Daphne odora Thunb.

PMDA Updates

February, 2015

News

1. APEC LSIF RHSC (January 28 to 31)

APEC-Life Science Innovations Forum (LSIF) - Regulatory Harmonization Steering Committee (RHSC) was held in Clark, Philippines, from January 28 to 31. Dr. Toshiyoshi Tominaga, Associate Executive Director (for International Programs), and a staff member from the Office of International Programs, PMDA, and Dr. Nobumasa Nakashima, International Planning Director, Ministry of Health, Labour and Welfare (MHLW), participated in the meeting. The committee was established in 2008 and has mainly discussed on regulatory harmonization of medical products including pharmaceuticals and medical devices in the APEC region. In the meeting, the committee has reached a consensus that the Multi-Regional Clinical Trial (MRCT) project that Japan plays a role as a champion will be jointly operated with the Good Clinical Practice (GCP) project that Thai FDA plays a role as a champion.

The next APEC-LSIF-RHSC will be held in August, 2016, in Philippines.

2. The 2nd PMDA Medical Devices Training Seminar (February 2 to 6)

PMDA held the 2nd PMDA Medical Devices Training Seminar for overseas regulatory officers from February 2 to 6. A total of 7 officials from Australia, Singapore, Taiwan and Brazil, and a staff member of U.S. FDA, who is currently training at PMDA under the Fellowship Program of the Mansfield Foundation, participated in the seminar. Lectures on 1) overview of the medical device regulations, 2) review of new/generic medical devices, including case studies, 3) Quality Management System (QMS) inspections, 4) Good Laboratory Practice (GLP)/Good Clinical Practice (GCP) inspections, 5) clinical trial for medical devices and post-market safety measures, 6) post-market surveillance system, and 7) overview of the third-party certification system by registered certification bodies were delivered. The participants of the training gave presentations on the medical device regulations in their own countries. On the fourth day of the seminar, a tour to a medical device manufacturing plant and an affiliated training facility was conducted. The participants and the staff members of PMDA actively exchanged their views throughout the seminar and cultivated friendly relationship. At the end of the seminar, Dr. Toshiyoshi Tominaga, Associate Executive Director (for International Programs), awarded the Course completion certificates to the participants, one by one.

Please refer to the following web site for the details of the 2nd PMDA Medical Devices Training Seminar.

http://www.pmda.go.jp/english/seminar/2nd_pmda_medical_devices_training_seminar.html

3. Asia Regulatory Conference (February 4 to 5)

Asia Regulatory Conference (ARC) was held in Taipei, Taiwan, from February 4 to 5. Dr. Toshiyoshi Tominaga, Associate Executive Director (for International Programs), and two staff members from Office of International Program, PMDA, and Dr. Nobumasa Nakashima, International Planning Director, MHLW, participated in the meeting. ARC is held every year as a place for the collection and exchange of the information of development and regulation of pharmaceuticals in Asia, hosted by Drug Information Association (DIA) and International Federation of Pharmaceutical Manufacturing & Associations (IFPMA). This year, the conference was cohosted by Taiwan Food and Drug Administration (TFDA). Discussion took place on Good Review Practice (GRP) and Good Submission Practice (GSubP) which Taiwan is working on as a leader country of APEC- LSIF-RHSC, under the theme of "Advancing Best Practices for Regulatory Review and Submission in Asia", etc.

4. PMDA delivers lecture for JST training program "Japan-Asia Youth Exchange Program in Science" (SAKURA Exchange Program in Science) Japan Medical Innovation Tour (February 19)

On February 19, PMDA accepted ten universities and academic research institution staff members from Taiwan, Singapore, Thailand, Philippines, Malaysia, Indonesia, Vietnam, and Mongolia, and provided lectures on 1) outlines of PMDA's organization, the role of PMDA in the pharmaceutical affairs, and international activities, and 2) Pharmaceutical Affairs Consultation on R&D Strategy. PMDA provided this training upon the request from Kyushu University which has undertaken the publicly-offered program "Japan-Asia Youth Exchange Program in Science" (SAKURA Exchange Program in Science), from Japan Science and Technology Agency (JST).

