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PMDA Updates

July, 2014

News

1. The 50th DIA Annual Meeting (June 15 to 20)

The 50th DIA Annual Meeting was held in San Diego from June 15 to 20. From PMDA, Dr. Tatsuya Kondo, Chief Executive, and 25 staff members (including 12 presenters), participated in the meeting.

Dr. Kondo; Dr. Tetsuo Nagano, Executive Director; Mr. Hiroshi Yamamoto, former Chief Safety Officer; and Mr. Masaru Hiraiwa, Director, Office of Planning and Coordination, made presentations in the "PMDA Town Hall" and "Asia Town Hall" sessions, chaired by Dr. Nobumasa Nakashima, Director, Office of International Programs.

In addition, Dr. Kondo participated in the "New Approaches to International Collaboration between Regulators" as a panelist, together with the executives of regulatory authorities from Europe, the U.S., and Canada. Both "PMDA Town Hall" and "Asia Town Hall" sessions had approximately 80 participants, representing the high interest in the pharmaceutical regulations in Asian countries, especially regulation in Japan. There were approximately 400 visitors to the PMDA's exhibition booth, and PMDA staff members had communication with them through distributing documents such as brochures of PMDA and answering their questions.

Dr. Kondo

2. The 4th ASEAN-USP Scientific Symposium (June 16 to 17)

The 4th ASEAN-USP Scientific Symposium was held in Da Nang, Vietnam, co-hosted by the National Institute of Drug Quality Control of Vietnam, Vietnamese Pharmacopoeia Commission, and the United States Pharmacopeia (USP), from June 16 to 17. Dr. Kyoichi Tadano, Special Technical Expert, Office of Standards and Guidelines Development, PMDA, participated in the symposium as a representative of Japanese Pharmacopoeia, and made a presentation and took part in a panel discussion.

This symposium is held once a year with the support of USP, aiming to improve, widely prevail, and harmonize the quality standard of pharmaceuticals in ASEAN. This year, representatives of regulatory authorities from 7 countries and more than 150 people participated in the meeting, and had active discussions. PMDA has resolved to proactively cooperate and contribute to the activities of ASEAN countries. Participation in this symposium is a part of the international activities of "Increasing leverage of Japanese Pharmacopoeia" described in "Road map for the PMDA International Vision".

The next symposium will be held in Philippines, in 2015 around the same period as this year.

3. Pharmacopoeial Discussion Group meeting (June 25 to 26)

The meeting of Pharmacopoeial Discussion Group (PDG) was held at headquarters of USP in Rockville, from June 25 to 26, and three staff members participated in the meeting from the Office of Standards and Guidelines Development, PMDA. The PDG is a regular discussion group meeting for the international harmonization of general chapters and excipient monographs, held by the European Directorate for the Quality of Medicines and HealthCare, USP, and the Ministry of Health, Labour and Welfare (MHLW)/PMDA of Japan. In this meeting, drafts for harmonization were discussed and reached consensus, i.e. a new draft (Thermal Analysis) and a revised draft (Polyacrylamide Gel Electrophoresis) in General Chapters, and a new draft (Glucose Anhydrous/Monohydrate) and 5 corrected drafts (Hypromellose, Mannitol, etc.) in excipient monographs. At present, 29 of the 36 General Chapters and 46 of the 62 excipient monographs of the current work program for harmonization have been harmonized.

Among other topics, the three Pharmacopoeias agreed to adopt a test, "Measurements of particle size in liquid by dynamic light scattering" as a new General Tests for harmonization. PDG also agreed on promoting concrete actions to improve its work procedures and improve transparency to stakeholders. Based on this agreement, a summary of the outcome of the meeting will be made available on the web sites of the three pharmacopoeias in the near future.

The next PDG regular meeting will be held in Strasbourg, France, in November, 2014.

