



Hydrangea macrophylla

PMDA Updates

June, 2014

News

1. Japan Officially Joins PIC/S (May 15 to 16)

The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) Committee meeting was held in Rome from May 15 to 16. Mr. Haruo Akagawa, Director, Pharmaceutical and Food Safety Bureau, the Ministry of Health, Labour and Welfare (MHLW), Dr. Shingou Sakurai, Director, Office of GMP/QMS Inspection, and 2 staff members of PMDA, participated in the meeting. At the Committee meeting, the accession of Japanese regulatory authorities, represented by MHLW, PMDA and 47 prefectural inspectorates, was approved, and Japan will become the 45th PIC/S participating authority as of July 1, 2014. Mr. Akagawa expressed his appreciation for the accession to PIC/S and the willingness to engage in the activities of PIC/S in the future.

The PIC/S are the framework of the cooperation among the pharmaceutical inspection authorities, aiming to lead the international development, implementation and maintenance of harmonized Good Manufacturing Practice (GMP) Standards and quality systems of inspectorates in the field of medicinal products. The PIC/S are currently recognized as the world standard in the field of GMP. Japanese regulatory authorities applied for the PIC/S membership in March, 2012. A paper assessment was conducted, followed by an on-site inspection visit in September, 2013, by the PIC/S inspection team.

As an activity after the accession, PMDA will host a PIC/S Expert Circle on Quality Risk Management (QRM), a training course for the GMP inspectors from regulatory authorities, from December 8 to 10 in Tokyo.

For the detail of the PIC/S Expert Circle on QRM, refer to the following web site.

<http://www.picscheme.org/expert-circles.php>



Second from left to right, Dr. Joey Gouws (PIC/S Chairperson, South Africa's Medicine Control Council), Mr. Akagawa, Dr. Sakurai

2. PMDA provides training program to officials from Thai FDA, Thailand (May 26 to 30)

PMDA accepted four officials from the Thai Food and Drug Administration (Thai FDA), Thailand, from May 26 to 30. Lectures on post-marketing safety measures for drugs and medical devices, and On-the-Job Trainings were provided by the Office of Safety I and Safety II. The officials of Thai FDA also gave a lecture to PMDA staff members on outlines of Thai FDA and Pharmacovigilance system in Thailand. Throughout the training, officials of both Thai FDA and PMDA exchanged views actively and deepened mutual understandings.

3. PMDA provides a training program to officials from CINP, Malaysia (May 26 to June 20)

PMDA accepted two officials from the Centre for Investigational New Product (CINP), National Pharmaceutical Control Bureau (NPCB), Ministry of Health, Malaysia, from May 26 to June 20. The

training program was given by the Offices of New Drug I, New Drug II, Cellular and Tissue-based Products, Conformity Audit, and GMP/QMS Inspection. Lectures on the reviews of non-clinical studies, first-in-human studies, etc., and On-the-Job Trainings were provided by each responsible office. Officials of both CINP and PMDA exchanged views actively and deepened mutual understandings.

4. The 6th meeting of IGDRP (May 26 to 28)

The 6th International Generic Drug Regulators Pilot Meeting (IGDRP), was held in Yilan, Taiwan, from May 26 to 28. Thirty participants from 9 countries and EU, including one staff from the Pharmaceutical and Food Safety Bureau, MHLW, and five staff members from Office of OTC/Generic Drugs and one staff member from Office of International Programs, PMDA, joined the meeting. The participants shared progress of currently operating working groups regarding Biwaiver and Drug Master File, and actively discussed the direction of the project. The next meeting will be held in Singapore from November 2 to 6, 2014.

5. ICH meeting held in Minneapolis (May 31 to June 5)

The ICH meeting was held in Minneapolis, from May 31 to June 5. Dr. Nobumasa Nakashima, Director, Office of International Programs, PMDA, and 27 experts from MHLW/PMDA joined the Steering Committee and the Expert Working Groups. In the Steering Committee, participants discussed the operational issues of ICH, including establishment of 5 task force groups to make ICH as a Legal Entity. Eight new topics has been agreed to progress, and MHLW/PMDA will lead discussions in three of the eight topics as a rapporteur/regulatory chair. In addition, M7 (assessment and control of DNA reactive impurities) and M8 (Version 1.26 of the eCTD Change Request Q&A document) reached Step 4 in this meeting. Next ICH meeting will be held at Lisbon, Portugal from November 8 to 13, 2014.

