



Hydrangea macrophylla
at Hasedera Temple

PMDA Updates

June, 2016

News

1. Opening ceremony of PMDA Hokuriku Branch (June 9)

On June 9, PMDA launched Hokuriku Branch in Toyama Prefecture, and an opening ceremony was held at Toyama Prefectural Civic Centre on the same day. At the ceremony, greetings were brought by Dr. Tatsuya Kondo, Chief Executive and Mr. Takakazu Ishii, Governor, Toyama Prefecture. Then congratulatory speeches were delivered by the guests including Mr. Kazuhiko Mori, Councilor for Pharmaceutical Affairs, Minister's Secretariat of Ministry of Health, Labour and Welfare (MHLW), which made all attendees have high expectation for enhanced cooperation between PMDA and Toyama Prefecture with a long history of pharmaceutical area.



Dr. Kondo (Right) and Mr. Ishii

Through providing seminar facilities for PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) at Hokuriku Branch and facilitating seminars on GMP inspection etc., PMDA will promote regulatory capacity building and harmonization in Asia and other emerging countries, and facilitate further development of cooperation.

2. 3rd International Generic Drug Regulators Programme (IGDRP) Meeting (May 9 to 12)

From May 9 to 12, the 3rd International Generic Drug Regulators Programme (IGDRP) meeting was held in Strasburg, France, which was attended by about 40 participants from 16 countries/regions/organizations. Mr. Naoyuki Yasuda, Office Director, Office of International Programs, a staff from Office of International Programs and the one from MHLW participated in the Steering Committee meeting from Japan. In addition, 4 staffs from Office of Generic Drugs and Office of International Programs participated in the Biowaivers and Active Substance Master File (ASMF)/Drug Master File (DMF) Working Group meetings. The updates on activities of such Working Groups were provided by participating regulatory agencies, and the future action policy was discussed in the Steering Committee meeting.

The next IGDRP meeting will be held in Mexico City, Mexico on October 17-20, 2016.

The details of the IGDRP are available at the following URL.

<http://www.igdrp.com/>

3. Special Lecture by Executive Director of EMA (May 11)

On May 11, Professor Guido Rasi, Executive Director, European Medicines Agency (EMA), visited PMDA and gave a special lecture entitled "Global Regulatory Challenges: role of EMA" to PMDA staffs. The topics outlined and explained in the lecture included an overview of EMA and EU, EMA regulatory challenges, EMA initiatives to promote drug development as well as initiatives for globalization. The participants gained a deeper understanding of the role of EMA in pharmaceutical regulation through the presentation and the active questions and answers.



Dr. Kondo (Right)
and Professor Rasi

4. PMDA provides training to Korea Institute of Drug Safety and Risk Management (KIDS) (May 16 to 18)

From May 16 to 18, PMDA provided training to 5 staffs from Korea Institute of Drug Safety and Risk Management (KIDS) at PMDA in Tokyo. This training was offered at the request of KIDS, which was established in 2012 as an auxiliary organization of Korea Ministry of Food and Drug Safety. This 3 day-training included sessions for lectures, questions and answers, case study and demonstration of relief system regarding advice services and public affairs, relief fund services, investigation and contribution collection to conduct Relief Service for Adverse Drug Reactions. Throughout the training, KIDS staffs learned a lot about the relief service in Japan and staffs of both regulatory authorities deepened mutual understandings.



Group Phot of trainees and PMDA staffs (Trainees from KIDS, Mr. Nobutaka Ikemoto, Chief Relief Officer and Mr. Masato Saito, Office Director of Office of Relief Funds on the front line)

5. 1st India-Japan Medical Products Regulation Symposium (May 18 to 19)

From May 18 to 19, the 1st India-Japan Medical Products Regulation Symposium was held in New Delhi, India between Ministry of Health and Family Welfare/Central Drugs Standard Control Organization (CDSCO) of India and MHLW/PMDA of Japan. This symposium was initiated as part of the cooperation activities as set out in the "Memorandum of Cooperation on Medical Products Regulation Dialogue and Cooperation Framework" signed between CDSCO and MHLW in December 2015.

