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PMDA Updates

November, 2014

News

1. The 5th PMDA Training Seminar (October 6 to 10)

PMDA held the 5th PMDA Training Seminar for regulatory officers from October 6 to 10. The Training Seminars are held on pharmaceuticals and medical devices once a year, respectively, and this year the main theme was review of new drugs (including biopharmaceuticals and tissue and cellular products). Lectures on outlines of PMDA's services were delivered by staff members from the Offices of Planning and Coordination, GMP/QMS Inspection, Conformity Audit, Standards and Guidelines Development, Review Management, Safety II, Relief Funds, and International Programs. The staff members from the Offices of New Drug and Cellular and Tissue-based Products delivered lectures on new drug review methodologies in the field of quality evaluation, toxicology, biostatistics and so on, and regulation of biopharmaceuticals and cellular and tissue-based products, respectively. On the third and fourth day of the seminar, group works entitled "Pharmacokinetics in Drug Development" and "Product Review Regarding Type 2 Diabetes Mellitus" were conducted and staff members from the Office of New Drug I and IV joined and led the works.

Upper: Group photo, Lower left: Group work,
Lower right: a certificate of completion conferment

A total 22 officials from 10 regulatory agencies (Brazil, Indonesia, Korea, Malaysia, Saudi Arabia, Singapore, Taiwan, Thailand, the United Sates, and Vietnam) participated in the seminar. The participants of the seminar learned the pharmaceutical regulations in Japan through the lectures and group works and enhanced relationship with PMDA staff members by actively exchanging opinions throughout the seminar.

Please refer to the following web site for the details of the 5th PMDA training seminar.
http://www.pmda.go.jp/english/seminar/5th_pmda_training_seminar.html

2. PMDA provides training program to officials from DAV, Vietnam (October 6 and 10)

On October 6, PMDA welcomed five officials from the Drug Administration of Vietnam (DAV). They participated in a part of the 5th PMDA Training Seminar to learn the outline of the pharmaceutical regulation in Japan, and communicated with the participants of the seminar from various countries.

On October 10, staff members from the Office of OTC/Generic Drugs delivered lectures on generic drugs, Over-the-Counter (OTC) drugs, and quasi drugs to the officials from DAV. There was an active discussion during the Q & A sessions.

A lecture by Office of OTC/Generic Drugs

3. The 50th Anniversary symposium of the European Pharmacopoeia（October 6 to 8）

The 50th Anniversary symposium of the European Pharmacopoeia (EP) was held in Strasbourg, France, from October 6 to 8, hosted by the European Directorate for the Quality of Medicines and Healthcare (EDQM). Dr. Toru Kawanishi, Director General, National Institute of Health Sciences (NIHS), Japan, and two staff members from the Office of Standards and Guidelines Development, participated in the symposium. This symposium was held to celebrate the 50th anniversary of the establishment of EP, and Nearly 300 delegates and experts from 45 countries including representatives from Pharmacopoeias, officials from pharmaceutical regulatory agencies, and representatives from industries, participated in the symposium. The plenary session was held, and then 12 topics were discussed in the workshop, and proposal for the future activities of EDQM was addressed. There were active discussions on the establishment of framework for collaboration among pharmacopoeias and necessity of the international harmonization of pharmacopoeias. Dr. Kawanishi delivered a presentation at workshop session on Pharmacopoeial Harmonization as well as expressed his opinions at the panel discussion in the plenary session on behalf of Japanese Pharmacopoeia (JP) committee, and it became a valuable opportunity to show the presence of JP to foreign countries.

Please refer to the following web site for the information of the press release and presentation documents of the symposium.

http://www.edqm.eu/en/50th-Anniversary-of-the-EDQM-Key-outcomes-from-the-international-conference-1587.html?mbID=234

4. The 4th International Meeting of World Pharmacopoeias （October 8 to 10）

From October 8 to 10, the 4th International Meeting of World Pharmacopoeias was held, co-hosted by World Health Organization and EP at the conference room of EDQM in Strasbourg, France, inviting representatives of pharmacopoeias from each country. Dr. Toru Kawanishi, Director General, NIHS, Japan, and a staff member from the Office of Standards and Guidelines Development, as representatives of JP, participated in the meeting. The main subjects of this meeting were discussions and editing for making a draft Good Pharmacopoeial Practices (GPhP) which explicitly indicates existence values and making standards of Pharmacopoeias. The representatives of JP expressed opinions as the member of working group for drafting GPhP. The discussions took place on the opinions provided by JP. Drafts specifically describing drug substances and preparations of chemical entities were made, and there was a significant progress toward making the main text of GPhP. The schedule that GPhP will be finalized in the next meeting in April, 2015, after reviewing of public comments from secretariats of pharmacopoeias and stakeholders in the world was confirmed.

