Snowmen

PMDA Updates

January, 2017

News

1. Chief Executive Dr. Kondo's New Year Message for 2017

I would like to wish you all a Happy New Year.

I would also like to share some thoughts for the New Year with you. PMDA has grown steadily since its establishment in 2004, and is now comparable to its European and American counterparts. I believe that this accomplishment is the direct result of the hard work and passion of each and every PMDA staff member, and we must strive to not only maintain, but continue to improve our efforts.

What will happen in 2017 and beyond? Looking at the rest of the world, various factors arising during the previous year are creating a global atmosphere of caution and uncertainty. 2017 may also prove to be a year of continuing discord. It will be important for us to carefully consider the balance of domestic and international activities.

The transition to a new presidency in the United States has already had an impact on many people, and will continue to bring changes around the world. This will also be true for the U.S. FDA and the EMA. In this circumstance as well, PMDA's working relationships with European and American regulatory agencies continue to be firmly rooted in the principles of regulatory science. In addition, we must continue to muster our existing relationships and strive to create new, sound collaborations with regulatory agencies in emerging nations in continental Asia and beyond, through our activities such as the "Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs", as well as the many ways that we share our accumulated knowledge and experience to continuously make meaningful contributions to the health and well-being of people around the world. In other words, we can navigate any uncertainty we encounter in the future by seeing our existing and future initiatives through.

The pharmaceutical and medical device industry are entities that "require direction and wisdom in order to grow strong". This wisdom comes from our national character. With effective guidance and wisdom, this industry can grow to bring health as well as enormous wealth to people. We must carry out our operations without ever forgetting the critical role that PMDA plays in its unique position at the center of an industry built on three pillars: wisdom, health, and wealth.

Now is the time for Japan to advance not one, but two steps ahead of the rest of the world. I pledge to use my experience in clinical practice as a neurosurgeon to lead PMDA's efforts to promote "Rational Medicine" initiative, under which the paternalistic, authoritarian approach to medicine will be cast off, and in its place we will create a new and improved paradigm founded on rational judgment.

Once again, I wish you all health, prosperity, and happiness in the New Year.

2. PMDA-ATC GMP Inspection Seminar 2016 (December 5-9)

From December 5 to 9, PMDA held a seminar entitled "PMDA-ATC GMP Inspection Seminar 2016" in Toyama prefecture, which was facilitated with the support of Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S), and by PMDA Hokuriku Branch.

This seminar was the first PMDA-ATC seminar specifically focusing on GMP, designed for GMP inspectors from regulatory authorities overseas, and participated by 19 regulators from Brazil, Hong Kong, Kazakhstan, Latvia, Malaysia, Mexico, Myanmar, Philippines, Singapore, Slovenia, Taiwan and Thailand.

In the seminar, lectures were delivered by PMDA staff and PIC/S instructors on the topics including Risk-based Inspection and Data Integrity. The seminar also included group discussions and a mock inspection with the cooperation of an actual manufacturing site recommended by Japan Pharmaceutical Manufacturers Association (JPMA), and the participants had active discussions throughout the seminar.

Please refer to the following web site for the details of PMDA-ATC GMP Inspection Seminar 2016.
http://www.pmda.go.jp/english/symposia/0093.html

3. The 4th Joint Conference of Taiwan and Japan on Medical Products Regulation (December 7-8)

On December 7-8, the 4th Joint Conference of Taiwan and Japan on Medical Products Regulation was held in Tokyo, co-hosted by Taipei Economic and Cultural Representative Office in Japan and Interchange Association, supported by PMDA, Japan Pharmaceutical Manufacturers Association (JPMA), and others. Japanese participants included: Dr. Tatsuya Kondo, Chief Executive, Mr. Haruo Akagawa, Senior Executive Director, Dr. Toshiyoshi Tominaga, Associate Executive Director (for International Programs), Mr. Naoyuki Yasuda, Office Director, Office of International Programs, and 16 staff members from PMDA; Mr. Kazuhiko Mori, Councilor, and 9 officers from Ministry of Health, Labour and Welfare (MHLW). Taiwanese participants included: Dr. Shiow-Ing Wu, Deputy Director-General and 11 staff members from Taiwan Food and Drug Administration (TFDA), Dr. Churn-Shiouh Gau, Executive Director and 4 staff members from Center for Drug Evaluation (CDE), and 15 people from other relevant organizations.

