# PMDA Updates

May 2023

# News

## 1. ICH Management Committee Interim Meeting

The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) held a Management Committee Interim Meeting on March 27 and 28, 2023, in Lausanne, Switzerland. Dr. NAKASHIMA Nobumasa (Associate Executive Director for International Programs, PMDA) and Mr. YASUDA Naoyuki (Office Director, Office of International Regulatory Affairs from the Ministry of Health, Labour, and Welfare (MHLW)) attended this meeting with other officers from the MHLW and PMDA.

The purpose of this meeting was to efficiently implement the process of adopting new topic proposals by the ICH Assembly, which will be held in Vancouver, Canada in June 2023. Seizing this opportunity, we also discussed the efficiency of ICH operations and training. Active discussions were held for each issue, thereby significantly contributing to the efficiency of the discussion in the ICH Assembly/Management Committee in June 2023, and it was a very meaningful meeting.

The next in-person ICH meeting is scheduled for June 10 to 13, 2023, in Vancouver, Canada.

## 2. The 23rd IMDRF Management Committee Meeting

The 23rd International Medical Device Regulators Forum (IMDRF) Management Committee (MC) Meetings were held between March 27 and March 31, 2023. Mr. TAKAHATA Masahiro from the Ministry of Health, Labour and Welfare MHLW), Dr. KUSAKABE Tetsuya, an International Coordination Officer, and four staff members from the PMDA attended them in person. The meetings, chaired by the EU, took place in Brussels, Belgium.

On March 27, a joint workshop was held between the IMDRF and industry groups, The Global Diagnostic Imaging, Healthcare IT & Radiation Therapy Trade Association (DITTA), and Global Medical Technology Alliance (GMTA). In this workshop, under the topic of "The life cycle of medical devices: the importance of post-market-related activities," regulators and industry groups shared their experiences and challenges for the international regulatory harmonization on post marketing vigilance, the utilization of real-world evidence and real-world data (RWE/RWD), and post-market improvement for software including artificial intelligence (AI).

The IMDRF Stakeholder Forum attended by regulators, industry stakeholders, and international organizations was held on March 28. The presentations on the latest information from each IMDRF country and region, progress reports of each Working Group (WG), and the interests and concerns from industry groups were held at this forum. The MHLW reported on marketing approval in emergencies, the need for medical device software regulation, and actions and fundamental reforms toward them from a regulatory perspective.

The joint workshop and IMDRF Stakeholder Forum were streamed online, and around 300 people participated in person, while over 200 individuals joined virtually and exchanged their views actively.

On March 29, an open meeting was held in the morning. Each regulatory member (invited observers) and the members of the Regional Harmonization Initiative (RHI) presented their activities and exchanged views on how industry groups got involved in each IMDRF activity.

In the afternoon of the same day, the Regulatory Authority Council (RAC) meeting of the Medical Device Single Audit Program (MDSAP) was held. Japan led the discussions on confirming the MDSAP utilization status in the MDSAP member countries and problem-solving in connection to the governance of the MDSAP as a chair.

On March 30 and 31, a closed meeting was held for regulatory members and official observers to discuss the draft guidance documents. At the meetings, two guidance documents by Cybersecurity WG, Principles and Practices for the Cybersecurity of Legacy Medical Devices (N70), and Principles and Practices for Software Bill of Materials for Medical Device Cybersecurity (N73), and two guidance documents by Personalized Medical Devices WG, Personalized Medical Devices – Regulatory Pathways (N58), and Personalized Medical Devices – Production Verification and Validation (N74) were approved as the final documents. The public consultation periods for Non-In Vitro Diagnostic Device Regulatory Submission Table of Contents (nIVD ToC) (N9) and In Vitro Diagnostic Device Regulatory Submission Table of Contents (IVD ToC) (N13) have been extended by 45 days. In addition, a

minor revision on Post Market Surveillance National Competent Authority Report (NCAR) Exchange Criteria and Report Form (N14) proposed by the NCAR Secretariat, which PMDA had been leading since January 2023, was approved by the MC.

The applications of Swissmedic, Switzerland as an IMDRF Official Observer, and South African Health Products Regulatory Authority (SAHPRA), South Africa as IMDRF Affiliate Member, were approved. Finally, the MC agreed to the rotation of the IMDRF secretariat and Chair to the US FDA in 2024, followed by Japan in 2025.

The next IMDRF MC Meeting, chaired by the EU, Europe, will be held in Berlin, Germany, from September 25 to 29, 2023. The detailed outcomes of the 23rd IMDRF MC Meeting are available on the following website:
https://www.imdrf.org/documents/imdrf-23rd-mc-meeting-brussels-march-2023-outcome-statement

## 3. Regulatory Harmonization Steering Committee (RHSC) Meeting

The Regulatory Harmonization Steering Committee (RHSC) held a face-to-face meeting for the first time in four years in Oakland, US, from April 13 to 14. From the PMDA, Dr. NAKASHIMA Nobumasa (Associate Executive Director for International Programs) and Mr. KOGA Daisuke (Division Director, Planning and Management Division, Office of International Programs) participated in the meeting with a staff member of the Ministry of Health, Labour and Welfare (MHLW) and experts from other regulatory agencies in APEC economies; representatives from industry associations in the area of pharmaceuticals, biopharmaceuticals, and medical devices, including the Japan Pharmaceutical Manufacturers Association (JPMA) and the Japan Medical Imaging and Radiological Systems Industries Association (JIRA); and experts from academia.

