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PMDA Updates

August, 2019

News

1. Japanese delegation visits China

From July 2 to 3, high-level meeting and forum between Japanese delegation and China National Medical Products Administration (NMPA) were held in Beijing, China. This is a part of annual event, in which Japanese government and industry visit China together and develop Japan-China cooperation in the area of public health through political dialogue. Participants from Japanese government side included Dr. Yasuhiro Fujiwara (Chief Executive), Dr. Nobumasa Nakashima (Senior Director for International Programs) from PMDA; and from Ministry of Health, Labour and Welfare (MHLW), Dr. Yasuhiro Suzuki (Vice-Minister for Health, Chief Medical & Global Health Officer) and Mr. Naoyuki Yasuda (Office Director, Office of International Regulatory Affairs) participated.

Front row from right to left, Ms. Jiao (3rd), Dr. Fujiwara (6th)

Ms. Jiao Hong (Commissioner of NMPA) introduced regulatory reform and development in China, and Dr. Fujiwara introduced the latest regulatory trends in Japan. Furthermore, both countries shared the view that cooperation between regulatory agencies is important.

This opportunity expected to enhance reliability to each other's regulatory systems and promote Japan-China cooperation.

2. PMDA-ATC & U.S. FDA Pediatric Review Seminar 2019

From July 8 to 11, PMDA convened a seminar entitled "PMDA-ATC & U.S. FDA Pediatric Review Seminar 2019". This seminar was designed for regulatory officials from overseas regulatory authorities involved in the review of pediatric clinical trial applications and/or new/generic drug applications for pediatric populations. A total of 26 participants from Bangladesh, Brazil, Chile, India, Indonesia, Malaysia, Myanmar, Nigeria, Papua New Guinea, Russia, Singapore, Sri Lanka, Thailand, and WHO (World Health Organization) joined the seminar.

Front row from left to right, Dr. Junko Sato (Office Director, Office of International Programs) (1st), Dr. Catherine Lee (U.S. FDA) (2nd), Dr. John Alexander (U.S. FDA) (4th), Dr. Donna Snyder (U.S. FDA) (5th), Dr. Yoshikazu Hayashi (Director Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs) (6th), Dr. Nakashima(7th), Dr. Michiyo Sakiyama (Seminar Coordinator) (9th), and Dr. Eriko Fukuda (Office Director, Office of International Cooperation) (10th)

The seminar included lectures by staff members from PMDA, U.S. FDA and academic institutions. The topics included the PMDA Introduction and Updates in Pediatrics, U.S. FDA organizational structure and U.S. pediatric regulations, physiology and clinical pharmacology in pediatric populations,

extrapolation of efficacy from other population data (e.g. adults, foreign child), ethical considerations for clinical trials in children, and review of the ICH E11 guideline.

Besides the lectures, group work included case studies to explore topics such as the review of a pediatric application, extrapolation and ethical issues in pediatric clinical trial design. Seminar participants presented information on the pediatric drug development programs in their individual countries/regions. The participants actively engaged in all discussions throughout the seminar.

At the end of the seminar, Dr. Fujiwara handed the course completion certificate to each participant.

After the seminar, individual agency meetings were held among PMDA/U.S. FDA and participants from 6 countries & WHO to discuss general issues specific to the participants' region related to pediatric drug development.

Please refer to the following web site for the details of PMDA-ATC & U.S. FDA Pediatric Review Seminar 2019.
http://www.pmda.go.jp/english/symposia/0144.html

3. 2nd ChP-JP Forum

On July 10, "the 2nd Chinese Pharmacopoeia (ChP) – Japanese Pharmacopoeia (JP) Forum" was held in Chengdu, China hosted by Chinese Pharmacopoeia Commission and MHLW/PMDA. This forum is based on the Memorandum of Cooperation (MOC) signed between MHLW and ChP in September 2016 and was attended by about 230 people including industry and government in China and Japan.

