*Berberis japonica*

# PMDA Updates

October, 2017

# News

## 1. AMDC-PMDA Standard Workshop 2017

Group photo of participants at workshop in Indonesia

PMDA has implemented "Innovative medical device promotion project to achieve international standardization" (formerly known as "Medical device international standardization strategy promotion project"). As one of its acts, PMDA has proposed to provide workshops on use of standards with the aim of advancing regulatory framework for medical devices in ASEAN countries and its proposal was approved for implementation In ASEAN Medical Device Committee (AMDC) Meeting held in Brunei in December last year. The first round of workshops were held in Vietnam (on August 14), Indonesia (on September 5-6) and Malaysia (on September 13), and common agenda toward the implementation of AMDD were identified and concrete cooperation for AMDC/each country was explored. The outcomes and issues of the first round of workshops will be fed back to the next AMDC meeting and a discussion toward next workshop will be held.

## 2. Regulatory Affairs Professionals Society (RAPS) 2017

Regulatory Affairs Professionals Society (RAPS) has started since 1976 and become a place for information exchange and education on the latest regulatory science of medical products (mainly medical devices).

From September 9 to 12, RAPS 2017 annual conference and associated workshops were held in National Harbor, U.S.A., and was participated by 2 PMDA staff from Office of Regulatory Science and Office of Manufacturing/Quality and Compliance.

The formal sessions of RAPS were held from the evening of September 10 to 12. In the session entitled "Medical Device Single Audit Program (MDSAP)" held on September 11, a staff from Office of Manufacturing/Quality and Compliance delivered a presentation outlining MDSAP Audit. There was a large audience and an active question and answer session.

The next RAPS annual conference will be held in Vancouver, Canada from October 1 to 4, 2018.

## 3. PIC/S Committee Meeting

PIC/S Committee Meeting was held from September 11 to 12 in Taipei, Taiwan. The proposal to hold 2019 PIC/S Committee Meeting and Seminar in Japan in October 2019 was accepted in the meeting. This meeting was attended by 40 out of 49 PIC/S Participating Authorities as well as by Applicants and Associated Partners, etc. under the chairmanship of Mr. Paul Hargreaves (United Kingdom's Medicines and Healthcare products Regulatory Agency; MHRA). The participants from Japan included 1 staff from Office of Manufacturing/Quality and Compliance and Office of International Programs, PMDA and 1 staff from Ministry of Health, Labour and Welfare (MHLW).

In the meeting, Iran Food and Drug Administration (IFDA), the Turkish Medicines and Medical Devices Agency (TMMDA), and Mexico's Federal Commission for the Protection from Sanitary Risks (COFEPRIS) were approved to join the Scheme as PIC/S' 50th, 51st and 52nd Participating Authority, respectively, as from January 1, 2018. Also, Boon Meow Hoe (Singapore / HSA) was elected as Chairman of the PIC/S Committee for the period 2018-2019.

As for PMDA-ATC (PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs) training facilitated with the support of PIC/S, an update was reported on the workshop held in Yamaguchi Prefecture from July 31 to August 4 this year, which was received with keen interest.

The next PIC/S Committee Meeting will be held in Geneva, Switzerland in April, 2018.

## 4. The 12th IMDRF Management Committee Meeting

From September 19 to 21, the 12nd International Medical Device Regulators Forum (IMDRF) Management Committee (MC) Meeting was held in Ottawa, Canada, and three staff from PMDA's Office of International Programs along with a staff from Ministry of Health, Labour and Welfare (MHLW) attended as the MC Members. The first and the third day of the meeting were dedicated to the closed sessions for regulators and officially invited observers only, where, in addition to the guidance documents developed by each working group, new work items were discussed. In this meeting, the final documents of the Medical Device Adverse Event Terminology Working Group (chaired by PMDA) were approved. These documents include IMDRF Terminologies for Categorized Adverse Event Reporting (2nd edition) and Terminologies for Cause Investigation Guidance (Annex B-D).

On the second day, an open IMDRF Stakeholder Forum was held with approximately 180 participants including members from MC and industry, and active discussions were held on issues of interest to industries such as use of real world evidence in medical device filed. The MC members from Japan provided an outline of recent regulatory efforts, and a progress report of the Medical Device Adverse Event Terminology Working Group.