The RHSC was inaugurated in June 2009 to promote "a strategic approach to regulatory harmonization by undertaking activities of the greatest value to regulatory authorities and regulated industries," and it is co-chaired by Dr. NAKASHIMA, along with Dr. Michelle Limoli from the US FDA. Seven Priority Work Areas (PWAs) were identified by the RHSC as key areas for achieving regulatory convergence for pharmaceutical and medical device products, and Training Centers of Excellence for Regulatory Science (CoEs) were commissioned by the RHSC to meet the training needs of member economies in the PWAs. The PMDA is endorsed as a CoE on MRCT/GCP Inspection PWA, Pharmacovigilance PWA, and Medical Device PWA.

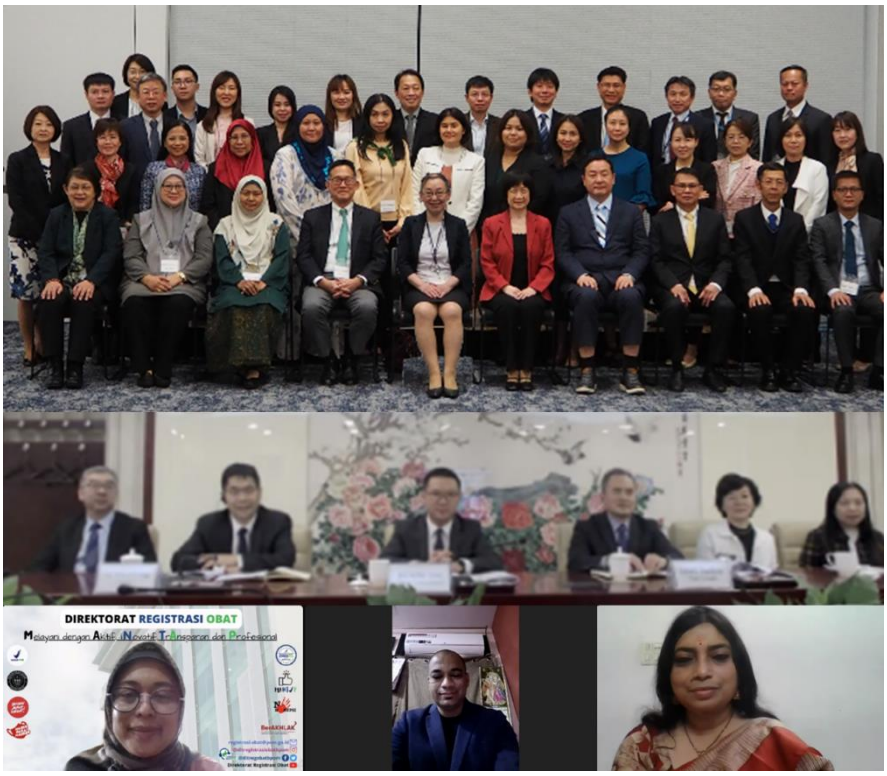
In the meeting, Mr. KOGA reported on the activities of the PMDA-ATC, including seminars held since the last RHSC meeting in October 2021, and planned this year for CoE workshops in the areas of MRCT/GCP Inspection PWA, Pharmacovigilance PWA, and Medical Device PWA, as well as the activities of Medical Device PWA as representatives of the champion economy of the PWA.

The next meeting is planned to be held this fall in the US.

## 4. The 5th Asian Network Meeting and Bilateral Meeting with Asian Countries

The Ministry of Health, Labour and Welfare (MHLW) and PMDA held the annual Asian Network Meeting on April 19, 2023. The fifth meeting was held in a hybrid manner, combining in-person and virtual participation. The meeting comprised top-level regulatory authorities. The MHLW, PMDA, and the regulatory authorities of China, India, and Singapore hosted the meeting and welcomed other Asian member countries, such as Indonesia, Korea, Malaysia, the Philippines, Thailand, and Vietnam. The participants agreed to facilitate cooperation on actions against future pandemics, build efficient regulatory systems in the Asian region from a high-level perspective, and hold another meeting next year.

In conjunction with the Asian Network Meeting, the MHLW and PMDA held bilateral meetings on April 17 and 20, with some participating countries. Opportunities for future collaborations to improve medical care in Asian countries were discussed in these bilateral meetings.




