*Grus japonensis*

# PMDA Updates

December, 2017

# News

## 1. 2017 APEC Good Registration Management Regulatory Science Center of Excellence Workshop

From Octover 31 to November 2, PMDA cohosted 2017 APEC Good Registration Management Regulatory Science Center of Excellence Workshop with Regulatory Affairs Professionals Society (RAPS) Taiwan Chapter and Taiwan Food and Drug Administration in Taipei. The objective of Good Registration Management (GRM) is for regulatory agencies and the industry to cooperatively promote Good Review Practice (GRevP) and Good Submission Practice (GSubP) to foster mutual communication and to contribute to effective product development and product review in APEC member economies. The workshop was designed for reviewers from regulatory agencies as well as applicants from the industry who make regulatory submissions. The participants included 30 officials from regulatory agencies from Indonesia, Malaysia, Papua New Guinea, Philippines, Singapore, Taiwan, Thailand and Vietnam. In the workshop, lectures and group discussions were conducted on topics such as regulator/ applicant communication, review management and points to be considered for a good review. Also, in the applicant-specific sessions, lectures by the representative of Japan Pharmaceutical Manufacturing Association and group discussions were held, and the attendees participated actively in the discussions throughout the workshop.

## 2. PMDA-ATC Medical Devices Seminar 2017

From November 6 to 10, PMDA held PMDA-ATC Medical Devices Seminar 2017. This seminar was designed for medical devices and in vitro diagnostics reviewers from overseas regulatory authorities, and participated by a total of 30 regulators from 12 regulatory agencies (i.e. Azerbaijan, Bangladesh, India, Indonesia, Malaysia, Philippines, Singapore, Sri Lanka, Taiwan, Tanzania, Thailand and Turkey). In the seminar, lectures were delivered by PMDA staff on the topics including medical device and in vitro diagnostic product reviews, consultations, Good Clinical Practice (GCP) and Good Laboratory Practice (GLP) inspections, Quality Management System (QMS) inspections, post-marketing safety measures, registration system, standards for medical device (utilization of international standards, etc.) and collaboration with U.S. Food and Drug Administration (FDA). Marketing approval holder's training facility tour helped participants to understand the importance of user's training program which aims realizing a proper use, in order to maintain safety of medical devices. And, PMDA staff and participants exchanged knowledge and culture of regulatory activities through the introduction of each participant country's regulatory authority in the seminar. The participants and PMDA staff actively engaged in discussions throughout the seminar.

Front row from left to right, Dr. Kensuke Ishii, International Senior Training Coordinator/Office Director, Office of Medical Devices II (3rd ), Mr. Haruo Akagawa, Director Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (4th), Dr. Junko Sato, Office Director, Office of International Cooperation (5th)

On the final day of the seminar, the course completion certificates were handed to each participant by Dr. Tatsuya Kondo, Chief Executive.

## 3. ICH Meeting in Geneva

The 5th International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) met in Geneva, Switzerland from November 11 to 16. The attendees included 39 staff in total from

PMDA, including Dr. Toshiyoshi Tominaga, Associate Executive Director for International Programs; and Mr. Naoyuki Yasuda, Office Director, Office of International Programs,

Group photo of participants

as well as staff from Ministry of Health, Labour and Welfare (MHLW) including Dr. Nobumasa Nakashima, Office Director, Office of International Regulatory Affairs. At the Assembly, Ms. Lenita Lindstrom (EC) and Dr. Tominaga were unanimously reelected as Assembly Chair and Assembly Vice Chair, respectively, for a two-year term. Also at the Management Committee, Dr. Theresa Mullinun (USFDA) and Dr. Tominaga were unanimously reelected as Management Committee Chair and Management Committee Vice Chair, respectively, for a one-year term. The ICH Assembly approved the Health Sciences Authority (HSA) of Singapore, a former Observer, as a new Member,

and the Colombian regulatory agency INVIMA and Bill & Melinda Gates Foundation as new Observers, bringing the total to 15 Members and 24 Observers. The Working Group meetings achieved many outcomes including E17 (Multi-Regional Clinical Trials), S3A Q&As (microsampling), M8 (eCTD) eCTD v4.0 Q&As, E2B (data elements and message specification for ICSR) EDQM terms user guide, which reached Step 4 of the ICH process, as well as Q12 (Pharmaceutical Product Lifecycle Management), which reached Step 2b of the ICH process.

