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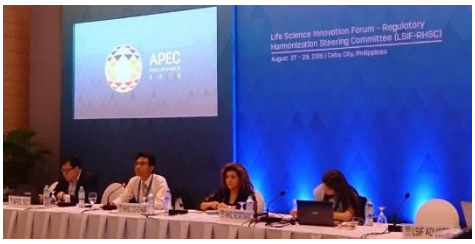
PMDA Updates

September, 2015

News

1. APEC-LSIF-RHSC (August 27 to 29)



Dr. Tominaga (The second left)

Asia-Pacific Economic Cooperation, Life Science Innovation Forum, Regulatory Harmonization Steering Committee (APEC- LSIF-RHSC) meeting was held in Cebu, Philippines from August 27 to 29. Key participants from Japan were Dr. Nobumasa Nakashima (International Planning Director, MHLW), Dr. Toshiyoshi Tominaga (Associate Executive Director for International Programs, PMDA) and Dr. Junko Sato (Office of International Cooperation, PMDA).

RHSC meeting aims for "Promotion of the strategic framework for the convergence of medical products regulation". Regulators from ten APEC economies, industry representatives (pharmaceuticals, bio-pharmaceuticals, medical devices, generics), and representatives from academia participated at the meeting. Dr. Tominaga co-chairs the RHSC with the US, and has led the discussion on path forward for the 6 working areas, including Multi-Regional Clinical Trials / GCP Inspection in which Japan plays its leadership role, Good Review/Submission Practice, Cell therapy, and Pharmacovigillance.

Next APEC-LISF RHSC meeting will be held in Peru, in January to February, 2016.

2. PMDA provides training program to medical doctors from Jiangsu Province, China (September 1)

PMDA accepted ten medical doctors from Jiangsu Province, China on September 1, and provided them with a training program on reviews of pharmaceuticals, post-marketing safety measures, relief for adverse health effects, and international activities, etc. This training program was provided upon the request from Japan International Cooperation Center (JICE), a general incorporated foundation, based on the Memorandum of Understanding, regarding friendship and cooperation between JICE and Jiangsu People's Association for Friendship with Foreign Countries. This was the fourth training course since 2013.

3. Celebrating MHLW's and PMDA's New International Strategic Plans "Toward further promotion of regulatory science and global capacity building" (September 3)

PMDA announced its new strategic plan titled "PMDA International Strategic Plan 2015" and Ministry of Health, Labour and Welfare (MHLW) also announced "International Pharmaceutical Regulatory Harmonization Strategy" on the same day, June 26, 2015. To mark the launch of both strategic plans, PMDA and MHLW co-hosted the conference Celebrating MHLW's and PMDA's New International Strategic Plans "Toward further promotion of regulatory science and global capacity building" on September 3, 2015.

Group photo of invited speakers and executives of MHLW and PMDA including Dr. Tatsuya Kondo, Chief Executive (the 5th left on the frontline) and Mr. Kanda (the 6th left on the front line)

Mr. Yuji Kanda, Director General, Pharmaceutical and Food Safety Bureau, MHLW and Dr. Toshiyoshi Tominaga, Associate Executive Director for International Programs, PMDA presented their respective new international strategic plans and the visions to further reinforce cooperation with countries in Asian, European and American regions and to promote international regulatory harmonization. The representatives of the world-leading regulatory authorities including U.S.FDA, EMA, and the representatives of regulatory authorities in Thailand, Malaysia and Singapore as well as the representatives of Japan Agency for Medical Research and Development (AMED) and industry in Japan expressed their expectations for the international strategies of MHLW and PMDA and their focused intention to cooperate to promote international harmonization.