5. MDEpiNet Annual Meeting（October 14 to 16）

The annual meeting of Medical Device Epidemiology Network (MDEpiNet) was held from October 14 to 16 at U.S. FDA, and a staff member of Office of International Programs participated in the meeting. MDEpiNet is the project launched by U.S. FDA in 2010, for the purposes of deepening the understanding of the evaluation of safety and efficacy of medical devices throughout their lifecycles, by developing methodologies for collection and analysis of registry data with the cooperation among regulatory authorities of each country, industry, academia and medical institutions, and citizens.

At this meeting, in addition to the presentation of various study results in the past four years, the current issues and the future direction of activities towards more effective and useful registries were discussed in the areas of cardiovascular and orthopedic. About 200 people participated in the meeting, and active discussions took place.

Please refer to the following web site for the detail of MDEpiNet.

http://www.mdepinet.org/wp/

6. The 2nd Joint Conference of Taiwan and Japan on Medical Products Regulation（October 31）

The 2nd Joint Conference of Taiwan and Japan on Medical Products Regulation was held co-hosted by Taipei Economic and Cultural Representative Office and Interchange Association, Japan, supported by PMDA, Japan Pharmaceutical Manufacturers Association (JPMA), and others. Many regulators from regulatory authorities from both country including following representatives participated in the conference: from PMDA, Dr. Tatsuya Kondo, Chief Executive; Dr. Taisuke Hojo, Senior Executive Director; Dr. Toshiyoshi Tominaga, Associate Executive Director (for International Programs); Dr. Daisaku Sato, Office Director of Cellular and Tissue-based Products; Dr. Takatoshi Nakamura, Office Director of OTC/Quasi-drugs; Mr. Naoyuki Yasuda, Office Director of Conformity Audit; Mr. Kaoru Misawa, International Coordination Officer for Pharmaceuticals; and Mr. Teruyoshi Ehara, Office Director of International Programs, from Ministry of Health, Labour and Welfare (MHLW), Mr. Masatoshi Narita, Councilor of Pharmaceutical Affairs, from Taiwan FDA (TFDA), Ms. Li-Ling Liu, Director, Division of Medical Products and Ms. Pei-weng Tu, Director, Division of Medical Devices and Cosmetics, from Center for Drug Evaluation (CDE), Prof. Churn-Shiouh Gau, Executive-Director.

In the meeting, three sessions, i.e. 1) Pharmaceuticals session, 2) Health Insurance session, and 3) Medical Devices Session, were held and the following presentations were delivered.
1) Pharmaceuticals session: Multi-Regional Clinical Trials (MRCT) and New Drug Review, Regenerative Products, Nanomedicine and Products, and Over-the-counter (OTC) Drugs, 2) Health Insurance session: Access to New Drugs, and Separation of Medical and Dispensary Practice, 3) Medical Devices Session: Post Marketing Surveillance (PMS), Product Registration, Quality System Documentation (QSD) / Quality Management System (QMS).

On November 1, the next day of the conference, a bilateral meeting was held between TFDA/CDE and MHLW/PMDA and views on pharmaceutical regulatory system and future collaboration were proactively exchanged. The 3rd conference is scheduled to be held in Taiwan in 2015.

Please refer to the following web site for the details of the 2nd Joint Conference of Taiwan and Japan.

http://www.pmda.go.jp/english/events/2014taiwan_sympo.html

7. The 7th IGDRP Meeting (November 4 to 5)

The 7th International Generic Drug Regulators Pilot (IGDRP) meeting was held in Singapore on November 4 and 5, and 3 staff members from Office of OTC/Quasi-drugs and a staff member from Office of International Programs, participated in the meeting. In the meeting, discussions took place on the evaluation of performances and future directions in the currently ongoing working groups of Biowaiver and Drug Master File. Approximately 40 people from 13 countries participated in the meeting and opinions were actively exchanged.

Next IGDRP meeting will be held in the Republic of South Africa from May 25 to 29, 2015.

8. The Science Board Activity Update (April to October)

From April 2014, the second term of the Science Board has started. In addition to the members in the first term of the Science Board, who were all re-appointed (reelected biennially and re-appointed once), 10 new members were added, and there are currently 26 members in total.

The 2nd term Science Board was firstly held on April 24, followed by two additional meetings on June 12 (document-based confirmation) and August 7.