In this conference, progress updates were presented on the activities of each of the 6 working groups (of New Drugs, GCP, Generic Drugs, OTC Drugs, Product Registration(medical device), QMS/QSD) , which Japan and Taiwan had been working on in collaboration with each other.

This conference covered a range of topics of strong interest including "quality control and safety measures" (in the pharmaceutical sessions) and "medical device software" and "in vitro companion diagnostic devices" (in the medical devices sessions), and active participation was achieved during lecture and discussion sessions. The next conference is scheduled to be held in Taiwan in the fall of 2017.

Group phot of participants.
From the 4th left in the front row, Dr. Kondo, Dr. Wu. and Mr. Mori.
Mr. Yasuda (4th left), Dr. Tominaga (7th left) and
Dr. Nakashima (8th left) are in the back row.

MHLW's press release is available at the following link.
http://www.mhlw.go.jp/stf/houdou/0000147140.html
The program and presentations are available at the following link.
http://www.pmda.go.jp/english/symposia/0097.html

4. International Medical Device Regulators Forum (IMDRF) Adverse Event Terminology Working Group Meeting (December 13-16)

From December 13 to 16, a meeting of IMDRF Adverse Event Terminology Working Group was held at PMDA and a total of 16 members from regulatory authorities from the US, Canada, Australia, EU, Kazakhstan and Japan (PMDA and MHLW) participated. This working group was established in March 2015, and since then, under the chairmanship of PMDA, it has been working on the development of the adverse event terminologies for medical devices, which is intended to be utilized in the medical device adverse event reporting to be submitted to the regulatory authorities. In this meeting, Medical Device terms/codes, Cause Investigation terms/codes, and maintenance methodology for IMDRF AE terminologies were mainly discussed. This was the third face-to-face meeting of the group.

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
Mulpleta	lusutrombopag	December 28
Olanedine	olanexidine gluconate	January 6
Cerdelga	eliglustat tartrate	January 6
Xiaflex Inj.	collagenase (Clostridium Histolyticum)	January 16

Regenerative Medicines (cellular and tissue-based products)

http://www.pmda.go.jp/english/review-services/reviews/approved-information/0004.html

Brand Name	Generic Name	Posting date
Temcell	human (allogeneic) bone marrow-derived mesenchymal stem cells	December 27

Safety Information

Pharmaceuticals Revisions of PRECAUTIONS, January 10, 2017

- Iguratimod
- Lenalidomide hydrate
- Interferon beta-1b (genetical recombination)

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

Risk Information which some safety measures might be taken (January 20, 2017)

- Hydroxyzine Hydrochloride (Injection)
- Hydroxyzine Hydrochloride (Tablets)
- Hydroxyzine Pamoate (Powders)
- Hydroxyzine Pamoate (Capsules/Dry Syrup)

- Hydroxyzine Pamoate (Syrup)
- Hydroxyzine Pamoate (Tablets)
- Vemurafenib

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
February 2-3	The 4th Thailand-Japan Symposium	Bangkok
February 6-9	PMDA-ATC Pharmacovigilance Seminar 2017	Tokyo
February 9-10	PIC/S (Pharmaceutical Inspection Cooperation Scheme)	Geneva
February 19-21	Cardiovascular Research Technologies (CRT) 2017	Washington, D.C.
February 19-21	APEC RHSC (Regulatory Harmonization Steering Committee)	Nha Trang
February 22	APEC RHSC LSIF (Life Science Innovation Forum)	Nha Trang

Reports from overseas

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

Activation of discussions for patient registries

Discussions on patient registries are ongoing in EU, not just in Japan where, for example, consideration of registries related to regenerative medicine products and the Clinical Innovation Network (CIN, which aims at utilization of registry information at product development stage) are promoted.