The news release is available at the following PDF file.
http://www.pmda.go.jp/english/pharmacopoeia/pdf/jpdata/pdg_press_release_en.pdf

Events

Conferences/Meetings PMDA hosts or participates in:

Date	Title	Location
August 2	The 1st Brazil-Japan Seminar on Pharmaceuticals and Medical Devices Regulations	Sao Paulo
August 21-22	Global Coalition for Regulatory Science Research (GCRSR)/Global Summit on Regulatory Science (GSR) 2014	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 16-18	International Medical Device Regulators Forum (IMDRF)	Washington D.C.
September 19	HBD Think Tank West	Washington D.C.
September 27 -October 1	Regulatory Affairs Professionals Society (RAPS) Annual Meeting	Austin
October 6-10	The 5th PMDA Training Seminar (Pharmaceuticals)	Tokyo
October 15-16	The 2nd Thailand-Japan Joint Symposium	Bangkok

Reports from overseas

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

A Modelling and Simulation (M&S) Working Group was established in EMA to aim for utilization of M&S in developing medicines in January, 2013 (Refer to Letters from the liaison officers of March 2013 issue) [1]. Recently, as a part of the Working Group activities, EMA announced that the workshop will be held from December 4 to 5, this year, aiming to discuss in order to reach agreements of the methodology of dose-response relationship estimation and dose range-finding, and the significance of utilization of M&S for the company, the regulator, the prescriber and the patient [2].

PMDA set up cross-sectional project working groups for standards development to systematize the result of research such as review information and regulatory science and to develop standards and guidelines. Within these working groups, PMDA has also been studying the utilization of M&S under the project on innovative statistical strategies for new drug development [3].

With the advent of greater utilization of M&S, more efficient drug development by applicants is expected as well as the establishment of optimized utilization of M&S in review, and improvement of prediction of efficacy and safety in post-marketing phase.

For the details of the M&S Working Group, the workshop, and the project on innovative statistical strategies for new drug development, see following web sites.

1) M&S Working Group
http://www.ema.europa.eu/ema/index.jsp?curl=pages/contacts/CHMP/people_listing_000122.jsp&mid=WC0b01ac058063f485
2) Workshop on dose finding at the EMA
http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/06/news_detail_002128.jsp&mid=WC0b01ac058004d5c1
3) Project on innovative statistical strategies for new drug development
http://www.pmda.go.jp/kijunsakusei/tokei.html (Japanese text only)

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

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"Q&A for conducting First in Man trial of nanomedicine"

Nanotechnology has been expected to be an important technique for the area of medicines and medical devices, and research regarding nano drug delivery system and nano medical devices are already ongoing. Swissmedic staff have been involved in domestic and international working groups on nanotechnology since 2006, and established an expert working group in the agency in 2009.

Swissmedic published "Information Sheet: First-in-Man (FIM) Clinical Trials with Nanomedicines" [1] on June 19, 2014. In the Q&A of this Information Sheet, Swissmedic answers 10 questions such as "Which authorities need to provide approval to conduct a FIM trial in Switzerland?", "What are the requirements within Switzerland while proposing and conducting FIM trials (for example, trial registration)?" The requirements for FIM trial with Nanomedicine in Switzerland are basically the same as other medicines. Therefore, vital points for review is assuring safety and quality of the products.

For news related to the nanotechnology in Japan, MHLW/EMA published "Joint MHLW/EMA reflection paper on the development of block copolymer micelle medicinal products" [2] last January. I would like to keep paying attention to the trends of nanotechnology products in the regulatory authorities in the world.

Please refer to the following web sites for the details of the Information Sheet and the Joint MHLW/EMA reflection paper.

1) Information Sheet: First-in-Man Clinical Trials with Nanomedicines
https://www.swissmedic.ch/aktuell/00673/00688/01453/index.html?lang=en&download=NHzLpZeg7t,lnp6I0NTU042l2Z6ln1ad1IZn4Z2qZpnO2Yuq2Z6gpJCDdoN3f2ym162epYbg2c_JjKbNoKSn6A--

2) Joint MHLW/EMA reflection paper.
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/01/WC500159411.pdf

PFSB/ELD Notification No.0110-1 of the Evaluation and Licensing Division, PFSB, MHLW, dated January 10, 2014
http://www.pmda.go.jp/kijunsakusei/file/tsuchi/20140110-1.pdf

Dr. Jun Kitahara
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Health Canada is planning the use of review reports written by the foreign regulatory agencies. As the background, the international harmonization of regulatory requirements has been progressing, and Health Canada is aiming for further improvement of qualities and acceleration of decision making in its review and evaluation services. The project covers reviews of approval application of new drugs, generic drugs and medical devices (Class III and IV), and also the evaluation of Periodic Safety Update Report (PSUR) and Periodic Benefit-Risk Evaluation Report (PBRER) in the post-marketing section. According to the Draft Guidance Document released in 2012, when a foreign review report is submitted from an applicant, Health Canada can select the usage from the four types of methods for the use of foreign review reports as follows.