1. The chairperson and the vice-chairperson were re-appointed.
   Chairperson: Tatsuro Irimura (Director, Institute for Medical Innovation, St. Luke's International University)
   Vice-chairperson: Kazuhiko Yamamoto (Professor, Graduate School of Medicine, the University of Tokyo)
2. The five Subcommittees were newly set up by the themes as listed below, and has started actual activities. Please refer to the following web sites for the meeting agenda and handouts.
   1) Subcommittee on Placebo-controlled Studies
      http://www.pmda.go.jp/english/scienceboard/placebo.html (English)
      http://www.pmda.go.jp/guide/kagakuiinkai/placebo-senmonbukai.html (Japanese)
      The 1st Subcommittee meeting was held on October 3.
   2) Subcommittee on Non-clinical Studies
      http://www.pmda.go.jp/english/scienceboard/non-clinical.html (English)
      http://www.pmda.go.jp/guide/kagakuiinkai/hirinsyo-senmonbukai.html (Japanese)
      The 1st Subcommittee meeting was held on August 4.
   3) Subcommittee on Application of Numerical Analysis to Non-clinical Evaluation
      http://www.pmda.go.jp/english/scienceboard/analysis.html (English)
      http://www.pmda.go.jp/guide/kagakuiinkai/kaiseki-senmonbukai.html (Japanese)
      The 1st Subcommittee meeting was held on August 4.
   4) Subcommittee on Evaluation of Medical Devices in Pediatric Use
      http://www.pmda.go.jp/english/scienceboard/pediatric.html (English)
      http://www.pmda.go.jp/guide/kagakuiinkai/shouni-senmonbukai.html (Japanese)
      The 1st Subcommittee meeting was held on October 17.
   5) CPC (Cell Processing Center) Subcommittee
      http://www.pmda.go.jp/guide/kagakuiinkai/cpc-senmonbukai.html (Japanese)
      http://www.pmda.go.jp/english/scienceboard/cpc.html (English)
      The 1st Subcommittee meeting was held on June 12.
      The 2nd Subcommittee meeting was held on September 16.

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
December 8-10	PIC/S Expert Circle on QRM	Tokyo
January 26	CMC Strategy Forum January 2015	Washington D.C.
January 27-29	The 19th Symposium on the Interface of Regulatory and Analytical Sciences for Biotechnology Health Products	Washington D.C.
February 2-6	The 2nd PMDA Training Seminar (Medical Devices)	Tokyo
February 23	Harmonization By Doing (HBD)	Washington D.C.
March 10	The 1st Japan-Malaysia Symposium	Kuala Lumpur
March 24-26	International Medical Device Regulators Forum (IMDRF)	Tokyo

Safety Information

Pharmaceuticals and Medical Devices Safety Information No.317, October 28, 2014

1. Guidelines for the Use of Mobile Phones in Medical Institutions
2. Change in the Submission Place of Reports in the Safety Information Reporting System
3. Important Safety Information
   (1) Imatinib Mesilate
   (2) Pregabalin
4. List of Products Subject to Early Post-marketing Phase Vigilance

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

Blue Letter

1. Sovriad Capsules 100 mg and Hyperbilirubinaemia (October 24, 2014)

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

English translations of review reports

The followings are current information about English version of review reports on PMDA web site.

Pharmaceuticals http://www.pmda.go.jp/english/service/drugs.html

Brand Name	Generic Name	Posting date
Stelara	Ustekinumab (genetical recombination)	November 17

Reports from overseas

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

Publication of discussion paper on the clinical investigation of medicines for the treatment of Alzheimer's disease and opening EMA workshop

EMA published a guideline on medicinal products for the treatment of Alzheimer's disease in July 2008. After that, a draft concept paper on the need for revision of the Alzheimer's guideline was released for public consultation from October 2013, and based on up-to-date scientific developments, a new discussion paper on the clinical investigation of medicines for the treatment of Alzheimer's disease and other dementias was published in 30th October 2014.

The discussion paper aims to take these developments into account and discusses new diagnostic criteria for Alzheimer's disease including early and asymptomatic disease stages on clinical trial design, the choice of parameters and need for assessment tools with regard to the different disease stages in Alzheimer's disease, biomarkers and their temporal relationship with the different phases of Alzheimer's disease in different stages of drug development (mechanism of action, diagnostic test, and stratification for subgroup, etc.), design of long term efficacy and safety studies, usefulness of combination therapy and corresponding study design.

EMA also held a workshop on Alzheimer's disease with representatives from the pharmaceutical industry, academia, patients and regulators to discuss the discussion paper on 24-25 November 2014. Meanwhile, PMDA prepared a document on Alzheimer's disease and presented its views in the workshop. The output of the workshop will be taken into account in the development of the draft revision of the guideline which will then be released for public consultation. These materials of the workshop such as presentations are to be published on EMA website.

In the aging society the need to develop medicinal products for neurological disorder has been more significant. I think exchanges of opinions among regulatory authorities with regard to the future guideline on medicines for the treatment of Alzheimer's disease can lead to establishment of better guideline, which contributes to accelerating the research and development of medicines in this field. This is the real contribution towards innovation from the regulatory authorities' point of view. As a liaison officer, I would like to play a part to make this contribution.