For details of the commemorative lecture meeting, please refer to:
http://www.pmda.go.jp/english/symposia/0080.html

For details of MHLW's "International Pharmaceutical Regulatory Harmonization Strategy – Regulatory Science Initiative", please refer to:
http://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/150827-01.html

For details of the "PMDA International Strategic Plan 2015", please refer to:
http://www.pmda.go.jp/english/int-activities/outline/0017.html

4. Special training given by staff from EMA (September 8)

On September 8, Dr. Segundo D Mariz from the European Medicines Agency, visited PMDA and gave a special training for PMDA staff members, which was entitled "Orphan Medicine Designation and development in Rare Diseases". In the training, Dr. Mariz from the perspective of scientific officer at the Orphan Medicines Office, explained the outline of Orphan Medicine Designation System in Europe and also introduced the cooperation between the regulatory authorities and the Committee for Orphan Medicinal Products (COMP) and incentives and special measures in reviewing applicable after being designated as an orphan medicine. The participants gained a further understanding of the support measures to promote research and development of orphan medicines and to accelerate getting their approvals.

5. PMDA delivers lectures for JST training program "Japan-Asia Youth Exchange Program in Science" (SAKURA Exchange Program in Science) The 2nd Japan Medical Innovation Tour (September 9)

On September 9, PMDA delivered lecture for JST training program "Japan-Asia Youth Exchange Program in Science" (SAKURA Exchange Program in Science) The 2nd Japan Medical Innovation Tour. Nine universities and academic research institution staff members from Hong-Kong, Indonesia, Malaysia, Myanmar, Philippine, Singapore, Taiwan and Vietnam, participated in the training program. PMDA delivered lectures on outlines of PMDA's organization, the role of PMDA in the pharmaceutical affairs, international activities and notification of clinical trials. 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).

6. The 2nd Brazil-Japan Seminar on Regulations on Pharmaceuticals and Medical Devices (September 10)

On September 10, the 2nd Brazil-Japan Seminar on Regulations on Pharmaceuticals and Medical Devices was held in Tokyo, co-hosted by PMDA, Agência Nacional de Vigilância Sanitária (ANVISA) and Japan External Trade Organization (JETRO), and supported by the Federation of Pharmaceutical

Manufacturers' Associations of JAPAN (FPMAJ), Japan Federation of Medical Devices Associations (JFMDA) and Japan Pharmaceutical Manufacturers Association (JPMA).

Those who participated in the meeting included: Mr. Katsunori Hara, Vice-Minister for the Ministry of Health, Labour and Welfare (MHLW), Mr. Keiya Iida, Assistant Minister for Promotion of Healthcare Industries and Global Expansion of Healthcare, Mr. Kazuhiko Mori, Director, Evaluation and Licensing Division, and Dr. Nobumasa Nakashima, International Planning Director from MHLW, and Dr. Tatsuya Kondo, Chief Executive, Dr. Taisuke Hojo, Senior Executive Director, Ms. Tomiko Tawaragi, Chief Safety Officer, Dr. Takao Yamori, Director of Center for Product Evaluation, Dr. Shingou Sakurai, Office Director, Office of Manufacturing/Quality and Compliance, and Mr. Naoyuki Yasuda, Office Director, Office of International Programs from PMDA.

This seminar was held following the first one held in August 2014 in Sao Paulo, Brazil, and there were presentations on the following themes: 1)Making Japanese and Brazilian Industries Closer, 2)Enhancing Review Efficiency, 3)QMS/GMP System and International Collaboration, 4)Pharmaceutical Regulations of Advanced Therapy. About 160 people from regulatory agencies in Brazil and Japan, as well as from industries participated, and actively exchanged their opinions at question and answer sessions, and the seminar was fruitful for both Japanese and Brazilian participants.

For the details of the Japan - Brazil seminar on Regulations on Pharmaceuticals and Medical Devices, please refer to:
https://www.pmda.go.jp/english/symposia/0081.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/review-services/reviews/approved-information/drugs/0001.html

Brand Name	Generic Name	Posting date
Adempas	riociguat	September 11
Pradaxa	dabigatran etexilate methanesulfonate	September 16

Safety Information

Pharmaceuticals and Medical Devices Safety Information No. 326, September 15, 2015

