Camellia japonica

PMDA Updates

January, 2015

News

1. PMDA Chief Executive Dr. Kondo's New Year message for 2015

Dr. Kondo

A Happy New Year to all of you.

PMDA has been promoting regulatory science through the operation of three major services, which are relief services for adverse health effects, product reviews, and safety measures in an integrated manner, ever since its establishment in 2004. The problem of drug lag and device lag which were expected to be improved from the time of its establishment has been practically resolved by all PMDA employees' efforts toward the common goal to improve the situation, and the quality of review service of PMDA has now become a world leading class. PMDA has steadily implemented Pharmaceutical Affairs Consultation on R&D Strategy, post-marketing safety measures utilizing Risk Management Plan of pharmaceuticals, etc., acceleration of relief services for adverse health effects and so on, and these actions are highly regarded in the world. In addition, toward providing the practical application of innovative pharmaceuticals and medical devices ahead of the world, PMDA is promoting utilizations of advanced review and consultation with electronic data, database system and related network constructed by the project for developing the medical information database infrastructure (MID-NET) and so on to improve the quality of review and post-marketing safety measures. Furthermore, PMDA will adequately utilize newly established *SAKIGAKE* Designation System, and provide more effective and safer products to clinical practice, while cooperating with Japan Agency for Medical Research and Development (AMED) which will start its operation in the future. Through the promotion of regulatory science research which is the basis of these projects, PMDA continues to evolve to meet future challenges.

We will stay motivated and make further efforts to provide faster, accurate and high-quality service as with in the past in the future.

2. CMC Strategy Forum Japan 2014 (December 8 to 9)

On December 8 and 9, the 3rd CMC Strategy Forum was held in Tokyo, supported by PMDA. Dr. Takao Yamori, Director, Center for Product Evaluation; Dr. Daisaku Sato, Director, Office of Cellular and Tissue-based Products; and other 4 staff members participated as speakers or panelists. The Forum has been organized by the California Separation Science Society (CASSS), a non-profit professional membership society, annually held since 2002 in the US and 2007 in the Europe, providing an arena to discuss emerging issues and the latest findings on CMC and regulation of biologics. About 130 representatives from regulatory agencies including U.S. FDA and EMA, as well as pharmaceutical companies and academia from Japan and other countries participated in the Forum.

3. PIC/S Expert Circle on QRM (December 8 to 10)

PIC/S Expert Circle was held at PMDA, Tokyo, from December 8 to 10, and Dr. Tatsuya Kondo, Chief Executive; Taisuke Hojo, Senior Executive Director; Shingou Sakurai, Director, Office of Manufacturing/Quality and Compliance; many other staff members from the Office of Manufacturing/Quality and Compliance, PMDA; GMP inspectors of prefectural governments; and 64 officials of regulatory agencies in about 20 countries participated.

The Pharmaceutical and Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S) are the cooperative framework among inspection authorities aiming at international harmonization, development, implementation and maintenance of Good Manufacturing Practice (GMP). PIC/S member countries host seminars and expert circles toward realization of cooperation, sharing information and experience, mutual education, and development of GMP guidelines among inspection authorities. Japanese regulatory authorities were accepted as a PIC/S member in July 2014 and this was the first PIC/S Expert Circle that Japan hosted.

The PIC/S Expert Circle at PMDA provided trainings focusing on case studies of Quality Risk Management (QRM), which has increased its importance in the world ever since recent implementation of ICH Q8, 9, and 10. The participants had an active discussion on 1) inspections of levels of QRM implementation at manufacturing sites and 2) decision of inspection plans based on QRM by regulatory authorities. Three trainings on QRM are scheduled to be held in total; the second training will be held in the U.S, in 2015 and the third one in Europe following the first one in Japan.