At the Forum, ChP and MHLW/PMDA shared the latest information on own pharmacopoeias: MHLW/PMDA made presentations including on the history and future perspective of the JP and on the outline of the Supplement II to the JP17 edition (JP17-2) published in June 2019. From ChP, the outline of ChP 2020 edition was presented. Following the Forum, closed meeting between ChP and MHLW/PMDA was held and both agreed to deepen mutual understanding further in the pharmacopoeia field. Please refer to the following website for the 2nd ChP-JP Forum (In Japanese).

https://www.pmda.go.jp/rs-std-jp/symposia/0013.html

4. The 4th Korea-Japan Medical Products Regulation Symposium

On July 16, the 4th Korea-Japan Joint Symposium on Medical Products was held in Seoul, Korea. Representatives from PMDA, MHLW, Ministry of Food and Drug Safety (MFDS), and industries attended it. The symposium is held regularly as part of cooperation based on the August 2015 "Memorandum of Cooperation between the MFDS of the Republic of Korea and the MHLW of Japan on Medical Products Regulatory Dialogue and Cooperation Framework."

In the symposium, regulators from both countries presented their latest information on medical product regulations in their countries. After the information presentations, in pharmaceutical sessions, topics included clinical examinations (including design and data source), cell and tissue-based products (status of products development and the regulatory system) and in medical device sessions, topics included *in vitro* diagnostics (including the regulatory system and the review process), and clinical evaluation and substantial equivalence of medical devices.

On the following day, the regulators of Korea and Japan exchanged opinions on Korea-Japan regulatory cooperation and international regulatory harmonization.

5. PMDA-ATC & WHO Pharmaceuticals Review Seminar 2019

From July 22 to 26, PMDA and WHO jointly held a seminar entitled "PMDA-ATC & WHO Pharmaceuticals Review Seminar 2019". This seminar was designed for Pharmaceuticals reviewers from overseas regulatory authorities and 29 regulators from Bangladesh, Chile, DR Congo, Hong Kong, India, Indonesia, Laos, Malaysia, Maldives, Myanmar, Philippines, Saudi Arabia, South Africa, Singapore, Sri Lanka, Taiwan, Thailand, Uganda, and Vietnam participated.

Front row from left to right, Dr. Fukuda (1st), Dr. Wataru Asakura (Senior Training Coordinator) (2nd), Dr. Hayashi (3rd), Dr. Fujiwara (4th), Dr. Nakashima (5th), Ms. Emer Cooke (WHO) (6th), and Dr. Samvel Azatyan (WHO) (7th)

This is the first time to hold the seminar jointly with WHO and the officials of WHO, including Ms. Emer Cooke (Head of Regulation of Medicines and other Health Technologies), have also joined. In Days 1 to 3, in addition to the lectures on the topics including the outline of PMDA, review of new drugs, generic drugs and biosimilars, innovative review pathways, CMC (Chemistry, Manufacturing and Control), pharmacovigilance and case study on generic drug review presented by PMDA, recent activities of WHO and its efforts to promote reliance, as well as recent activities of U.S. FDA were introduced by WHO and U.S. FDA, respectively, thus promoting deeper understanding on the international efforts among participants. Moreover, the seminar included participation in the symposium for the draft revision on the ICH E8 "General Considerations for Clinical Trials" to learn consideration points in the clinical trials in Day 4, and also manufacturing site visit in Toyama prefecture to understand the efforts by manufacturers, as well as the lecture by a staff member of Toyama prefectural government on the regulatory systems at prefectural level to learn comprehensive regulatory systems in Day5. At the end of the seminar in Toyama, the course completion certificates were handed to each participant by Dr. Eriko Fukuda (Office Director, Office of International Cooperation).

Please refer to the following website for the details of PMDA-ATC & WHO Pharmaceuticals Review Seminar 2019; https://www.pmda.go.jp/english/symposia/0147.html.

6. Symposium for the draft revision on the ICH E8 "General Considerations for Clinical Trials"

The symposium for the draft revision on the ICH E8 "General Considerations for Clinical Trials" was held at Yurakucho Yomiuri Hall (Chiyoda-ku, Tokyo) on July 25. More than 1,000 people, mostly from the pharmaceutical industry and the academia attended the symposium. In Japan, the draft revision of E8 guideline is under public consultation (https://search.e-ov.go.jp/servlet/Public?CLASSNAME=PCMMSTDETAIL&id=495190053&Mode=0) and, the symposium was held to facilitate understanding of the draft revised guideline with the financial support from ICH (Program and presentation materials are available on the following link; https://www.pmda.go.jp/english/symposia/152.html.)