1. Epidemiological Survey on Vaccination and Sudden Death of Infants
2. Important Safety Information
   (1) sterile talc
   (2) panitumumab (genetical recombination)
3. Revision of Precautions (No. 267)
   Hydroxyzine hydrochloride and hydroxyzine pamoate (and 4 others)
4. List of Products Subject to Early Post-marketing Phase Vigilance (as of August 2015)

http://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0013.html

Pharmaceuticals Revisions of PRECAUTIONS, September 15, 2015

- amantadine hydrochloride
- ipragliflozin L-proline
- luseogliflozin hydrate
- tofogliflozin hydrate
- canagliflozin hydrate
- dapagliflozin propylene glycolate hydrate
- empagliflozin
- fingolimod hydrochloride
- nivolumab (genetical recombination)
- azithromycin hydrate (Fine Granules)
- azithromycin hydrate (250 mg, 500 mg Tablets)
- azithromycin hydrate (600 mg Tablets)
- azithromycin hydrate (Capsules)
- azithromycin hydrate (Dry Syrup)
- azithromycin hydrate (Injection)
- asunaprevir
- daclatasvir hydrochloride

http://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0003.html

Medical Devices Revisions of PRECAUTIONS

- Medical devices and in vitro diagnostics for blood glucose measurements using enzymatic electrodes (September 1 , 2015)
- Electrosurgical devices and Intraocular lens (September 7 , 2015)

http://www.pmda.go.jp/english/safety/info-services/0015.html

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
October 12-13	Global Summit on Regulatory Science (GSRS15)	Parma
October 19-23	6th PMDA Training Seminar	Tokyo
November 10-13	10th International Summit of Heads of Medicines Regulatory Agencies & International Coalition of Medicines Regulatory Authorities (ICMRA) meeting	Mexico City
November 15-17	12th Annual Meeting DIA JAPAN 2015	Tokyo
December 13-18	APEC Multi-Regional Clinical Trials (MRCT) Regulatory Science Center of Excellence Pilot Workshop	Singapore

Reports from overseas

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

Interest in Japan's Pharmaceuticals and Medical Devices Act (PMD Act) and regenerative medicines

A symposium on regenerative medicine in Japan and the United Kingdom (UK) was held at the Japanese Embassy in London, on September 9, 2015. About 100 participants from academia, pharmaceutical industry and regulators attended the symposium, which included lectures by Dr. Daisaku Sato, the PMDA Director of Office of Cellular and Tissue-based Products and academia from Japan. The European Medicines Agency (EMA) has expressed an interest in finding out more about conditional and term-limited approval under the Japanese PMD Act, which came into effect in November 2014, particularly in light of the EMA recommendation in December 2014 for conditional approval of corneal epithelium as an advanced therapy medicinal product (ATMP). In light of this, I have actively translated and shared information with European colleagues on the seminar early on, together with opinion about regenerative medicines adopted by the Regenerative Medical Product and Biologics Committee, Pharmaceutical Affairs and Food Sanitation Council in the previous week. Three EMA colleagues from the quality of medicines department attended the symposium, with one of them asking a question about the concept of data collection after conditional and time-limited approval. It can be said that this led to encouragement of debate in the symposium.

Information exchange and sharing between EU and Japan is one of the most important parts of the Liaison Officer's work. Through this person-to-person exchange of information, I consider that I was able to contribute to promoting information exchange and sharing between our agencies.

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

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USP Workshop on Glycosylation Analysis for Biopharmaceuticals

The USP workshop on Glycosylation Analysis for Biopharmaceuticals was held on August 25-26 at the USP headquarters 1). USP has been working on developing new enforceable general chapters regarding glycosylation analysis. Therefore many stakeholders, who are from industry, academia and regulatory agencies, participated in this first workshop on glycosylation analysis. One of the Japanese Pharmacopoeia Expert Committee members, Dr. Akira Harazono who works at the National Institute of Health Science (NIHS) attended the workshop from Japan. Dr. Harazono presented a poster about glycosylation analysis of glycoprotein, monosaccharide analysis and oligosaccharide analysis/profiling which are to be newly included in the Japanese Pharmacopoeia Seventeenth Edition (JP17), entitled "New Japanese Pharmacopoeia General Test and General Information for Glycosylation Analysis of Glycoprotein". There were many informative presentations and discussions regarding to the role of glycosylation analysis for biopharmaceuticals, current technologies, and perspective for glycosylated biosimilars from manufacturer and regulatory agencies. In addition, USP presented the current status of its general chapters for glycosylation analysis, <212> Oligosaccharide Analysis will be official in USP38 second supplement and <210> Monosaccharide Analysis will be published in Pharmacopeial Forum (PF) in 2016, etc. Although General chapter for glycosylation analysis is not target item for harmonization in the Pharmacopoeial Discussion Group (PDG) at the moment, in accordance with the increase of biopharmaceuticals, it is considered that harmonization of its related general chapter will become more important. Therefore I expect that General chapter for glycosylation analysis will be targeted for harmonization in PDG activity.