The next ICH meeting will be held on June 2-7, 2018 in Kobe, Japan.

## 4. The 5th Joint Conference of Taiwan and Japan on Medical Products Regulation and related meetings

On December 1, the 5th Joint Conference of Taiwan and Japan on Medical Products Regulation was held in Taiwan, hosted by the Japan-Taiwan Exchange Association and the Taiwan-Japan Relations Association. This conference was attended by more than 300 people from regulatory agencies and industry from Taiwan and Japan. Japanese participants included Mr. Seiichi Inoue, Executive Director; Mr. Naoyuki Yasuda, Office Director, Office of International Programs; and 8 staff from PMDA as well as Mr. Yoshihiko Sano, Deputy Director, Office of International Regulatory Affairs; and 3 officers from Ministry of Health, Labour and Welfare (MHLW). Taiwanese participants included Dr. Shou-Mei Wu, Director-General with about 40 staff from Taiwan Food and Drug Administration (TFDA), as well as Dr. Churn-Shiouh Gau, Executive Director with about 40 staff from Center for Drug Evaluation (CDE). In this conference, regulatory updates in Japan and Taiwan were provided by PMDA's Mr. Inoue and TFDA's Dr. Wu, and also progress updates were presented on the activities of each of the 6 working groups (of new drugs, generic drugs, OTC drugs, information sharing, product registration (medical device), QMS/QSD), which Japan and Taiwan had been working on in collaboration with each other. The conference covered a range of topics including multi-regional clinical trials, latest approaches to quality assurance, big data utilization (in the pharmaceutical session) and post-market evaluation of efficacy and safety, and trends on regulatory convergence (in the medical devices session), which were presented with active question and answer sessions.


Group photo of participants

The next conference is scheduled to be held in Japan in the first half of October, 2018.

MHLW's press release is available at the following link.

http://www.mhlw.go.jp/stf/houdou/0000187640.html

The program and presentations are available at the following link.

http://www.pmda.go.jp/english/symposia/0120.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 |
|---|---|---|
| Cyramza<br>[Partial Change Approval] | ramucirumab<br>(genetical recombination) | November 16 |
| Idelvion | albutrepenonacog alfa<br>(genetical recombination) | November 30 |
| Nucala | mepolizumab<br>(genetical recombination) | December 4 |
| Livalo<br>[Partial Change Approval] | pitavastatin calcium hydrate | December 6 |

# Safety Information

## Pharmaceuticals Revisions of PRECAUTIONS, November 28, 2017

- Clozapine
- Gadoxetate sodium
- Gadoteridol
- Meglumine gadoterate
- Gadobutrol
- Gadodiamide hydrate
- Meglumine gadopentetate

http://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0005.html

## Medical Devices Revisions of PRECAUTIONS

Revision of Precautions in the Package Inserts of Medical Devices Containing Chlorhexidine Gluconate or Chlorhexidine Hydrochloride
(Posted on November 30, 2017, Originally Posted in Japanese on November 2, 2017)

http://www.pmda.go.jp/english/safety/info-services/devices/0002.html

## Risk Information which some safety measures might be taken (December 8, 2017)

- Edoxaban tosilate hydrate
- Aripiprazole
- Aripiprazole hydrate
- Teriparatide acetate
- Teriparatide (genetical recombination)
- Ipilimumab (genetical recombination)
- Lenvatinib mesilate