Safety Information

Pharmaceuticals and Medical Devices Safety Information No. 320, January 29, 2015

1. Cabazitaxel Acetonate and Severe Febrile Neutropenia
2. Use of Capsule Endoscopy for Small Intestine Screening in Pediatrics and Geriatrics
3. Important Safety Information
   (1) cabazitaxel acetonate
   (2) sodium-glucose co-transporter 2 inhibitors
   (3) freeze-dried live attenuated mumps virus vaccine
   (4) levetiracetam
4. Revision of Precautions (No. 262)
   (1) Linagliptin (and 2 others)
5. List of Products Subject to Early Post-marketing Phase Vigilance (as of January 2015)

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

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
March 10-11	The 1st Japan-Malaysia Symposium	Kuala Lumpur
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 20-21	The 9th DIA Annual Conference in Japan for Asian New Drug Development	Tokyo

Reports from overseas

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

20th Anniversary of EMA

EMA was founded in January 1995 and welcomes its 20th anniversary on 26th January this year (2015). Since its foundation, unification of regulations for medicines within the EU has been conducted by expanding its area such as the introduction of central authorisation system for new medicines starting in 1995, followed by medicines for rare diseases in 2000, herbal medicines in 2004, medicines for children in 2006, and advanced-therapy medicines in 2007. The number of staff in the Agency has increased from initial less than 70 officers to at present more than 780. On 26th January, the 20th anniversary event took place in EMA and an Extraordinary General Assembly was held following related events such as a ribbon-cutting ceremony. In this General Assembly, speeches were made by four persons of Mr. Andreas Pott, Deputy Executive Director; Sir Kent Woods, Chair of the EMA Management Board; Professor Tomas Salmonson, Chair of CHMP; and Professor Guido Rasi, Principal Adviser in charge of strategy, and they mentioned EMA's achievements have been contributed to the unification of regulations among member states.

From the Japanese point of view, EMA has very complex structure, in collaboration with European Parliament, European Commission, and regulatory authorities of European Economic Area (EEA, 3 countries) and EU member states (28 countries), while cooperating with WHO, ICH and other outside regulatory authorities such as the United States and Japan. EMA implements activities on efficacy and safety of human and veterinary medicines with supports from 7 Science Committees, more than 30 working parties, and more than 4,500 experts in various fields from member states. In terms of those collaborations, the point that really intrigues me in the speeches is that a huge amount of meetings relating to approval of new medicines and pharmacovigilance are held in the Agency. For example, in 2015, about 500 meetings, 9,000 participants, and 3,600 telephone, video, and web-conferences aimed at saving time and travel costs. Once again, I have respect for the EMA colleagues working for such huge activities.

EMA has implemented remarkable actions such as participations of representatives of patients and healthcare professionals to each of the Scientific Committees (see my liaison letter in August 2014) and safety monitoring of medicines across Europe (see my liaison letter in September 2014) in 2014, and publication of clinical trials data for improving transparency in January 2015 (see my liaison letter in October 2014). We need to continue to pay attention to them. As a liaison officer stationed at EMA, I will continue to report EMA's newest activities in the PMDA updates.

EMA 20th anniversary web site:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000628.jsp&mid=WC0b01ac058087addd

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

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Collaboration with patients/consumer groups for providing adequate information on therapeutic products

Proper use of pharmaceuticals and medical devices is important, therefore, every regulatory agency hopes that patients to be active, well-informed users rather than passive recipients of therapeutic products. Proper provision of information on therapeutic products is one of our duties. Providing precise information in package inserts to medical professionals is important, however, the information is often too difficult for patients to correctly understand since it requires special knowledges. I believe provision of easily understandable information for patients is also our duty.

Swissmedic is currently establishing collaboration with patients/consumers group. The key issues are;

- The proactive provision of information related to therapeutic products, in a form adapted to the needs of patients and consumers
- The use of appropriate communication methods
- The involvement of representatives of patients/consumers organisations in specific areas of Swissmedic's activities

As a first trial, pilot project for two years with representatives of regulatory authority and patients/consumers was established. In this project, they exchanged opinions and shared information about past experiences. The opinions and experiences of patients and consumers regarding issues related to therapeutic products may be included in Swissmedic's processes of information provision.

Necessary information differs among the recipients. As the nature of regulatory authorities, there are many medical doctors and pharmacists in the agency. However, it is relatively difficult to get opinions from patients/consumers sides. Therefore, I think that is a very good choice to collaborate with patients/consumers representatives, since they can make win-win relationships. PMDA also has representatives from patients group as members of our advisory board and receives many precious opinions, and this Swissmedic activity will be good consideration for us.

At the end, this report is my final report from Switzerland. Thank you for reading my reports for one year.