Group photo of the participants of the 5th Asian Network Meeting

# *English Translations of Review Reports*

*The following links provide the latest information on the English versions of the review reports on the PMDA website.*

## Pharmaceuticals

https://www.pmda.go.jp/english/review-services/reviews/approved-information/drugs/0001.html

| Brand Name | Non-Proprietary Name | Posting Date |
|---|---|---|
| Samtasu [Initial Approval] | tolvaptan sodium phosphate | April 14, 2023 |

## Medical Devices

https://www.pmda.go.jp/english/review-services/reviews/approved-information/devices/0003.html

| Brand Name | Term Name | Posting Date |
|---|---|---|
| Harmony Transcatheter Pulmonary Valve Replacement System [Initial Approval] | Transcatheter porcine pericardial valve | April 27, 2023 |

# *English Translations of Notifications and Administrative Notices*

*The following link provides the latest information on the English versions of the latest notifications and administrative notices published on the PMDA website:*

https://www.pmda.go.jp/english/review-services/regulatory-info/0003.html

| Issue Date | Document Type & No. | Title | Posting Date |
|---|---|---|---|
| March 31, 2023 | PSEHB/MDED Administrative Notice | Questions and Answers (Q&A) on Points to Consider for Ensuring the Reliability in Utilization of Data from Registry or Medical Information Database in Applications for Marketing Approval and Re-examination for Regenerative Medical Products | April 21, 2023 |

# *Safety Information*

## Pharmaceuticals and Medical Devices Safety Information No. 400 (April 20, 2023)

1. Revision of Drugs That May Cause Abuse, Etc.
2. Revision of Precautions for Antitubercular Agents
3. Important Safety Information
   (1) Borofalan ($^{10}$B)
4. Revision of Precautions (No. 340)
   Borofalan ($^{10}$B) (and 6 others)
5. List of Products Subject to Early Post-marketing Phase Vigilance

(Reference)
Terminology of "Phaeochromocytoma" in the Precautions of Drugs (Excluding in vitro Diagnostics)
https://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0021.html

## Pharmaceuticals Revisions of PRECAUTIONS (May 9, 2023)

- Azilsartan
- Azilsartan/amlodipine besilate
- Alacepril
- Aliskiren fumarate
- Imidapril hydrochloride
- Irbesartan
- Irbesartan/amlodipine besilate
- Irbesartan/trichlormethiazide
- Enalapril maleate
- Olmesartan medoxomil
- Olmesartan medoxomil/azelnidipine
- Captopril
- Candesartan cilexetil
- Candesartan cilexetil/amlodipine besilate
- Candesartan cilexetil/hydrochlorothiazide
- Temocapril hydrochloride
- Delapril hydrochloride
- Telmisartan
- Telmisartan/amlodipine besilate
- Telmisartan/amlodipine besilate/hydrochlorothiazide
- Telmisartan/hydrochlorothiazide
- Trandolapril
- Valsartan
- Valsartan/amlodipine besilate
- Valsartan/cilnidipine
- Valsartan/hydrochlorothiazide
- Benazepril hydrochloride
- Perindopril erbumine
- Lisinopril hydrate

- Losartan potassium
- Losartan potassium/hydrochlorothiazide
- Sacubitril valsartan sodium hydrate
- Mesalazine
- Zinc acetate hydrate
- Leflunomide
- Ampicillin hydrate
- Ampicillin sodium
- Ampicillin hydrate/cloxacillin sodium hydrate
- Ampicillin sodium/cloxacillin sodium hydrate
- Ioversol

https://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0011.html

# *Events*

## Conferences/Meetings that the PMDA will participate in or host

| Date | Title | Location |
|---|---|---|
| June 10–13 | ICH meeting | Vancouver |
| June 13–14 | IPRP meeting | Vancouver |
| June 16–19 | 15th DIA 2023 China Annual Meeting | Suzhou |
| June 25–29 | 59th DIA 2023 Global Annual Meeting | Boston |
| July 10–13 | PMDA-ATC & U.S. FDA Pediatric Review Seminar 2023 | Tokyo |

# *Reports from Overseas*

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

## Single-arm trials as pivotal evidence for the authorization of medicines in the EU

On 21st April 2023, EMA has opened a public consultation on a reflection paper "Reflection paper on establishing efficacy based on single-arm trials submitted as pivotal evidence in a marketing authorization" [1]. This paper discusses key concepts for single-arm clinical trials that are submitted as pivotal evidence in support of marketing authorization applications for medicines in the EU.

Randomized clinical trials in which a new treatment is compared against a placebo or an existing standard of care are widely considered as the gold standard for generating evidence needed by regulatory authorities to assess the efficacy and safety of a new medicine, but single-arm trials may be feasible to use due to very small number of target populations for certain treatments of rare diseases, including rare cancers.

This reflection paper outlines consideration on single-arm trials that are submitted as pivotal evidence to demonstrate efficacy in a marketing authorisation application. This also includes some suggestions to sponsors on how to design single-arm trials and strategies for minimizing bias in these trials to support new marketing authorization applications.

This public consultation will end on 30 September 2023 and the comments will be analysed. The final document is planned to be published in 2024. I will keep a close eye on this item that how many comments will be received and how the process will proceed, as I believe it will have no small impact on Japan.

1) Reflection paper on establishing efficacy based on single-arm trials submitted as pivotal evidence in a marketing authorization https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing_en.pdf

Ms. UEDA Mami
PMDA's International Liaison Officer stationed at EMA in the Netherlands