In the first half of the program, as the background of ICH E8 revision, three presentations were provided by three distinguished speakers (ICH Updates including GCP Renovation by Dr. Theresa Mullin, U.S. FDA, ICH Management Committee (MC) Chair; MHLW/PMDA International Activities by Dr. Nakashima, PMDA, ICH MC Vice-Chair; Current Status of ICH E Topics by Dr. Masafumi Yokota, JPMA MC member). In the latter half, experts who have worked for the revision presented the background and gist of the draft revised guideline, and representatives from the industries and the academia shared their expectations for the revised guideline. The panel discussion was held at the end of this symposium and not only speakers but also the audience actively participated in the discussion.

7. APEC-LSIF-RHSC opened website

Japan positively takes action for pharmaceutical and medical devices regulatory convergence, supporting to build capacity of regulatory authorities, etc. in Asia-Pacific Economic Cooperation-Life-Science Innovation Forum-Regulatory Harmonization Steering Committee (APEC-LSIF-RHSC), like for example leading the committee as Co-Chair. The public website to publish its own activities launched on 31 July 2019 (https://www.apec.org/RHSC). The website introduces the status of training implementation by Centers of Excellence (CoE)s and the schedule in 7 Priority Work Areas (PWA)s*. The activities of "Multi Regional Clinical Trial/Good Clinical Practice inspection" PWA, "Good Registration Management" PWA, and "Medical device" PWA that Japan leads are introduced. Moreover, PMDA's CoE workshops of "Multi Regional Clinical Trial/Good Clinical Practice inspection" PWA and "Pharmacovigilance" PWA, and CoE Pilot workshop of "Medical Device" PWA approved by APEC-LSIF-RHSC are also published on the website.

Reference: https://www.pmda.go.jp/english/int-activities/int-harmony/apec-lsif-rhsc/0001.html

*Table: APEC-LSIF-RHSC's work areas and their champion economies (As of March 1, 2019)

PWA	Leader economies
Multi Regional Clinical Trials and Good Clinical Practice Inspection	Japan, Thailand
Pharmacovigilance	Korea

Medical Device	Japan, the USA, Korea Sub-champions: Japan Medical Imaging and Radiological Systems Industries Association (JIRA) Advanced Medical Technology Association (AdvaMed)
Biotechnological Product	Korea
Advanced Therapies	Singapore
Good Registration Management	Chinese-Taipei, Japan
Global Supply Chain Integrity	the USA

8. Call for participation to PDG 30th Anniversary Symposium

MHLW and PMDA will host the international symposium, entitled "The PDG 30th Anniversary Symposium - The History and Future Perspective of PDG" (October 3, 2019 at Seiryo-Kaikan in Tokyo, Japan).

This symposium will be held to celebrate the 30th anniversary of the Pharmacopoeial Discussion Group (PDG). At the symposium, we will look back on the history of PDG's 30 years of activities, and give a lecture from experts on the latest situation and the role PDG has played in Europe, Japan, the United States, and the other country/region, along with the expectations for PDG. The symposium is open to the general public as well as the people involved. For details of the symposium and how to register, please refer to the following.

http://www.pmda.go.jp/english/symposia/0153.html.

9. Call for application to PMDA-ATC Medical Devices Seminar 2019 starts

PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) will hold the "PMDA-ATC Medical Devices Seminar 2019" from November 25 to 29. This seminar is designed for reviewers of medical devices and in vitro diagnostics from overseas regulatory authorities, and the objective of the seminar is to provide the participants with opportunities to further enhance the regulatory systems in their respective country/region by learning the basics of regulations and review/approval process, such as risk based classification, scientific review, GCP/GLP/QMS/standards and safety measures, as well as obtaining up-to-date information about international regulatory harmonization effort for medical devices, through lectures and manufacturing site visit.