Those who participated in the symposium from PMDA included Dr. Kazuhiro Shigeto (Executive Director), Dr. Toshiyoshi Tominaga (Associate Executive Director for International Programs), Dr. Daisaku Sato (Office Director, Office of Cellular and Tissue-based Products), as well as staffs from Office of Standards and Guidelines Development, Office of Manufacturing/Quality and Compliance and Office of International Programs. From CDSCO, Dr. G. N. Singh, Drugs Controller General and many other staffs participated in the symposium. There were presentations delivered by the regulators of both countries on the overview and updates on the regulations of pharmaceuticals, regenerative medical products and medical devices, and also by the industries on their activities related to the regulations. In addition, valuable information was inputted in the symposium, including the India's plan to introduce a third party certification system for low risk medical devices in a similar way to Japan.



Dr. Shigeto (left) and Dr. Singh (center)

6. PMDA provides training to staff from Ministry of Public Health Thailand and allied and network organizations (May 19)

On May 19, PMDA provided training on the regulation of herbal medicines including kampo medicines to 21 participants from Department for Development of Thai Traditional and Alternative Medicine (DTAM), Ministry of Public Health Thailand, and allied and network organizations. PMDA's Office of OTC/Quasi-drugs and Office of International Cooperation facilitated lectures covering a wide range of areas including regulatory control, safety, efficacy and quality review of a product, pharmacovigilance activities and relief services. The production and use of herbal products are promoted in Thailand, thus participants had particular interest to the regulation of kampo medicines, leading to lively discussions. PMDA hopes this training is of help to Thai regulatory authorities.



Dr. Takatoshi Nakamura, Office Director of Office of OTC/Quasi-drugs gave a lecture to trainees

7. Special training given by staff from U.S.FDA (May 24)

On May 24, Dr. Lawrence Yu from U.S.FDA visited PMDA and gave a special lecture entitled "FDA Quality Oversight, Quality Metrics, and BCS Biowaiver" to PMDA staff. From the perspective of Deputy Director, Office of Pharmaceutical Quality (OPQ), U.S.FDA Center for Drug Evaluation and Research, Dr. Yu explained the background about the establishment of OPQ, purpose of the quality assessment by Quality Review Team organized by multiple reviewers who have different specialties such as drug substance and drug product, and establishment of Emerging Technology Team to deal with state-of-the-art technology.



Dr. Yu

As an expert, Dr. Yu also explained Quality Oversight as well as Quality Metrics, on which a draft guidance for industry was issued in July, 2015 and Biowaiver based on the idea of Biopharmaceutics Classification System (BCS), which is one of the main topics for IGDRP. The audiences from PMDA gained further understanding of new challenge of product quality and manufacturing in U.S.FDA as well as the perspective about BCS-based Biowaiver.

8. Pharmacopoeial Discussion Group (PDG) Meeting (May 25 to 26)

From May 25 to 26, Pharmacopoeial Discussion Group (PDG) Meeting was held at the European Directorate for the Quality of Medicines & HealthCare (EDQM) headquarters (Strasbourg, France), where staff members of Office of Standards and Guidelines Development, PMDA attended as a part of representatives of the Japanese Pharmacopoeia (JP). PDG is an international discussion group comprised of the representatives of the EP, USP (U.S. Pharmacopoeial Convention), and JP. In this meeting, the excipient monograph for Hydroxyethylcellulose was newly harmonized. In addition, 8 items including Ethylcellulose and Cellulose acetate were agreed for revision or correction. By these agreements, 29 items in 36 general tests, 49 items in 62 excipient monographs have been agreed for harmonization to date. Moreover, five new excipient monographs (Isostearyl alcohol, Myristyl myristate, Polysorbate 65, Sodium cetyl sulfate and Calcium silicate) were added to the work program. Also, the commitment to harmonize the general tests for chromatography and elemental impurities was reaffirmed, and the information on approaches for the implementation of the ICH Q3D Guideline for Elemental Impurities was exchanged in the meeting.

