Cerasus

PMDA Updates

April, 2015

News

1. PMDA's staff size expanded (April 1)

The total number of executives and employees has increased by 67 from April 1, 2014 to 820 on April 1, 2015, of which 532 belong to the review department and 165 to the safety department. From April 3 onwards, the training program for the new recruits has been carried out. The newcomers will undergo an intensive two-month training program that includes orientation, interpersonal skills training, specialized training, and professional awareness training.

2. The 7th IMDRF Management Committee Meeting (March 24 to 26)

The 7th International Medical Device Regulators Forum (IMDRF) Management Committee (MC) Meeting was held in Tokyo from March 24 to 26, at which Japan takes the chair for CY 2015. The meeting was presided by Dr. Toshiyoshi Tominaga, Associate Executive Director (for International Programs), while Mr. Soichiro Isobe, Director, Medical Device and Regenerative Medicine Product Evaluation Division, Ministry of Health, Labour and Welfare (MHLW), and a staff member of Office of International Programs (OIP) attended as committee members, and one member each from MHLW and OIP served as secretariat.

The first and the third day of the meeting were dedicated to the closed sessions for regulators and officially invited observers only, whereas an open forum for all stakeholders including industry took place on the second day. During those sessions, the Strategic Plan of IMDRF, as well as the progress of each working group were reported and discussed, and the establishment of Adverse Event (AE) Terminology Work Group, proposed by Japan, was approved to pursue harmonization of AE terminology as a new work item. About 170 stakeholders attended the open forum and Mr. Yasuhisa Shiozaki, Minister of Health, Labour and Welfare, gave a congratulatory speech at the reception after the forum. Dr. Tatsuya Kondo, Chief Executive, expressed his appreciation as the closing remark of the meeting.

The next IMDRF MC Meeting will be held in Kyoto from September 15 to 17 this year.

The details of the 7th IMDRF MC Meeting and Press release from MHLW are available at following URL.

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

http://www.mhlw.go.jp/stf/houdou/0000080780.html (Japanese only)

3. Special training given by academic staffs from Medical University of Vienna (March 27)

On March 27, Dr. Peter Bauer, Professor Emeritus, Dr. Martin Posch, Professor and Dr. Franz König, Associate Professor from Medical University of Vienna, visited PMDA and gave a special training for PMDA staff members, which was entitled "Trends in adaptive design and statistical approaches to small population group trials in EU". In the training, Dr. König and Dr. Posch explained the outline of adaptive design as well as various regulatory issues regarding adaptive clinical trials and research initiatives to resolve them based on the results of the survey of scientific advice letters at the European Medicines Agency (EMA). Dr. Bauer raised issues on planning and evaluating for adaptive interim analysis. Following those lectures on adaptive design, Dr. Posch and Dr. König explained EU-funded projects (ASTERIX[1)], IDEAL[2)], InSPiRe[3)], and IDEAS[4)]) on designing and evaluating small population group trials. The participants gained a further understanding of adaptive design and other research initiatives to improve methodology for designing and evaluating clinical trials in EU.

1) ASTRIX: Advances in small trials design for regulatory innovation and excellence
   http://www.asterix-fp7.eu/
2) IDEAL: Integrated design and analysis of small population group trials
   http://www.ideal.rwth-aachen.de/
3) Inspire: Innovative methodology for small population research
   www.warwick.ac.uk/InSPiRe
4) IDEAS: Improving Design, Evaluation and Analysis of early drug development Studies
   http://www.ideas-etn.eu/


Left: Discussion at the Q & A session. Right: from the left Dr. Bauer, Dr. Posch and Dr. König,

4. ICMRA introduced on WHO Drug Information (April 2)

Dr. Tatsuya Kondo, Chief Executive coauthored an article entitled "The International Coalition of Medicines Regulatory Authorities (ICMRA)", which was published in the WHO Drug Information on April 2. In the article, ICMRA was introduced as "a voluntary, executive level entity that provides direction for a range of areas that are common to many regulatory authorities' missions in an increasingly globalized and complex regulatory environment". The authors also encouraged all WHO Member States to increase their understanding of ICMRA as well as to become engaged in its activity along with the transformation of the global regulatory landscape.

The aritcle is available at following URL (WHO Drug Information Vol. 29, No. 1, 3-6, 2015).
http://www.who.int/medicines/publications/druginformation/WHO_DI_29-1_RegulatoryCollaboration.pdf?ua=1

5. The 4th Asia Partnership Conference of Pharmaceutical Associations (April 9 to 10)

The 4th Asia Partnership Conference of Pharmaceutical Associations (APAC) was held in Tokyo from April 9 to 10. Dr. Tatsuya Kondo, Chief Executive, Dr. Daisaku Sato, Director, the Office of Cellular and Tissue-based Products, and 14 staff members (including Executives and Directors) from PMDA participated in the conference. Presentations and panel discussions were delivered under the theme of "To Expedete the Launch of Innovative Medicines for Peoples in Asia" with participants from regulatory authorities of Indonesia, Korea, Thailand, Taiwan, Philippines, Malaysia, and Myanmar.