6. The 2nd Taiwan-Japan Medical Device Exchange Seminar (June 10 to 11)

The 2nd Taiwan-Japan Medical Device Exchange Seminar was held in Taipei on June 10, 2014. One each staff member from the Pharmaceutical and Food Safety Bureau and Health Policy Bureau, MHLW, and one each of PMDA expert from the Offices of International Programs and GMP/QMS Inspection, participated in the Seminar. Approximately 90 people involved in medical device industry and relevant government service from Taiwan and Japan gathered, and opinions were lively exchanged during the seminar.

On June 11, the participants were divided into 4 working groups by topics such as Product Registration, Good Clinical Practice (GCP), Quality System Documentation (QSD)/Quality System Manual (QSM), and Post-Market Surveillance (PMS), and discussed how to proceed their works in the future. Moreover, in the meeting between administrative authorities from Taiwan and Japan, outcomes of the discussions in each working group were reported and future cooperative framework between Taiwan and Japan was confirmed. The next seminar is scheduled for November, 2014.

7. PhRMA-PMDA forum (June 11)

The PMDA-PhRMA Forum was co-hosted by PMDA and Pharmaceutical Research and Manufacturers of America (PhRMA) in New York on June 11. From PMDA, Dr. Tatsuya Kondo, Chief Executive, Dr. Takao Yamori, Director, Center for Product Evaluation, Dr. Nobumasa Nakashima, Director, Office of International Programs, and two staff members from Office of International Programs, attended the forum. In the forum, Dr. Kondo and Dr. Yamori gave presentations entitled "10-Year Achievements of PMDA and the Future" and "The 3rd Mid-term Plan of PMDA", respectively, along with the presentations by PhRMA executives on the current situations of Japanese pharmaceutical affairs regulations and expectations for PMDA. About 50 senior executives from the member companies of PhRMA attended the forum and vigorous questions and answers took place.



The third right, Dr. Kondo, the forth right Dr. Yamori

Safety Information

Pharmaceuticals and Medical Devices Safety Information No.313, May 27, 2014

1. Fatal cases with XEPLION® Aqueous Suspension for IM injection
2. Important Safety Information
(1) Paliperidone palmitate
3. Revision of Precautions (No. 256)
(1) Pentamidine isetionate
4. List of Products Subject to Early Post-marketing Phase Vigilance (as of May 2014)
http://www.pmda.go.jp/english/service/precautions_2014.html

Revision of precautions in drug package inserts

English translation of Summary of the investigation results for instruction of revision of the Precautions in drug package inserts are released on PMDA's English web site from FY 2014.

Instruction of revision as of June 3, 2014

1. Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers
2. Losartan
3. Rosuvastatin
4. Imidafenacin
5. Granulocyte colony-stimulating factors

<http://www.pmda.go.jp/english/service/revision.html>

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
August 2	Brazil-Japan Joint Seminar	Sao Paulo
August 21-22	Global Coalition for Regulatory Science Research (GCRSR)/Global Summit on Regulatory Science (GSR)	Montreal
August 24-29	International Conference of Drug Regulatory Authorities (ICDRA)	Rio de Janeiro
August 26-29	China International Medical Device Regulatory Forum (CIMDR)	Amoy
September 19	HBD Think Tank West	Washington D.C.
September 27 -October 1	Regulatory Affairs Professionals Society (RAPS) Annual Meeting	Austin

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
Topiloric/Uriadec	Topiroxostat	June 16

Reports from overseas

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

Publication of clinical trial data was covered in the letters from the liaison officers so far in December 2012 and May 2013. After that, a series of related information is published on the EMA website between May and June this year. Recent information published includes a requirement that any interventional clinical trials that ended on or after July 21, 2014, have to be submitted with their results to the European Clinical trials database (EudraCT) within six or twelve months following the end of the trial, and other trials that ended before the date have to be submitted retrospectively.

The Executive Director Guido Rasi and other colleagues point out in an article of the New England Journal of Medicines in October, 2013, as a background factor, there are several merits of publication of the clinical trials, with due consideration to the balance between securing the property rights and transparency of the clinical trials, such as 1) improving the design and analysis of subsequent trials for research-oriented pharmaceutical companies, 2) enhancing a drug's value in the marketplace by learning lessons from past trials, 3) more comparative-effectiveness information available by widely accessing to patient-level data, at a very limited cost as compared with before, soon after licensing, and 4) reducing the repetition of clinical trials by avoiding doomed trials from the outset.