The next PDG meeting will be held in Tokyo, hosted by the JP in the week of 24 October, 2016.

9. PMDA provides training to staff from Thailand FDA (May 25 to 26)

From May 25 to 26, PMDA provided training on eCTD management to a staff from Thai Food and Drug Administration. The training was facilitated by Office of Review Management, who instructed on eCTD review process, submission, validation, emergency plan including data backup and restore and system maintenance, using mockup eCTD. The operational know-how gained from PMDA through this training is expected to promote utilization of eCTD in Thailand where eCTD has been introduced recently.



Trainee (Left)
and Lecturer

10. Special CDISC Symposium: Smarter Research Through CDISC Standards for Therapeutic Areas (June 1)

On June 1, PMDA held a symposium entitled "Special CDISC Symposium: Smarter Research through CDISC Standards for Therapeutic Areas" at the University of Tokyo, cohosted by Clinical Data Interchange Standards Consortium (CDISC) and University Hospital Medical Information Network (UMIN) Center. The symposium aimed to promote the use of CDISC standards by academia, with academics as main target participants.

Dr. Mayumi Shikano, Associate Director of Center for Product Evaluation for Advanced Review with Electronic Data Promotion and Science Board, gave the opening remarks and outlined the system in Japan toward the use of CDISC standards and Therapeutic Area Standards, followed by lectures by CDISC experts on the significance of using CDISC Standards for clinical trials and clinical research, the overview and benefits of CDISC standards, generating procedure of Therapeutic Area Standards using

actual examples, and the progress and status, etc. During questions and answers sessions, academics and official CDISC trainers in Japan actively asked questions on selection criteria and generating and amending procedures of Therapeutic Area Standards. To conclude the symposium, cooperation was sought in working to reflect medical practice actual conditions in Japan into Therapeutic Area Standards. Through detailed explanations and active questions and answers sessions, about 150 participants were able to gain an in-depth understanding of the significance and method of using CDISC standards for clinical trials and clinical research, which is expected to facilitate further utilization of CDISC standards in Japan in the future.



Group Phot of Organizers and Speakers (Dr. Shikano is the 2nd from the right and Dr. Kush is the 3rd from the right)

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
Radicut Injection 30 mg, Radicut Bag for Intravenous Infusion 30 mg	edaravone	June 13

Safety Information

Pharmaceuticals Revisions of PRECAUTIONS, May 31, 2016

- Levetiracetam (Tablets)
- Levetiracetam (Dry Syrup)
- Levetiracetam (Injection)
- Alendronate Sodium Hydrate (Tablets)
- Alendronate Sodium Hydrate (Oral Jelly)
- Alendronate Sodium Hydrate (Injection)
- Ibandronate Sodium Hydrate (Tablets)
- Ibandronate Sodium Hydrate (Injection)
- Etidronate Disodium
- Zoledronic Acid Hydrate
- Pamidronate Disodium Hydrate
- Minodronic Acid Hydrate
- Risedronate Sodium Hydrate

<http://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0004.html>

Risk Information which some safety measures might be taken (June 10, 2016)

- Benzoyl Peroxide
- Clindamycin Phosphate Hydrate/Benzoyl Peroxide
- Apixaban
- Ombitasvir Hydrate/Paritaprevir Hydrate/Ritonavir
- Sofosbuvir
- Ribavirin
- Ledipasvir Acetate/Sofosbuvir
- Oxytocin
- Diclofenac Sodium (Oral Tablets)
- Diclofenac Sodium (Suppositories)
- Diclofenac Sodium (Capsules)