Reference: https://www.swissmedic.ch/aktuell/00673/01931/index.html?lang=en

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

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Using electronic medical records for post-marketing safety assessments

The U.S.FDA awarded a contract to the Harvard Pilgrim Health Care Institute to lead the Sentinel System, a program that uses electronic healthcare data to monitor the safety of drugs, on October 1, 2014. The Sentinel System will build upon the achievements of the Mini-Sentinel System, which was launched in 2008. Dr. Janet Woodcock, the Director of the Center for Drug Evaluation and Research at the U.S. FDA, mentioned the substantial accomplishments of Mini-Sentinel and raised expectations for the Sentinel System at the Sentinel Initiative Public Workshop held on February 5, 2015 in Washington, D.C. You can watch the meeting's presentations at the following web site:
http://www.brookings.edu/events/2015/02/05-fda-sentinel-initiative-workshop

The U.S. FDA has been using Mini-Sentinel to assess post-marketing safety concerns that are difficult to analyze only by individual case safety reports. For example, individual case safety reports are not sufficient to determine if the bleeding rates between warfarin and dabigatran are different. Similarly, they cannot determine if sprue-like enteropathy occurs with equal frequency across all members of the angiotensin II receptor blocker class. The transition from Mini-Sentinel to Sentinel will include further strengthening of the database, introduction of new data elements, and continued development of advanced analytical methods. The expansion may lead to improved accuracy and broader use of the system. Dr. Woodcock noted that the U.S. FDA will continue to support efforts to improve the Sentinel System. Please refer to the following web site for details of Mini-Sentinel's past activities: http://www.mini-sentinel.org/

In the area of post-marketing drug safety, using electronic medical records, which have real world data, has tremendous possibility to expand drug safety analyses. Such analyses might help improve the appropriate use of medications through a better understanding of a drug's characteristics. However, using electronic health records has limitations because the records are, in general, not optimized for post-marketing safety assessments. Therefore, it is important to convey accurately the results of these analyses so that they are not misinterpreted. In Japan, PMDA is also conducting the MIHARI project, which uses electronic medical records for safety assessments (http://www.pmda.go.jp/english/service/mihari_project.html). A comparison of the communication styles between the U.S. FDA and PMDA may allow us to think about the most suitable communication methods.

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

Medical Device Single Audit Program (MDSAP) Pilot

Medical Device Single Audit Program (MDSAP) was launched in 2012 with participation of the U.S., Canada, Australia and Brazil. This is a multi-national work sharing program where the member countries share their inspection resources with the intention of conducting more efficient inspections of medical devices manufacturers.

Inspections of medical devices manufacturers in each country are not always conducted by the regulatory authorities. In the U.S. and Brazil, regulatory authorities directly conduct inspections of medical devices manufacturers. On the other hand, in Europe and Canada, private inspection organizations called "the third-party certification bodies" conduct Quality Management System (QMS) audits. Those third-party certification bodies often have branch offices in various countries and have already built an operating platform for international inter-branches coordination. MDSAP aims for reducing redundant inspections by regulatory authorities by accepting audit results conducted by the third-party certification bodies.

Third-party certification bodies are private organizations, therefore, regulatory authorities need to confirm appropriateness of inspections by such organizations before assigning responsibilities of inspections to them. To continuously ensure the ability and fairness of the third-party certification bodies, member countries work together on assessing such organizations. At the same time, it is essential to build common rules on which member countries carry out operations in concerted manner. U.S. FDA is ambitiously working on setting up the program by assigning dedicated staff members.

Japan participates in this program as an official observer since the autumn in 2013, and PMDA exchanged opinions through its monthly Expert Meeting. It has been almost a month since I was dispatched to U.S. FDA. I always admire the constructive discussions among the staff members, and their unflagging efforts and expertise of U.S. FDA staff members. PMDA's Certified Body Assessment has just started in last November. I would like to learn U.S. FDA's procedures through this training, and make use of the acquired knowledge for the operations of the newly started PMDA's Certified Body Assessment.

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

Dispatch to Center for Drug Evaluation and Research, U.S. FDA

I am Masanobu Sato, Advanced Review with Electronic Data Promotion Group in PMDA. I have been dispatched to the Division of Pharmacometrics (DPM), Center for Drug Evaluation and Research (CDER), U.S. FDA in training program since October 2014. The dispatch period will be for 1 year.

In the DPM, reviewers mainly evaluate the results of quantitative data analysis in pharmacokinetics and clinical pharmacology area of application of pharmaceuticals including modeling and simulation for regulatory decisions. Furthermore, regulatory science research is conducted to create new knowledge based on the unique data available at U.S. FDA, e.g., data from New Drug Application (NDA) submission, and literatures for efficient and effective drug development and better regulatory decisions.

The objective of my dispatch is to learn the review process for new drugs and regulatory science research methodology utilizing submitted electronic data in U.S. FDA. I have attended to review teams for some NDA and also conducted regulatory science research. I hope the information would be useful for the advanced review in PMDA.

Dr. Masanobu Sato
PMDA's International Officer at U.S. FDA in the U.S.A.