With the promotion of global clinical trials, it may be said that we, including pharmaceutical industry and regulatory authorities, continue to pay close attention to the publication of the clinical trial data.

The publication of the clinical trials and the article of Executive Director Dr Rasi are available at following web sites.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/06/news_detail_002127.jsp&mid=WC0b01ac058004d5c1

<http://www.nejm.org/doi/full/10.1056/NEJMp1310771>

Mr. Yoshihiko Sano

PMDA's International Liaison Officer stationed at EMA in the United Kingdom

The Parliament of Canada is currently deliberating the Amendments to the Food and Drugs Act. This reform bill, also known as Vanessa's Law, aims to strengthen the post-marketing safety measures for pharmaceuticals and medical devices. For example, the proposed Amendments include the following new provisions:

1. The Health Canada has power to inquire manufacturers to conduct investigations and tests, and to report the results for product safety.
2. The Health Canada has power to inquire manufacturers to revise package inserts of their products when necessary to prevent injury to health.

3. The Health Canada has power to recall unsafe therapeutic products from the marketplace when the product presents an imminent or serious risk to health.
4. The healthcare institutions are obligated to report serious Adverse Drug Reactions (ADRs) and medical device incidents directly to Health Canada.

Especially on the above #4, reporting due date is scheduled to be set and the increase in number of ADRs and medical device incidents is expected. To deal with the increase, the responsible divisions in Health Canada are developing measures to receive and utilize the reports effectively. In Japan, Initiative to Develop Infrastructure for Medical Information Database is proceeding to comprehensively collect electronic medical records from medical institutions. Health Canada and PMDA face common challenges in collecting more medical information effectively and utilize them into strengthening the post-marketing safety measures, therefore, I believe it is useful for us to share each other's experiences.

For more information about Vanessa's Law, see following web site.
Amendments to the Food and Drugs Act (Bill C-17)

<http://www.hc-sc.gc.ca/dhp-mpps/legislation/unsafedrugs-droguedangereuses-eng.php>
<http://www.parl.gc.ca/Legisinfo/BillDetails.aspx?Mode=1&billId=6365510&Language=E>

Mr. Kosuke Haneda
PMDA's International Liaison Officer stationed at Health Canada in Canada

I had a chance to talk about compliance data with a staff member belonging to Office of Manufacturing and Product Quality, Office of Compliance, Center for Drug Evaluation and Research (CDER). PMDA collects post-market information on safety issues and adverse reactions for drugs. When a product recall from the market is necessary, marketing authorization holders provide the information for MHLW. FDA has established several information collecting systems for recording manufacturing problems with drug products: Field Alert Reports (FAR), Biological Products Deviation Reports (BPDR), and the Med Watch Program. The U.S. Code of Federal Regulations requires FARs to be submitted, when quality abnormalities (physico-chemical or other change in components, contamination, labeling, etc.) are found in post-market drugs. This applies for abnormalities in manufacturing processes of all products, including APIs, intermediates, and finished dosage forms. The reports should be submitted to the relevant FDA District Office within 3 working days after the identifying abnormalities with the product. Then the reports are sent to CDER for evaluation. For products that are manufactured at foreign manufacturing sites, the FARs are submitted to the appropriate FDA District Office by representatives of the manufacturing sites in the U.S. The FAR system has three types of reports, Initial, Follow up, and Final. Reported cases can be closed only after appropriate completion of root-cause analysis, and after taking corrective action and preventive action. The BPDR system is an information collecting system specifically for biological products. The reporting format is similar to the FAR system, but the reports are submitted to the Center for Biologics Evaluation and Research/CDER within 45 calendar days of the discovery of the abnormalities at a manufacturing site. The Med Watch Program allows everyone (including pharmacists, doctors, patients, and so on) to provide information to FDA when any quality abnormality is found in a post-market drugs. A database that collects the above mentioned reports has been created. The data base is useful for recognizing issues at early stage, such as identifying problems at manufacturing sites in advance of Good Manufacturing Practice inspections. From the discussions with the FDA staff member, I learned that there are various ways to collect manufacturers' information. I will continue to learn more through this kind of communications and share information I have learnt with you.

Ms. Mami Yabuki
PMDA's International Officer stationed at CDER, U.S.FDA in the U.S.A.