Left: Group discussion
Right: from left, Dr. Sakurai, Dr Kevin O'Donnell (Chairman of the PIC/S Expert Circle on QRM)

4. PMDA Workshop on Multi-Regional Clinical Trials in Global Drug Development –What Japan can contribute to new drug development – (December 15)

On December 15, PMDA Workshop entitled "Multi-Regional Clinical Trials (MRCT) –What Japan can contribute to new drug development –" hosted by the MRCT project team in PMDA was held in Tokyo, and Dr. Takao Yamori, Director of Center for Product Evaluation; Mr. Masanobu Yamada, Associate Center Director for New Drug Review, and many staff members from PMDA participated in the workshop. Many detailed examples of global drug developments were introduced by the experienced pharmaceutical companies, as well as the outline and focal points of the Administrative Notice on "Basic Principles for Conducting Phase I Trials in Japanese population prior to Global Clinical Trials" issued on October 27, 2014, were provided. Approximately 500 participants from the industry-government-academia participated and actively exchanged views on the significance in conducting phase I study in Japanese population prior to MRCT, the impact of the aforementioned Administrative Notice on drug development strategy, and issues in Japan in order to participate in global development from an early phase.

Please refer to the following web site for the detailed information.
http://www.pmda.go.jp/operations/shonin/info/report/workshop20141215.html (Japanese only)

5. PMDA provides JICA training program "Strengthening the National Regulatory Authorities (NRA) for Vaccine's Quality and Safety (Collaboration with WHO)" (January 15, 19, and 20)

On January 15, 19, and 20, PMDA accepted seven administrative officers/managing staffs of national control laboratory from Indonesia, Pakistan, Vietnam and Mongolia, and provided lectures on 1) outlines of PMDA's organization and the role of PMDA in the vaccine administration, 2) review service, 3) Good Clinical Practice (GCP), 4) Good Manufacturing Practice (GMP), and 5) post-marketing safety measures. PMDA provided this training upon the request from specified non-profit corporation (NPO) Bio-Medical Science Association (BMSA) which has undertaken the specific training program, "Strengthening the National Regulatory Authorities (NRA) for Vaccine's Quality and Safety (Collaboration with WHO), from Japan International Cooperation Agency (JICA). This was the second training course following the first one in 2014.

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
February 2-6	The 2nd PMDA Training Seminar (Medical Devices)	Tokyo
February 4-5	The 8th Asia Regulatory Conference (ARC)	Taipei
February 18-19	International Regulatory Endeavor towards Sound Development of Human Cell Therapy Products	Tokyo
February 23	Harmonization By Doing (HBD)	Washington D.C.
March 10-11	The 1st Japan-Malaysia Symposium	Kuala Lumpur
March 17-18	The 20th Anniversary Symposium of EMA	London
March 24-26	International Medical Device Regulators Forum (IMDRF) Management Committee Meeting	Tokyo
April 9-10	The 4th Asia Partnership Conference of Pharmaceutical Association (APAC)	Tokyo
April 13-15	The 27th Drug Information Association (DIA) EuroMeeting	Paris
April 16-17	The 8th Japan-China Medicine Manufacture Exchange Meeting	Tokyo

Safety Information

Pharmaceuticals and Medical Devices Safety Information No. 319, December 24, 2015

1. Summary of the Relief System for Sufferers from Adverse Drug Reactions and the Cases of Non-payment of Relief Benefits Due to Improper Use of Drugs
2. Revision of Precautions (No. 261)
   (1) Galantamine Hydrobromide
3. List of Products Subject to Early Post-marketing Phase Vigilance (as of December 2014)

(Reference) Handling of Fire during Long-term Oxygen Therapy

http://www.pmda.go.jp/english/service/precautions_2014.html

Administrative Notice and presentation document related to the issuance of the Act for Partial Amendment of the Pharmaceutical Affairs Law etc.