1) USP Workshop on Glycosylation Analysis for Biopharmaceuticals
http://www.usp.org/meetings-courses/workshops/glycosylation-analysis-biopharmaceuticals-workshop\

Dr. Chie Mizumaru
PMDA's International Liaison Officer stationed at USP in the U.S.A.

Programs for students and visiting scientists at the U.S.FDA

The U.S.FDA has a variety of programs that offer an opportunity for outside scholars, from undergraduate students through senior scientists, to learn about the U.S.FDA's work and to conduct regulatory science research[1)]. The U.S.FDA routinely has students, especially pharmacy students, shadowing experienced FDA staff in their daily jobs. This experience provides a wide range of knowledge related to drug regulation and assists with future career planning. More experienced scientists can conduct regulatory research using data that are available only at the agency. Results of such studies have the potential to have substantial impact. Although PMDA has a similar program, the U.S.FDA program might provide ideas to improve PMDA's program.

1) http://www.fda.gov/aboutfda/workingatfda/fellowshipinternshipgraduatefacultyprograms/default.htm

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

Introduction of the review case utilizing exposure-response analysis –Determination of appropriate dosing regimens for approval-

In my previous reports, I have described the review cases where pharmacokinetics (PK) profiles in plasma in untested condition (drug-drug interaction, PK in polymorphism subjects and so on) are predicted based on physiologically based PK (PBPK) modeling and those analysis results provide rationales for the product labeling. In this report, I would like to introduce the review case where an appropriate dosing regimen was determined based on exposure-response (E-R) analysis.

U.S. FDA approved an oncology drug Sonidegib in July 24th, 2015. In a randomized, double-blind trial for cancer patients, efficacy evaluated by overall response rate was demonstrated in both two dosing regimens of Sonidegib used in this registration trial. However only the lower dosing regimen was approved by U.S. FDA because E-R analysis for safety indicated musculoskeletal adverse reactions increased with higher sonidegib concentration while the lack of an E-R relationship was observed for efficacy. I think this is one of the typical cases where E-R analysis plays a critical role in selecting the appropriate dosing regimens under the circumstance where efficacy of both two dosing regimens was demonstrated in the registration trial.

The U.S.FDA's review reports of Sonidegib have been opened in FDA's website since August 28th1). Please take a look if you are interested in them.

1) Odomzo sonidegib Capsules Review
http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/205266Orig1s000TOC.cfm

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

Promoting the activity for utilizing real world data of registry by U.S.FDA

My name is Nobuhiro Handa, a principle reviewer of Office of Medical Device I. I have been stationed at Division of Epidemiology (DEPI), OSB, CDRH, FDA, since August 1, 2015. During my stay at DEPI, I have learned that DEPI is promoting the activities of Medical Device Epidemiology Network (MDEpiNET) which is a Public Private Partnership between FDA, and Harvard University, Cornell University and Duke University. MDEpiNET facilitates the assessment of safety and effectiveness of medical devices for total product life cycle by utilizing real world data of registry. In addition to collect further information during the rest of my stay, I will work to promote to keep a good relationship between FDA and PMDA.

Dr. Nobuhiro Handa
Visiting scientist, Division of Epidemiology, Office of Surveillance and Biometrics at CDRH, U.S. FDA in the U.S.A.