This seminar is offered as a Pilot Workshop of APEC-LSIF-RHSC (Asia-Pacific Economic Cooperation, Life Sciences Innovation Forum, Regulatory Harmonization Steering Committee), Center of Excellence (CoE), however, the seminar is open to non-APEC economies, as well. Please refer to the following web site for the details of PMDA-ATC Medical Devices Seminar 2019;

http://www.pmda.go.jp/english/symposia/0154.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	Non-proprietary Name	Posting date
Vyndaqel [Partial Change Approval]	tafamidis meglumine	August 14

Medical Devices

http://www.pmda.go.jp/english/review-services/reviews/approved-information/devices/0003.htm

Brand Name	Non-proprietary Name	Posting date
RFA System [Partial Change Approval]	radiofrequency ablation system	August 14
Cool-tip RFA System E Series [Partial Change Approval]	radiofrequency ablation system	August 14

Safety Information

PMDA Medical Safety Information No. 58 (July, 2019)

Introduction of Connectors to Prevent Misconnection (for Enteral Applications)
http://www.pmda.go.jp/english/safety/info-services/safety-information/0001.html

Pharmaceuticals and Medical Devices Safety Information No. 365 (August 6, 2019)

1. Review of Contraindications of Metformin including "renal impairment"
2. Safety Measures for Febuxostat
3. Guidance of Appropriate Medication for Elderly Patients [particular (by recuperation environment)]
4. Proper Use of Over-the-Counter (OTC) Drugs that May Lead to Abuse
5. Important Safety Information
   1. Nivolumab (genetical recombination)
   2. Palbociclib
6. Revision of Precautions (No. 305)
   Epoprostenol sodium (and 10 others)
7. List of Products Subject to Early Post-marketing Phase Vigilance

https://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0017.html

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
September 16-19	IMDRF Management Committee Meeting	Ekaterinburg
September 21-24	RAPS (Regulatory Affairs Professionals Society) Regulatory Convergence	Philadelphia
October 1-2	The 7th Joint Conference of Taiwan and Japan on Medical Products Regulation	Taipei
October 8-9	The 1st Vietnam-Japan Symposium・PMDA-ATC CMC/GMP Seminar 2019 in Hanoi, Vietnam	Hanoi
October 28-30	ICMRA Summit	Rome

Reports from overseas

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

US-FDA Workshop related to Real-World Evidence (RWE)

I attended the US Food and Drug Administration (FDA) Workshop "Leveraging Randomized Clinical Trials to Generate Real-World Evidence for Regulatory Purposes" on July 11 and 12, 2019, in Washington D.C.[1,2]. FDA defines Real-World Data (RWD) and RWE as follows[3]:

RWD are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

RWE is the clinical evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

FDA proceeds with the examination related to utilization of RWE in the clinical assessment of medical products[4].

In this Workshop, examples of clinical studies partially using RWD and RWE were introduced, and the experience and challenges/difficulties to conduct them were shared. The attendees mainly discussed following topics, which are important to use RWE practically:

Points to be considered for Outcome definition,

Necessity of blinding in randomized comparison of RWD

Population to be analyzed

Handling of missing data

Monitoring of sites in the case RWD are used for New Drug Application (NDA) / Supplemental NDA (sNDA) Process

Safety monitoring

FDA considers drafting a guidance based on the discussion of the Workshop.

In PMDA, Clinical Innovation Network WG[5] leads discussion on utilization of patient registries. In addition to Epidemiological study consultation[6], which is focused on studies for post-marketing surveillance, PMDA newly started consultation to advise appropriateness of development plan utilizing registry data and method of ensuring data reliability of registry data[7,8] from April 2019 for NDA/sNDA Process etc..

1) https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/leveraging-randomized-clinical-trials-generate-real-world-evidence-regulatory-purposes
2) https://healthpolicy.duke.edu/events/leveraging-randomized-clinical-trials-generate-real-world-evidence-regulatory-purposes
3) https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence
4) https://www.fda.gov/media/120060/download
5) https://www.pmda.go.jp/rs-std-jp/cross-sectional-project/0017.html [Japanese Only]
6) https://www.pmda.go.jp/review-services/f2f-pre/consultations/0076.html [Japanese Only]
7) https://www.pmda.go.jp/review-services/f2f-pre/consultations/0101.html [Japanese Only]
8) https://www.pmda.go.jp/review-services/f2f-pre/consultations/0102.html [Japanese Only]

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