Dr. Kondo delivered a keynote speech entitled "Advocacy of Regulatory Science and International Collaboration" and introduced PMDA's efforts in promoting regulatory science, regulatory harmonization, and dissemination of information on Japan's regulation system to Asian countries, and explained the importance of building win-win relationships between Japan and the other countries in the international activities. In the panel discussion session, Dr. Sato participated in the "Regulations and Approvals Session" as a panelist, where there was an active discussion under the theme of "Expectiations and Challenges for APAC Good Submission Practice Guidence".

The 5th APAC will be held in April 2016, in Tokyo.


Left: Dr. Kondo, Right: Dr. Sato (the third from the left)

6. DIA 27th Annual Euro Meeting (April 13 to 15)

From April 13 to 15, the DIA 27th Annual Meeting was held in Paris, and Dr. Taisuke Hojo, Senior Executive Director; Dr. Tetsuo Nagano, Executive Director; Ms. Tomiko Tawaragi, Chief Safety Officer; Dr. Toshiyoshi Tominaga, Associate Executive Director for International Programs; Dr. Yoshiaki Uyama, Director, Office of Medical Informatics and Epidemiology, Project Leader for Global Clinical Trials; 3 staff members from PMDA; and Dr. Nobumasa Nakashima, International Planning Director, Ministry of Health, Labour and Welfare, participated in the meeting. At the PMDA Updates session chaired by Dr. Tominaga, presentations on 1) the outline of PMDA's services based on the progress of the third mid-term plan of PMDA by Dr. Hojo, 2) PMD Act and Strategy of SAKIGAKE by Dr. Nakashima, 3) PMDA's efforts on review services focusing on the pharmaceutical affairs consultation on R&D strategy and science board by Dr. Nagano, and 4) Safety measures in Japan focusing on the risk management plan by Ms. Tawaragi, were delivered. At the Asia: Creative Possibilities for Clinical Development and Collaboration session chaired by Dr. Tominaga, Dr. Uyama and 2 other speakers delivered presentations. There were approximately 60 participants in both of the PMDA Updates session and Asia session, and active discussion took place.

Left: from the left, Dr. Tominaga, Dr. Hojo, Dr. Nakashima, Dr. Nagano and Ms. Tawaragi
Right: from the left, Dr. Hojo, Dr. Nagano and Ms. Tawaragi

7. The Science Board Activity Update (November 2014 to March 2015)

The activities from November 2014 to March 2015 of the five subcommitees of the second term of the Science Board, which statred in April 2014, are as follows. Please refer to the following web sites for the meeting agenda and handouts.

1) Subcommittee on Placebo-controlled Studies
http://www.pmda.go.jp/english/rs-sb-std/sb/subcommittees-2nd/placebo/0001.html (English)
http://www.pmda.go.jp/rs-std-jp/subcomm-2nd/placebo/0004.html (Japanese)
The 2nd Subcommittee meeting was held on January 9, 2015.
The 3rd Subcommittee meeting was held on March 6, 2015.

2) Subcommittee on Non-clinical Studies
http://www.pmda.go.jp/english/rs-sb-std/sb/subcommittees-2nd/non-clinical-studies/0001.html (English)
http://www.pmda.go.jp/rs-std-jp/subcomm-2nd/non-clinical-studies/0004.html (Japanese)
The 2nd Subcommittee meeting was held on December 18, 2014.
The 3rd Subcommittee meeting was held on February 4, 2015.
The 4th Subcommittee meeting was held on March 11, 2015.

3) Subcommittee on Application of Numerical Analysis to Non-clinical Evaluation
http://www.pmda.go.jp/english/rs-sb-std/sb/subcommittees-2nd/numerical-analysis/0003.html (English)
http://www.pmda.go.jp/rs-std-jp/subcomm-2nd/numerical-analysis/0004.html (Japanese)
The 2nd Subcommittee meeting was held on Novermber 14, 2014.
The 3rd Subcommittee meeting was held on February 25, 2015.