Discussion paper on the clinical investigation of medicines for the treatment of Alzheimer's disease published on October 30, 2014
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/10/WC500176827.pdf

Workshop on Alzheimer's disease held on November 24-25, 2014
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2014/04/event_detail_000932.jsp&mid=WC0b01ac058004d5c3

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

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Fight against Ebola

Until last summer, we have not found Dengue fever infection for almost 70 years in Japan. Number of patients who diagnosed as Dengue fever infection reached 160. Public parks in Tokyo were temporarily closed since the places were suspected to be the places of infection. However, with decrease of temperature, activities of mosquitoes which transmit Dengue fever virus, become less active and then, people's life turns back to normal. On the other hand, current outbreak of Ebola virus disease (Ebola) started in West Africa at the end of 2013 is still spreading. Secondary infection amongst medical practitioners have been also found in Europe and the U.S. Chaotic condition is still continuing such as closure of borders and disruption of airplane services to countries where infections are occurring. It has been passed nearly 40 years of first recorded infection of Ebola, but limited pharmaceutical companies try to develop drugs for Ebola, and no authorized drugs nor vaccines to treat or prevent this disease exist. International Coalition of Medicines Regulatory Authorities (ICMRA), strategic organization of regulatory agencies, concern the situation and announced its commitment to enhanced cooperation with concentrating the expertise against Ebola.

As already reported by the media in the end of October, clinical trial for Ebola vaccine will be conducted in Lausanne University Hospital, Switzerland. Prior to the clinical trial, clinical trial notification was submitted to Swissmedic in the end of September and the document was reviewed. The investigational vaccine was designated as a priority review item, and conducting of the clinical trial was approved on October 27. In this first-in-human clinical trial, the investigated vaccine will be administered to healthy medical practitioners who will be dispatched to infected countries to see the safety and immune response.

In addition, at the time of writing this article, Swissmedic just approved another Ebola vaccine clinical trial which will be conducted in University Hospital of Geneva, Switzerland. This trial will be a multi-regional clinical trial with the U.S., Germany, Gabon and Kenya.

Currently, ZMapp which is under development in the U.S., Favipiravir which is originally approved for influenza virus infection in Japan and some other experimental drugs are used to treat Ebola. I wish development of these vaccines and drugs continues smoothly and they become available as soon as possible.

There are so called "neglected diseases" such as contagious disease in the tropics and Ebola, which might threaten human being but still no drug to cure them exist. There seems to be many problems in development of drugs for such diseases including cost benefit balance and difficulties to conduct clinical trials etc. However, as interactions with other areas increase along with the globalization, infectious diseases will spread easily and outbreak areas will expand. Sooner or later, we need drugs for such kind of diseases. In Japan, the GHIT Fund has been launched and public, private and civil sectors work together to facilitate R&D of drugs, vaccines, diagnostics, and other products needed by the developing nations. Isn't it time to think about the development of such drugs?

Please refer to the following web sites for the information of the statement of ICMRA, Official announcements in the Swissmedic web sites, and GHIT Fund.

http://www.pmda.go.jp/english/international/statement-e.html
https://www.swissmedic.ch/aktuell/00673/02464/index.html?lang=en
https://www.swissmedic.ch/aktuell/00673/02472/index.html?lang=en
https://ghitfund.org/

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

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Introduction of Office of Surveillance and Epidemiology, CDER, U.S.FDA

Since October 1, 2014, I've been dispatched to the Center for Drug Evaluation and Research (CDER) at the U.S. FDA, where I am working in the Office of Surveillance and Epidemiology (OSE) in a training program. While OSE's primary responsibility is to monitor and assess the post-approval safety of drugs and therapeutic biologics, OSE is also actively involved in certain aspects of pre-approval review in areas such as medication error prevention, evaluation of risk evaluation and mitigation strategies, and development of post-approval safety studies. To accomplish this work, OSE works with multiple other offices within CDER, especially with the Office of New Drugs (OND). For example, OSE and OND work together on the evaluation of post-approvals safety signals and together arrive at a regulatory action. OND officials sign the regulatory letter to the company.

U.S. FDA's transparency initiatives allow those of us outside of U.S. FDA to understand U.S. regulations and FDA's rationale for its safety actions. Despite these initiatives, it is still difficult to understand U.S. FDA's actual internal activities and operations, such as how collaboration occurs between offices and what factors are considered when U.S. FDA decides on a safety action. So, I'm going to actively learn U.S. FDA's scientific and organizational approaches to these activities. I will also explain the Japanese system of drug safety activities to FDA staff. In learning the similarities and differences between the U.S. approach and the Japanese approach, I will be able to strengthen PMDA-FDA communications when I return. I will write this column on topics that I learn during this dispatch. I hope this information will be of some help to you.

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