- Diclofenac Sodium (Enema Ointment)
- Nintedanib Ethanesulfonate
- Carmustine
- Fingolimod Hydrochloride

<http://www.pmda.go.jp/english/safety/info-services/drugs/risk-communications/0001.html>

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
July 5-8	PIC/S Seminar / PIC/S Committee Meeting	Manchester
July 12-14	ICCR (International Cooperation on Cosmetics Regulation) Meeting	Washington D.C.
July 12-15	APEC MRCT/GCP Workshop	Beijing
July 25-29	PMDA-ATC Pharmaceutical Review Seminar 2016	Tokyo
August 15-18	APEC-LSIF-RHSC SOM3	Lima

Reports from overseas

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

Discussions on development of biosimilars and promotion of their use; key take-aways from 14th Annual Biosimilar Medicines Group Conference

The 14th Annual Biosimilar Medicines Group Conference was held on 28 - 29 April 2016 by Medicines for Europe³⁾, a generic drug industry. Worldwide stakeholders such as industry, academia, doctors, patient groups and regulatory authorities attended as speakers/panelists and had lively opinion exchanges with other participants about experience, current issues and future prospective for development of biosimilars and promotion of their use. I would like to introduce 3 particularly interesting discussions in the conference.

Firstly, the participants had the common perception that biosimilars can provide a solution for the sustainability issue of medical care systems due to highly priced drugs. It is assumed that market emergence of a biosimilars would cause lower drug prices of the reference product as well as other related biosimilars because of their competition. The market emergence of biosimilars is also stated as one of the areas where regulators can show contribution to sustainability of medical care system in the article of the New England Journal of Medicine by EMA's Executive Director Guido Rasi et al.²⁾. Though neither PMDA nor EMA is responsible for drug pricing, this point is still significant because appropriate approval of biosimilar can improve patients' access to drug.

The second point is why the switch from reference products to biosimilars has shown slow progress. Doctors and patients in the conference insisted on the need for more information for consideration of

the switches because of their less reliance on biosimilars. However, no one had an answer to what specific further information they want on biosimilars, which are reviewed with efficacy, safety and quality data and approved by regulatory authorities.

As a result of such discussions, the conference concluded that closer communication among stakeholders is important for further promotion of biosimilar use. The importance of information on generic drugs, including biosimilars, has been discussed for a long time in Japan as well, and still remains as an issue globally.

Finally, it is recognized that governments/public health authorities play an essential role for development of biosimilars and promotion of their use. The discussion that they should take measures to promote biosimilars was raised again and again through the conference. A presentation of survey results for relation between biosimilars-related policies in some EU countries and switch rates for biosimilars showed that the switch rate for biosimilars is actually higher in the countries that actively promote their use. In addition, much time was allocated to presentations and QA sessions by regulatory authorities in the conference, including an update on the situation and biosimilar concept in Japan by Dr, Daisaku Sato, Office Director of Office of Cellular and Tissue-based Products in PMDA.

Through participation in this conference, I have recognized again that regulators and other stakeholders around the globe face common issues and concerns, including those mentioned above. In order to address them, it is important to keep frameworks of collaboration with EMA such as Biosimilar Cluster³⁾.

- 1) Its original organization name was European Generic and Biosimilar Medicines Association (EGA), and name has been replaced since March 2016.
- 2) The following is URL of the related press release by EMA:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/05/news_detail_002529.jsp&mid=WCob01ac058004d5c
- 3) The framework to discuss regulatory issues/cooperation about biosimilar among regulatory authorities. From Japan, the Office of Cellular and Tissue-based Products in PMDA mainly take care of this cluster. U.S. FDA and Health Canada are also included in the cluster.
http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/general/general_content_000655.jsp&mid=WCob01ac0580953d98

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PMDA Website: <http://www.pmda.go.jp/english/index.html>

Contact: <http://www.pmda.go.jp/english/contact/0001.html>