1. The Canadian regulatory decision is based on a critical assessment of the foreign review.
2. The Canadian review is based on a critical assessment of the foreign review, referring to the data filed in Canada as necessary. The Canadian regulatory decision is based on the Canadian reviews.
3. The Canadian review is based on a critical assessment of the Canadian data package, with the foreign review as an added reference. The Canadian regulatory decision is based on the Canadian review.
4. The Canadian review is based on a critical assessment of the Canadian data package. The foreign review is not referred.

Although PMDA's review reports have not yet been listed as usable foreign reviews in the Draft Guidance Document, they will be usable when submitted with the English translations of the reports.

I completed the stay here for the initially scheduled three months and will return to Japan. I really appreciate the colleagues in Health Canada for sharing the valuable information.

Please refer to the following web site for the Draft Guidance Document.
The Use of Foreign Reviews by Health Canada.
http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/for_rev-exam_etr/draft_foreign_rev_ebauche_exam_etra-eng.php

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Currently, the Center for Drug Evaluation and Research (CDER) is developing a program to collect and analyze standardized quality manufacturing metrics (quality metrics) from pharmaceutical firms. Under recent U.S. legislation, the Food and Drug Administration Safety and Innovation Act (FDASIA), the FDA is authorized to collect records from manufacturers in advance of, or in lieu of, facility inspections. These data can provide measures of product and facility quality. This will improve FDA's Good Manufacturing Practice (GMP) surveillance program by providing information about which facilities and processes within facilities are at higher risk. The adoption of a quality metrics system should encourage a corporate culture that promotes quality manufacturing. It is anticipated that the use of quality metrics can have a great impact on patients by preventing product shortage and recalls.

During my dispatch period, I had an opportunity to participate with the Quality Metrics working group. This working group discussed what information (metrics) should be obtained from drug manufactures. Based on a recent workshop convened by the Brookings Institution, four consensus metrics have been proposed by FDA and other stakeholders: Lot Acceptance Rate, Product Quality Complain Rate, Confirmed Out-of-Specification Rate, and Product Recall Rate. Also, multiple meetings with Marketing Authorization Holders (MAHs) have been held to understand what information is currently collected and what data would be needed to evaluate the risks of products and manufacturing facilities more appropriately. In addition, the mechanism for collecting the quality metrics and the plan for managing and evaluating data were also discussed in the working group.

In addition, another workgroup is considering new protocols for pre-approval and periodic (surveillance) GMP inspection. This workgroup seeks to prepare criteria to enable inspectional observations at manufacturing sites to be expressed in a semi-quantitative manner.

CDER plans to establish a new office called the Office of Pharmaceutical Quality (OPQ) to integrate the evaluation of product quality. Currently, oversight of product quality is distributed through several offices in CDER and Office of Regulatory Affairs (ORA, the FDA's inspectorate). Within the OPQ, there will be a surveillance function that will be charged with the ongoing monitoring of the quality of regulated products. As I already wrote in PMDA Updates of June, I believe the quality of products can be managed more robustly if we can develop continuous monitoring methods and survey manufacturing sites more appropriately by obtaining deviation reports like Field Alert Reports and periodic quality metrics from manufactures, as mentioned above.

Though a 90-day dispatch is a short period, I succeeded at having an extremely meaningful experience through workgroup meetings, one-on-one meetings, briefings, training, and observing an inspection. I was able to share PMDA information related to GMP inspections and inspector training with my colleagues in CDER, Center for Biologics Evaluation and Research, and ORA. When I return to PMDA, I will do my best to contribute to PMDA's future advancement and make best use of the information and experiences obtained during my dispatch to FDA/CDER.

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