1. Q&A on Adverse Drug Reaction and Malfunction Reports of Combination Products (PDF)
   http://www.pmda.go.jp/english/service/pdf/mhlw/20141217-qa_en.pdf
2. Package insert notification system
   http://www.pmda.go.jp/english/service/pdf/mhlw/20150109-presentation_material_en.pdf

Reports from overseas

Our officers deliver lively reports of their activities at their stationed overseas authorities.

EMA's actions of medicinal products against Ebola Virus Disease

The outbreak of Ebola virus disease has spread mainly in West Africa since spring 2014. According to situation report of World Health Organization (WHO) dated on 7th January 2015, there are 2,775 cases and 1,781 deaths in Guinea, 8,157 cases and 3,496 deaths in Liberia, and 9,780 cases and 2,943 deaths in Sierra Leone; and for other countries outside Africa, 1 case in Spain, and 4 cases and 1 death in the United States, and 1 case in the United Kingdom.

There are no medicines or vaccines with regulatory approval against Ebola virus disease as of January 2015, although there are a number of potential candidates in the pipeline. Needless to say that the quality, efficacy and safety should be assured before approval of the medicinal products, just like any other. At the same time, under the current emergency situation with concerns of outbreak of Ebola virus disease with high fatality ratio spreading into the world, necessity and urgency on public health are also required to be further taken into consideration.

Under such circumstances, EMA has published documents and taken a number of actions regarding possible drugs and vaccines against Ebola virus disease since October 2014. First of all, on 20th October 2014, it is announced that developers of medicines or vaccines against Ebola virus disease are encouraged to apply for orphan designation to stimulate their developments and facilitate them placing on the market. Those medicines with orphan status can have access to incentives such as fee waivers and 10 years of market exclusivity after launch onto the market. In addition, as a special action for possible drugs against Ebola virus disease, free scientific advice and priority review are given from EMA. On 22nd October 2014, a rolling review was announced to allow companies to submit data as it becomes available leading to sequential assessments by experts, instead of waiting for the whole package data ready for application for approval. Based on the procedure, on 29th October 2014, it was announced that the first scientific advice had been given to GSK's vaccine. In addition, on 16th December 2014, , EMA published an interim assessment report of the Committee for Medicinal Products for Human Use (CHMP) review of currently available quality, preclinical and clinical data for 7 possible drugs against Ebola virus disease.

Recently, I had opportunities to attend related meetings about Ebola virus disease with regulatory authorities as a liaison officer. In the meetings, I keenly felt this issue should not be limited only in Africa and be dealt with globally, needless to say. At the same time, it is also pointed out its necessity that EMA swiftly implements necessary actions such as scientific advices and reviews by utilising existing regulatory frameworks and limited human resources as maximally and effectively as possible while taking care of intellectualizing these actions externally. For coming several months, we must continue to pay attention to the ongoing situation and discussion regarding possible drugs and vaccines in EMA. As a liaison officer I would like to contribute to accelerating approval by promoting further information exchange between both Japan and Europe.

Situation report of WHO dated of 7th January 2015
http://apps.who.int/iris/bitstream/10665/147112/1/roadmapsitrep_7Jan2015_eng.pdf?ua=1&ua=1

The information of publication of EMA's Ebola website and interim assessment report dated on 16th December 2014 are as follows:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000624.jsp&mid=WC0b01ac058041e30

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2014/12/WC500179062.pdf

Mr. Yoshihiko Sano
PMDA's International Liaison Officer stationed at EMA in the United Kingdom

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History of pharmaceutical regulations in Switzerland

In Switzerland, pharmaceutical industries developed with the help of geographical advantages such as bordering other European countries, abundant water supply from River Rein which also provides capacity of mass transportation. There are several headquarters of global pharmaceutical companies in Switzerland, and now Switzerland is one of the centers of pharmaceutical industries in the world.

