discussions between the Japanese government and industry associations

Key changes to Japanese medical device regulation

The PMD Act introduces several changes to the way medical devices will now be regulated. Among these, the three most significant are: 1) streamlining of the quality management system (QMS) and the shift from a licensing system to a registration system for the medical device manufacturer, 2) the regulation of standalone (software) programs as medical devices, and 3) evaluation system on performance of usage.

1) QMS and the shift from a licensing system to a registration system

For the purposes of this article, it is important to clarify the difference between "marketing authorization holders (MAH)" and "manufacturers."

Up till now, manufacturers of medical devices have been required to obtain a license. However, this step is no longer needed under the PMD Act; instead, manufacturers are now only required to register. Generally, a license can be obtained after the manufacturer passes an examination; on the other hand, registration just entails the manufacturer submitting the necessary information. But while the required procedure for manufacturers has been simplified, it is not accurate to regard this change as just a simple deregulation.

Medical devices are machines or materials, and the improvement cycle for medical technologies is much shorter than that of drugs. A system that is appropriate for managing such products with frequent improvement cycles would not need to individually control the manufacturing processes of each manufacturer. Instead, it would look at the "whole" system of manufacturing and quality control of the devices. Based on this concept, having manufacturers undergo a registration procedure will be enough to maintain quality and safety of the products.

Consequently, the person in charge of managing the whole quality system of devices is obliged to be

highly responsible. In this case, an MAH is supposed to assume the responsibility. Therefore, an MAH, capable of obtaining product approval and clearance, is responsible for managing the whole quality management system (QMS), including manufacturer systems.

For manufacturers, the classification of manufacturing facilities (general, sterilization, organisms, packaging and labelling etc.) has been abolished under the new PMD Act. However, the types of manufacturers have also been revised. For example, design manufacturers will need to be registered.

In addition, the system's operations have been streamlined, including the case that QMS examinations can be omitted when the registered manufacturing facilities (a combination pattern, if multiple facilities exist) and the products produced at manufacturing facility have matching product groups.

The updated system assumes that an MAH is responsible for the QMS and for managing manufacturers.

It is relatively easy to coordinate steps when an MAH and a manufacturer exist as one company. However, it becomes more complex if a manufacturer was the parent company located overseas, and the Japanese MAH is its subsidiary. Legally, a manufacturing supplier is responsible for the whole QMS, including the parent company's manufacturers, even if it is a subsidiary. In reality, however, a subsidiary must follow the policies of its parent company (this is even more relevant if the subsidiary has a relationship with another company based on just a business agreement). Sharing roles is required to bring together the need for compliance and reality.

It is important to understand carefully the details of the PMD Act and clarify the sharing of roles between a Japanese MAH and an overseas manufacturer. Then, it would be possible to streamline the quality management system by properly organizing the registered manufacturing facilities and the product groups, as mentioned earlier. Employees responsible for managing the quality system at each company are expected to act positively in this aspect.

2) Standalone programs regulated as medical devices

Under the previous PAL, standalone programs could not be regulated as medical devices but the amendment has changed that. A standalone program is defined as a program that is installed on a PC for the purpose of being used as a medical device. Previously this type of program was not approved unless it was together with PC hardware. However, the amendment now states that a standalone program "can be a medical device" so can be regulated, approved and sold as such. This puts Japan on par with Europe and the US, where standalone programs are already treated as medical devices.

That said, a standalone program in Japan does not mean a system control program mounted on a medical device. Therefore, a system control program cannot be extracted for sale because it needs to be approved as part of a medical device.

For example, previously, a treatment planning program used in radiotherapy to determine radiation dose and positioning would not have been accepted as a medical device. This is because under the legal interpretation, a program itself cannot provide treatment. Pursuant to the amended act, however, such a program shall be accepted as a medical device. Similarly, due to the recent fitness boom, a large number of programs relating to health and medicine have become widely available on smartphones or tablet devices. There is the possibility that such programs are (or, can be) accepted as medical devices depending on their claims and risks. For programs originally developed for medical purposes, as initially mentioned, specific contents of application documents are now under review. For programs where it is difficult to judge whether they can or cannot be accepted as medical devices, the criteria to determine their eligibility is continuously under discussion. Particularly in the IT field, there is also a possibility that unexpected programs will be developed. The Japanese government is, together with industry associations, required to formulate an operation rule that is flexible and not bound to the existing regulations with hardware based on the unique characteristics of programs, in order to allow real technology development in this field. On the other hand, applicants need to ensure they keep up with the trend of relevant regulations and operation rules.