4) Subcommittee on Evaluation of Medical Devices in Pediatric Use
http://www.pmda.go.jp/english/rs-sb-std/sb/subcommittees-2nd/devices-in-pediatric-use/0001.html (English)
http://www.pmda.go.jp/rs-std-jp/subcomm-2nd/devices-in-pediatric-use/0003.html (Japanese)
The 2nd Subcommittee meeting was held on December 19, 2014.
The 3rd Subcommittee meeting was held on March 12, 2015

5) CPC (Cell Processing Center) Subcommittee
http://www.pmda.go.jp/english/rs-sb-std/sb/subcommittees-2nd/cpc/0005.html (English)
http://www.pmda.go.jp/rs-std-jp/subcomm-2nd/cpc/0005.html (Japanese)
The 3rd Subcommittee meeting was held on December 2, 2014.
The 4th Subcommittee meeting was held on March 12, 2015.
The 5th Subcommittee meeting was held on February 12, 2015.

Safety Information

Pharmaceuticals and Medical Devices Safety Information No. 321, March 30, 2015

1. Lamotrigine and Serious Skin Disorders
2. Abiraterone Acetate and Hypokalaemia
3. The MIHARI Project
4. Important Safety Information
   (1) abiraterone acetate
   (2) lamotrigine
   (3) apixaban
   (4) memantine hydrochloride
5. Revision of Precautions (No. 263) Montelukast sodium and telaprevir
6. List of Products Subject to Early Post-marketing Phase Vigilance (as of March 2015)

(Reference) The Drug and Medical Devices Safety Information Reporting System
- Reporting via e-Gov will be closed
http://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0010.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
Betanis	Mirabegron	April 28
Cedartolen	-	April 28

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
May 26	DIA China 7th Annual Meeting	Shanghai
May 27-28	IGDRP MEETING PRETORIA 2015	Pretoria

May 28	Japan Promoting Policy and Approval System of Innovative Drugs Symposium	Beijing
June 6-11	ICH Week	Fukuoka
June 14-18	DIA 2015 51st Annual Meeting	Washington D.C.
June 22-26	MDSAP RAC, MDSAP Forum 2015	Washington D.C.
June 30-July 1	Pharmacopoeial Discussion Group Meeting	Tokyo
July 20-Aug 1	CVIT2015 HBD Session	Tokyo

Reports from overseas

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

Participation at OECD technical meeting facilitating international co-operation and quality assurance in clinical trials

The OECD technical meeting of 'Facilitating international co-operation and quality assurance in clinical trials' was held in Paris on April 9-10. The objective of the meeting was, with regard to global clinical trials conducted under different regulations among each countries, to contribute to benefit for healthcare systems and patients worldwide by improving regulatory collaboration and ensuring steady implementation of clinical trials. Over 30 regulatory, academic and patient representative stakeholders from Asia, North and South America, Africa and Europe attended the meeting. Participants worked in 6 small-group breakout sessions covering (1) infrastructure and funding, (2) global core competences of medical institutions necessary for conducting global clinical trials, (3) ethics committees, (4) patient involvement, (5) comparative effectiveness research, and (6) regulatory harmonisation, and conducted closed discussion. I attended the 6th session on regulatory harmonisation and contributed to clarification of issues to be considered in future in collaboration with other regulators from the US, EU, France and Switzerland. Participants of each group presented the results of their discussions in plenary session on the last day of the meeting.

The discussion at this technical meeting has just started and should be continued in future. Core competences and ethics committee were the points that intrigued me through this small-group and plenary discussions. In terms of core competences, to promote global clinical trials, how to ensure the level of system and abilities of healthcare professionals to promote clinical trials in each country, and to include this as a part of education systems impressed me.

With regard to ethics committees, how to ensure the quality of evaluation and review of ethics committee globally was so impressive, because nature of ethics committees varies in distinctive ways between countries (e.g. a country such as Hungary with one central ethics committee, and Italy with hundreds ethics committees) in the context of variation of thinking and perception towards medication and system for providing medical services across countries or regions.

It would be beneficial for Japan to continue contributing to this meeting.

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

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Japanese expert gave a presentation at USP Workshop

The United States Pharmacopeial Convention (USP) hosted a workshop regarding Alternative Microbiological Methods on March 16-17 at the USP Headquarters. In this workshop, one of the members of the Microbiology Expert Committee, Dr. James Akers acted as a chairperson and interested parties including industry, academia, and governmental bodies (U.S. Food and Drug Administration, and European Directorate for the Quality of Medicines, etc.) attended. From Japan, Dr. Nobuyasu Yamaguchi, Associate Professor, Osaka University, attended this workshop as one of the speakers on behalf of the Japanese Pharmacopoeia Expert Committee. He gave a presentation on rapid microbiological methods, etc., entitled "Current JP Perspectives", which is to be newly included in the Japanese Pharmacopoeia Seventeenth Edition (JP 17). The validation of alternative microbiological methods and the current status of each pharmacopoeia's work on rapid/modern microbiological methods, etc., were discussed actively throughout the workshop.