The history of pharmaceutical regulation in Switzerland is said to date back to 100 years ago. Switzerland established an agency called Interkantonale Kontrollstelle für Heilmittel (IKS) in which each cantons (administrative districts) cooperates to protect consumers from cheating and deception related to pharmaceuticals. The basic system that decisions by IKS are enforced by each canton was developed, and the system lasted long with some modifications. However, in the 1990s, it was pointed out that this system was old-fashioned compared with the systems in other countries. In the latter half of the 20th century, collaboration among agencies of other countries has increased its importance and modernized legal basis has become essential to cope with the internationalization of the development, production and distribution of pharmaceuticals and related regulations, especially with rapid development of internationally harmonized standards. To fulfill such requirements, Swissmedic was established as an institute under Swiss federal law, and current regulation system launched in which pharmaceuticals are regulated by confederation instead of canton since 2002.

In Japan, the revised Pharmaceutical Affairs Act, "the Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics" came into force on November 26th, last year. Revision of the Swiss Therapeutic Product Act (TPA), and the respective ordinances is also currently ongoing here in Switzerland. I would like to keep my eyes on how pharmaceutical regulations of Switzerland, a country with global pharmaceutical companies, will be harmonized.

Dr. Jun Kitahara
PMDA's International Liaison Officer stationed at Swissmedic in Switzerland

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Single, Shared system Risk Evaluation and Mitigation Strategies

In the last issue, I wrote about the difficulty of measuring the effectiveness of risk minimization actions. An additional challenge in managing the risks of medicines occurs when several products include the same active ingredient, have the same indication, and need the same risk minimization actions. If the manufacturer of each product developed its own system to implement the risk minimization actions, the varying operations implemented across companies could create confusion and burden for patients and practitioners. For example, it is easy to imagine that multiple restricted distribution systems for an innovator drug and generics versions of that drug would cause some confusion in clinical settings. In these situations, U.S. law states that the innovator drug and the generic drugs shall use a single, shared system Risk Evaluation and Mitigation Strategy (REMS) when elements to assure safe use are required. In certain cases, FDA may waive the requirement for a single, shared system. In other cases, multiple companies that manufacture a class of drugs may use single, shared system REMS to reduce the burden on the health care system. Six single, shared-system REMS have been approved by the U.S. FDA. You can find information on these REMS at the following website:http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm#Shared

In Japan, MHLW/PMDA also accepts a single Risk Management Plan submitted jointly by multiple companies that collaborate on their pharmacovigilance activities and risk minimization activities for their products. The opportunity to use a single plan might increase since the requirement for a Risk Management Plan for generic drugs became effective in August 2014 in Japan. I have ever heard that collaboration between companies has many obstacles. If this is the case, we might expect that there will not be many such collaborations. So that patients and healthcare providers can focus on the most important aspects of using a drug safely and not be burdened unnecessarily by multiple risk management systems, it would be good to begin exchanging experiences between Japan and the U.S.

Ms. Shohko Sekine
PMDA's International Officer at CDER, U.S. FDA in the U.S.A.

Dispatch to Center for Devices and Radiological Health, U.S. FDA

I am Kenichi Ishibashi, Office of Manufacturing/Quality and Compliance, stationed at Center for Devices and Radiological Health (CDRH), U.S. FDA. The dispatch period will be for 3 months from January 14 to April 10. Throughout my stay in CDRH, I will belong to the Division of International Compliance Operations (DICO), and work on exchanging opinions regarding the Medical Device Single Audit Program (MDSAP) Pilot, which intends to realize single audit of medical devices using third-party certification bodies. Although 3 months of dispatch period seems to be short term for me, I would like to make the best use of the information obtained from this pilot program facilitated by U.S. FDA cooperating with Health Canada (Canada), Therapeutic Goods Administration (Australia), and ANVISA (Brazil), for the improvement of the method for Registered Certification Body Assessment. I wish the information I will deliver to you will be beneficial for you.

Mr. Kenichi Ishibashi
PMDA's International Officer at CDRH, U.S. FDA in the U.S.A.