A workshop on patient registries was held at EMA on 28 October 2016. The workshop had a variety of stakeholders, including industry, academia, health technology assessment (HTA) bodies, and regulators, with discussion of the current situation, challenges and future of patient registries.

In EU, as each HTA body may request collection of additional data after a drug approval, one of unique and big challenges is how appropriate registries and data to satisfy requirements from both regulators and HTA bodies are established.

On the other hand, other challenges raised included sustainability, including cost burden, suitable quality of registry, access to registry by a company, ownership of registered data. Since the challenges are same as those considered in Japan, I believe that international opinion exchanges and experience sharing will become important.

At the workshop, for the purpose of ensuring quality of registry, the idea that regulators conduct inspections, certifications or validity studies was proposed. It is interesting that regulators are expected to play a new role for patient registries.

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

Analytical Procedure Lifecycle

The United States Pharmacopeial Convention (USP) has published a Stimuli Article for a new proposed USP general chapter entitled "The Analytical Procedure Lifecycle <1220>" in PF 43(1), which is the current issue1). Pharmacopeial Forum (PF)2) is an online publication to seek public comments on new and proposed USP standards. The current concepts of general chapters address a portion of the analytical procedure lifecycle. On the other hand, the purpose of this proposed new chapter is to more fully address the entire procedure lifecycle and define concepts that may be useful. It is expected that the adoption of the concept of Quality by Design (QbD)3) as described in The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Q8, Q9, Q10, and Q11 and control of analytical methods by using the Analytical Target Profile (ATP), which states performance requirements for analytical procedure, will lead to improved understanding of the procedures and control of sources of variability in the procedures. I believe that this concept of quality assurance is important for continuous improvement of analytical procedures and application of emerging technologies, which have uncertainty, in pharmaceutical production and analysis.

1) Pharmacopeial Forum43 (1)
   http://www.usp.org/usp-nf/pharmacopeial-forum/pf-table-contents
   Stimuli to the Revision Process: Proposed New USP General Chapter: The Analytical Procedure Lifecycle <1220>
   http://www.usppf.com/pf/pub/data/v431/GEN_STIMULI_431_s201784.html#GEN_STIMULI_431_s201784 * A one-time registration is required to access PF.
2) http://www.usp.org/usp-nf/pharmacopeial-forum
3) 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

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

Postmarketing Reporting of Adverse Drug experiences in the U.S.

The Code of Federal Regulations defines the rules regarding reporting to U.S.FDA adverse drug events occurring in the course of the use of a drug product in the postmarketing period[1)]. Marketing authorization holders (MAHs) must submit to U.S.FDA all adverse drug experience information regardless of its seriousness; on the other hand, health care professionals and patients may submit reports voluntarily. To submit such information, three MedWatch Forms are provided; 1) Form FDA 3500 for use by healthcare professionals, consumers and patients, 2) Form FDA 3500B, a consumer-friendly version, and 3) Form FDA 3500A for use by manufacturers. The Form 3500 and 3500B are sent to U.S.FDA by postal mail or FAX. Also, healthcare professionals, consumers and patients are able to report adverse drug experiences via the U.S.FDA's website[2)]. Since 2000, U.S. FDA has accepted MAH's electronic submissions of adverse drug experience reports prepared in accordance with ICH E2B and from June 2015, U.S.FDA is requiring that MAHs electronically submit all adverse drug experience reports. All of the reported information is stored in the FDA Adverse Event Reporting System (FAERS) and utilized for the pharmacovigilance screening and analysis. About 95% of adverse drug events are reported by MAHs. While the proportion of direct reports from healthcare professionals is small in the U.S., the absolute number is increasing. Healthcare professionals' reports are considered quite important for pharmacovigilance analysis.

1) Code of Federal Regulations Title 21 Sec. 314.80
2) https://www.accessdata.fda.gov/scripts/medwatch/index.cfm?action=reporting.home

Mr. Takashi Misu
PMDA's Officer at CDER, U.S. FDA in the U.S.A.