To improve global health, the USP promotes various activities around the world including workshops like the current one, online training courses for experts in academia and industry and healthcare professionals, in addition to publishing the United States Pharmacopeia-National Formulary (USP-NF). PMDA also actively holds workshops for industry and PMDA staff members give presentations at symposia organized by scientific society to inform interested parties of current status of the JP. For further international development of the JP, as a PMDA's International Liaison Officer, I would like to learn the know-how about USP's international training program which is the specialty of them. The workshop "2nd Excipient Workshop: Focus on Excipient Quality, Compendial Testing, and Regulatory Impact", which is organized by the excipients team I belong to, will be held on November 18-19. There I would like to provide information on Japanese standard and regulatory system positively.

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

Risk minimization and the Safe Use Initiative

Labeling is a fundamental risk minimization tool, because it contains the information necessary for proper use of a drug. For example, risk minimization via labeling can be achieved through information on the type of patients who should not use a product, recommendations for laboratory testing before or during treatment, or a description of adverse drug reactions for which early detection may lead to reduced harm. When additional risk minimization beyond labeling is necessary to ensure that the benefits of a drug outweigh its risks, the U.S. FDA may require the drug's manufacturer to develop a Risk Evaluation and Mitigation Strategy (REMS). However, it is difficult to manage some types of risk only by labeling and REMS. Because the medication use system is a complex network of stakeholders, including patients, physicians, pharmacists, nurses and others, targeted outreach to these groups can promote the safe use of medicines in a way that goes beyond an individual drug. To address this need, the U.S. FDA has developed an effort called the Safe Use Initiative, which is operated by the Professional Affairs and Stakeholder Engagement (PASE) staff in the Center for Drug Evaluation and Research (CDER). As the U.S. FDA notes on its website, "The goal of the Safe Use Initiative is to reduce preventable harm by identifying specific, preventable medication risks and developing, implementing and evaluating cross-sector interventions with partners who are committed to safe medication use" (http://www.fda.gov/Drugs/DrugSafety/SafeUseInitiative/default.htm). To achieve this purpose, they interact with multiple stakeholders. They also offer funding opportunities for research related to safe use of medications. The Office of Surveillance and Epidemiology, whose main responsibilities are postmarket risk assessment and risk management, collaborates closely with PASE. I'd like to consider the possibility of further collaboration amongst stakeholders to strengthen efforts to protect Japanese patients from preventable harm.

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

Guidances to be published by CDER in 2015

Recently, Center for Drug Evaluation and Research (CDER) released a new list of 90 guidance documents it plans to publish in 2015. (Guidance Agenda: New & Revised Draft Guidances CDER is Planning to Publish During Calendar Year 2015 : http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM417290.pdf). The latest guidance agenda includes a wide variety of fields such as Advertising, Biopharmaceutics, Biosimilarity, Clinical/Medical, Clinical Pharmacology, and so on.

In clinical pharmacology area, 8 revised guidances (Clinical Lactation Trials, Content and Format of the Clinical Pharmacology Section, Exposure-Response Relationships, In vitro Drug Interactions, In vivo Drug Interactions, Pharmacokinetics (PK) in Patients with Impaired Renal Function, PK during Pregnancy and the Postpartum Period, and population PK) and 1 new guidance (Dose Selection in Drug Development) are in process to be published within 2015.

Several guidance documents are also in process in biopharmaceutics area including food effects guidance (Food effect on human PK). The food effect guidance was first published in 2002. In early February 2015, U.S. FDA, American Association of Pharmaceutical Scientists (AAPS), American College of Clinical Pharmacy (ACCP), and American Society for Clinical Pharmacology and Therapeutics (ASCPT) co-sponsored a workshop to provide a forum for open discussion on the revision of the given guidance (http://www.aaps.org/FDAfood/). The workshop focused on issues related to food effect assessment such as risk of food effects on clinical pharmacology, standardization of meal content, and study design. U.S. FDA will draft the revision of the guidance document on food effect assessment based on the input from this workshop. Such workshop co-sponsored by a regulatory agency and scientific societies appears to be a good occasion to share current scientific approaches and information among relevant stakeholders for creating and/or revising a regulatory guidance.

Creating guidelines/guidances contributing to efficient drug development is one of the important roles of regulatory authorities. PMDA has a plan to accept electronic clinical trial data from fiscal year 2016 (tentative) as well as to publish regulatory guidelines/guidances by utilizing the database created by PMDA in the future (http://www.pmda.go.jp/english/review-services/reviews/advanced-efforts/0002.html). In order to create effective guidelines/guidances, it would be very useful for PMDA in the future to enhance open discussion regarding the results of cross products analyses conducted by PMDA per se with participants from academia and industries like the workshop introduced above.

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