It is important to note that programs which correspond to Class I medical devices would not be regulated as devices and therefore need not be submitted for regulatory clearance. However, discussions with the regulatory authority must still be conducted on how to advertise the effectiveness of these programs. Operations have already begun under the voluntary guidelines created by industry associations for programs not accepted as medical devices. So the key to success for new players in this field is to "use" the regulations in considering their individual business strategy.

3) Evaluation System on Performance of Usage

The Post-Marketing Surveillance System (PMS) has been renamed the 'Evaluation System on Performance of Usage' under which each applicable case and the duration of each case is now determined individually.

Under the previous PAL, it was uniformly specified that the applicable cases were all "new medical devices", and that the applicable period should be, in principle, three years (four years for new structure medical devices; seven years for medical devices that are used to treat rare diseases). This is now changed under the new Evaluation System on Performance of Usage of the PMD Act, so that the applicable medical device and the surveillance period can be specified for each case. In other words, there is a possibility that while a "new medical device" may not be subject to the new Evaluation System, an "improved medical device" may be subject to the evaluation. This shall be judged in the product review process and will depend on the device's individual characteristics.

This system change has given rise to pros and cons. While it is reasonable that the system is not uniformly applied, potentially, this will depend on the judgment made by the Pharmaceuticals and Medical Devices Agency (PMDA) reviewers or the reviewing doctors requested by the PMDA. It would then be harder to predict the burden of the evaluation

system on performance of usage for which heavy cost is required. Therefore, the government and industry associations will be required to hold in-depth discussions in the future to clarify the judgment criteria of the applicable case of the evaluation on performance of usage and the transparency of the decision process.

Conclusion

Prior to the PMD Act, the last amendment to the PAL was enacted in 2002. At that time, companies were given a transition period of three years before the amended PAL came into force. With the PMD Act, the transition between promulgation and enforcement has only been one year. As a result, the act has been enforced without sufficient review of the actual operation. In terms of QMS, some problems remain unsolved regarding the actual method of surveillance. Other issues may also be identified after operations are conducted. These issues may be in areas such as the unit programs and the evaluation system on performance of usage as mentioned previously.

That said, compared with the previous amendment in 2002, it seems to have achieved more fruitful, mutual discussions between the Japanese government and industry associations aiming to specify the operation rules based on the concepts of the new PMD Act. A remaining challenge will be whether both the applicant and the reviewer (especially the PMDA and the third-party certification agents i.e. notified bodies) can implement a reasonable operation that keeps in mind what is most needed. Medical devices are no longer managed under the PAL, which had previously followed the rules for pharmaceutical products. The applicant is now responsible and authorized to develop their medical devices and apply for approval by understanding the purpose of the relevant regulations and complying to these new requirements; conversely, the reviewer is required to make new judgments in accordance with the specific characteristics of medical devices, and not take into account review precedents that had applied to previous drug regulations. It should also be noted that the development and submission of medical devices will not be achieved without a profitable business.

In conjunction with the amendment, the action program aiming to accelerate product reviews – which was implemented for five years – was renamed as a five year "collaboration plan" in 2014, to support the acceleration of product reviews. The number of PMDA reviewers has increased as planned, but an improvement in submission procedures and review quality is still required. Proper implementation by "collaboration" will be the key for success of this amendment.

**Masanori Otake is the chairman of the regulatory affairs and quality assurance committee at American Medical Device and Diagnostics Manufacturers' Association in Tokyo. He is also regulatory affairs and policy manager, healthcare, at GE Japan. For more information, contact the AMDD at http://amdd.jp/en/index.html*

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