On September 18, prior to the IMDRF meeting, a workshop sponsored by DITTA (Global Diagnostic Imaging, Healthcare IT and Radiation Therapy Trade Association) was held, where PMDA staff gave a presentation titled "Value of International Standards in Japan". Medical Device Single Audit Program (MDSAP) Regulatory Authority Council (RAC) meeting was also held in the afternoon and Japanese delegates attended as a member country.

The next IMDRF MC Meeting will be held in Shanghai, China, in March 2018.

The details of the 12nd IMDRF MC Meeting are available at the following web site.

http://www.imdrf.org/meetings/meetings.asp

## 5. PMDA-ATC Pharmaceuticals Seminar 2017 in Hanoi, Vietnam

From October 3 to 4, PMDA held a seminar entitled "PMDA-ATC Pharmaceuticals Seminar 2017 in Hanoi, Vietnam." This seminar was designed for drug application reviewers from Drug Administration of Vietnam and 30 reviewers participated.

Group photo of participants and PMDA directors
Front row from left to right,
Dr. Wataru Asakura, International Senior Training Coordinator/Office Director, Office of New Drug IV (4th),
Dr. Junko Sato, Office Director, Office of International Cooperation (5th)

In the seminar, lectures were delivered by PMDA staff on consultations, clinical trials, GCP/GLP inspections, product reviews (for new/generic drugs), package inserts, safety measures, Risk Management Plan (RMP), the relief system for sufferers from adverse drug reactions and the post-marketing drug safety measures using electronic healthcare database. Professor Tatsuo Iiyama from NCGM (National Center for Global Health and Medicine) delivered a lecture on Drug proper use and surveillance for anti-microbial. Besides these lectures, the program included group discussions on the review of clinical study.

On the final day, the course completion certificates were handed to each one of the participants by Dr. Wataru Asakura, International Senior Training Coordinator/Office Director, Office of New Drug 4.

Please refer to the following web site for the details of PMDA-ATC Pharmaceuticals Review Seminar 2017 in Hanoi, Vietnam.

http://www.pmda.go.jp/english/symposia/0116.html

## 6. Call for application to PMDA-ATC Pharmacovigilance Seminar 2018 starts

PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) will hold a seminar entitled "PMDA-ATC Pharmacovigilance Seminar 2018" from February 5 to 8, 2018. This four-day seminar is designed for regulatory authority officials who are engaged in pharmacovigilance activities. The Seminar includes lectures, group discussions with the objective of acquainting the participants with the topics such as pharmacovigilance legislation in Japan, EU and the US, pharmacovigilance plan and risk minimization activities for important safety specifications (Risk Management Plan), the way of risk communication for risk minimization activities, e.g., package insert, and the review of pharmacovigilance plan, i.e., studies and surveillances.

The Seminar is held as a workshop of the Asia-Pacific Economic Cooperation, Life Sciences Innovation Forum, Regulatory Harmonization Steering Committee (APEC-LSIF-RHSC) Center of Excellence ; however, the Seminar is open to non-APEC economies as well.

Please refer to the following web site for the details of PMDA-ATC Pharmacovigilance Seminar 2018.
http://www.pmda.go.jp/english/symposia/0118.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 |
|---|---|---|
| Risperdal [Partial Change Approval] | risperidone | September 11 |
| Zagallo | dutasteride | October 17 |

# *Safety Information*

## Pharmaceuticals and Medical Devices Safety Information No. 347, October 10, 2017

1. Summary of the Relief System for Adverse Drug Reaction and Request of Cooperation for the System
2. Important Safety Information
   (1) Dabigatran etexilate methanesulfonate
3. Revision of Precautions (No. 288)
   Dabigatran etexilate methanesulfonate (and 2 others)
4. List of Products Subject to Early Post-marketing Phase Vigilance
   (Posted on October 10, 2017)

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

## Pharmaceuticals Revisions of PRECAUTIONS, October 17, 2017

- Levetiracetam
- Chlorhexidine hydrochloride/diphenhydramine salicylate/hydrocortisone acetate/benzalkonium chloride concentrated solution 50
- Chlorhexidine gluconate
- Products containing chlorhexidine gluconate or products containing chlorhexidine hydrochloride (OTC drugs)
- Linagliptin
- Amoxicillin hydrate
- Lansoprazole/amoxicillin hydrate/clarithromycin
- Lansoprazole/amoxicillin hydrate/metronidazole
- Rabeprazole sodium/amoxicillin hydrate/clarithromycin
- Rabeprazole sodium/amoxicillin hydrate/metronidazole
- Vonoprazan fumarate/amoxicillin hydrate/clarithromycin
- Vonoprazan fumarate/amoxicillin hydrate/metronidazole
- Potassium clavulanate/amoxicillin hydrate
- Moxifloxacin hydrochloride (oral dosage form)