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

## PMDA Medical Safety Information No. 52 (December 20, 2017)

Precautions When Using an Open Ventricular Drainage Circuit

http://www.pmda.go.jp/english/safety/info-services/safety-information/0001.html

# Events

## Conferences/Meetings PMDA hosts or participates in:

| Date | Title | Location |
|---|---|---|
| January 15-18 | PMDA-ATC Multi-Regional Clinical Trials Seminar 2018 | Tokyo |
| February 5-8 | PMDA-ATC Pharmacovigilance Seminar 2018 | Tokyo |

# Reports from overseas

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

## Participation in TOPRA Annual Symposium

TOPRA works for increased professionality of regulatory affairs for medicines and medical devices in mainly EU by, for example, hosting workshops and providing training, and many people, including industries, academia, patient groups and regulators, join its annual symposium.

The annual symposium was held on 2 – 4 October 2017 and covered highly interesting topics in EU (and globally) such as utilization of real-world evidences, patients' involvement in regulatory processes, regulations on combination products, including companion diagnostics, and Brexit. Actually it was a very informative symposium.

There was also a session about global regulatory collaborations, where I had an opportunity to present not only collaborative activities between Japan and EU but also those with other regulators in mainly Asia. As many participants showed interest in what Japanese regulatory authorities are doing, I recognized the importance of information dissemination through such an international conference.

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

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## Workshop on ICH Q3D Elemental Impurities Co-sponsored by PQRI and USP

PQRI/USP Workshop on ICH Q3D Elemental Impurities Requirements was hosted by Product Quality Research Institute (PQRI), which is a non-profit consortium organizations serving as a forum for industry, government and academia to work cooperatively to conduct pharmaceutical product quality research and to support development of public guidance and standards[1)], and United States Pharmacopeial Convention (USP) on November 2-3[2)]. ICH Q3D Guideline for Elemental Impurities shows processes which control elemental impurities in drug products using the principles of risk management considering their toxicity, likelihood of occurrence in drug products, and potential source as well as administration of drug products[3)]. In this workshop, topics focused on, but not limited to the regulator experience with implementation of new drug applications in the U.S., EU, Canada and Japan, as well as recent compendial activities related to elemental impurities, pharmaceutical industry's challenges, and initiatives in implementing the guideline. Also, the attendees discussed the relationship between this guideline and the existing standards for elemental impurities, the challenges regarding availability of data which is required for implementing the guideline, the possibility of sharing the data among companies, and the acceptable risk assessment strategies.

The Japanese Pharmacopoeia (JP) has moved the discussion for implementation of the guideline forward with accordance to the specific work plan which is described in the Basic Principles for Preparation of JP 18th

Edition[4]. Also, the chapter on analytical procedures for elemental impurities has been discussed for harmonization among the Pharmacopoeial Discussion Group (PDG) pharmacopoeias[5].

This guideline requires establishing limits and control methods based on risk management considering various elements. Therefore, it is predicted that challenges can arise out of elements such as (1) availability of data required for risk assessment, (2) resources for risk management for many drug products, (3) adjustment of relationship between the new guideline and the existing related standards for controlling same elements, when the pharmacopoeia implements the standards stated in the guideline. I will continue to pay attention to the international trends related with this guideline.

1) Product Quality Research Institute (PQRI)
http://pqri.org/wp-content/uploads/2017/06/PQRI-Overview-June-2017.pdf
2) PQRI/USP Workshop on ICH Q3D Elemental Impurities Requirements
http://pqri.org/pqriusp3rdeiworkshop/
3) ICH Harmonised Guideline: Guideline for Elemental Impurities Q3D
http://www.pmda.go.jp/files/000197758.pdf
4) Basic Principles for Preparation of JP18: 2-6. Development of Standards for Control of Impurities in Response to International Trends
http://www.pmda.go.jp/files/000220938.pdf
5) PDG September 2017 Rockville Meeting Highlights: 3 PDG Work Programme
http://www.pmda.go.jp/files/000220887.pdf

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

 