http://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0005.html

# Events

## Conferences/Meetings PMDA hosts or participates in:

| Date | Title | Location |
|---|---|---|
| October 30-November 3 | 6th IGDRP Meeting | Brasilia |
| November 1-16 | ICH Week | Geneva |
| November 6-10 | PMDA-ATC Medical Devices in Tokyo (PMDA) | Tokyo |
| November 30-December 2 | 5th Joint Conference of Taiwan and Japan on Medical Products Regulation | Taipei |
| December 7 | HBD East 2017 Think Tank Meeting in Tokyo | Tokyo |
| December 12-15 | PMDA-ATC Pharmaceuticals Review Seminar 2017 in Bangkok, Thailand | Bangkok |

# Reports from overseas

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

## First EMA International Awareness Session

Under the coordination of the International Affairs Team in EMA, the first EMA International Awareness Session was held at EMA on 18-19 September 2017. The session was targeted at international regulators and non-profit organization staff and aimed at introducing regulations on medicinal products in EU and EMA's roles and activities. Despite this being the first such event, a lot of people, including regulators outside EU, took part in the session, with many others following the live webcast.

The 2-day session was very intensive, and it was a good opportunity to comprehensively learn not only about the EMA's business but also the whole EU regulatory framework, and the relationship between EMA, European Commission and regulatory authorities in EU. The session also provided the participants with valuable inputs about the future direction of EMA and EU, with current interesting topics in EMA (and EU) such as clinical data publication and patients' engagement included.

As the session allows for understanding of basic EU regulations and EMA activities efficiently, which Japanese stakeholders including regulators should know, it is interesting to know that these sessions are planned to be organised every 6 months in the future.

Mr. Hideyuki Kondo
PMDA's International Liaison Officer stationed at EMA in the United Kingdom

## USP Bioassay Workshop

The USP's 7th Bioassay Workshop – Bioassay: A Lifecycle Approach was held on September 25-26 at the USP (United States Pharmacopeial Convention) headquarters[1)]. Bioassay is a bioanalytical procedure which evaluates the attributes of molecules of interest by using a biological system such as animals and cells, and is also used as

an analytical method for characterization and quality control of potency, toxicity and others on biotechnological/biological products. This workshop focused on approach incorporating lifecycle management and QbD (Quality by Design) [2)] concepts into bioassays for characterization and quality control. The scientific, statistical, and regulatory perspectives and the presentations of case studies at each stage (Stage 1; Method Design and Development. Stage 2; Procedure Performance Qualification, and Stage 3; Continued Procedure Verification) were provided. Also, the attendees discussed what is different in lifecycle approach versus traditional approach as described in the International Council for Harmonization of technical Requirements for Pharmaceuticals for Human Use (ICH) Q2 guideline[3)].

By attending this workshop, I was able to learn that (1) design and development based on understanding of analytes, analytical methods, and mechanism of action, (2) statistical analysis of test results including multiple variation factors, and (3) continuous improvement of variability and uncertainty in analytical procedures based on knowledge gained through analytical lifecycle are important for bioassay and enhance reliability of methods because analytes and methods are complex and have high uncertainty in most cases of bioassay. In recent years, bioassay technology for biotechnological/biological products has been improved remarkably. Since I expect that pharmacopeias, which describe requirements for analytical methods, will need to respond to the technological advancements, I will pay attention to trends of bioassay in the U.S. including related USP chapters and regulations.

1) USP's 7th Bioassay Workshop – Bioassay: A Lifecycle Approach
http://www.usp.org/events-training/workshops/usp-7th-bioassay-workshop-bioassay-lifecycle-approach
2) ICH Harmonised Tripartite Guideline: Pharmaceutical Development Q8(R2), Part II, 4. Glossary Quality by Design (QbD)
http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf
3) ICH Harmonised Tripartite Guideline: Validation of Analytical Procedures: Text and Methodology Q2(R1)
http://www.pmda.go.jp/files/000156867.pdf

Dr. Yujiro Kameyama
PMDA's Liaison Officer stationed at USP in the U.S.A

 