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PMDA Updates

October, 2019

News

1. The 16th IMDRF Management Committee Meeting

From September 17 to 19, the 16th International Medical Device Regulators Forum (IMDRF) Management Committee (MC) Meeting was held in Ekaterinburg, Russia, and 2 staff members from PMDA's Office of International Programs along with a staff from Ministry of Health, Labour and Welfare (MHLW) attended as the MC Members.

On the first day, an open IMDRF Stakeholder Forum was held with approximately 270 participants including members from MC and industry, and updates were given for the IMDRF member countries and progress reports were made by the Working Groups (WGs) in addition to the issues of interest to industries. The MC members from Japan provided an outline of recent Japanese regulatory efforts (among others, Guidance for evaluation of artificial intelligence–assisted medical imaging systems for clinical diagnosis) and a progress report of the Medical Device Adverse Event Terminology Working Group (chaired by Japan). The second and the third day of the meeting were dedicated to the closed sessions for regulators and observers (either official or invited) only, where, in addition to the guidance documents developed by each working group, new work items were discussed.

In this meeting, the MC approved 3 final documents on clinical evaluation proposed by the Clinical Evaluation WG as final documents. The document on principles and practices for medical device cybersecurity for public consultation submitted by the Cybersecurity WG was also approved.

On September 16, Medical Device Single Audit Program (MDSAP) Regulatory Authority Council (RAC) meeting was held and Japanese delegates attended as a member country. The next IMDRF MC Meeting will be held in Singapore, Republic of Singapore, in March 2020.

The details of the 16th IMDRF MC Meeting are available at the following website.

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

2. Swissmedic staff visits PMDA

Dr. Marco Menna, Head of Infrastructure at Swissmedic, the regulatory authority for pharmaceuticals and medical devices in Switzerland, visited PMDA from September 17 to 20 to exchange information, including on PMDA's approach to digital transformation and AI. PMDA and Swissmedic have been reinforcing cooperation through mutual staff fellowship and bilateral meeting. During his stay, Dr. Menna was briefed on the practice at PMDA. The PMDA staff members from Office of International Programs, Office of Medical Devices, Office of Advanced Evaluation with Electronic Data, Office of Research Promotion, Office of Review Management, and Office of Informatics and Management for Safety took part in sharing their experience and discussing various topics with Dr. Menna. On the last day of his stay, Dr. Menna gave a lecture for the PMDA staff members. His presentation covered innovation at Swissmedic, current challenges, and digital transformation. As part of the session, he also took questions from the PMDA staff members.



Discussion with PMDA staff members of Office of Research Promotion (Right: Dr. Menna)



Lecture given for the PMDA staff members (Dr. Menna, standing at left of the screen)

3. Regulatory Affairs Professionals Society (RAPS) 2019

The Regulatory Affairs Professionals Society (RAPS) 2019 annual conference was held in Philadelphia, the U.S., from September 21 to 24. Participants from PMDA included Dr. Nobumasa Nakashima (Senior Director for International Programs) and 7 staff members. In addition, 1 staff member from MHLW participated.

A session titled "Japan Updates" was chaired by Dr. Nakashima. In this session, staff members of PMDA and MHLW delivered presentations on the revision of Pharmaceutical and Medical Devices Act (PMD Act) and the RWD utilization including MID-NET. About 120 participants attended this session, exceeding the number of last year greatly.

In a session titled "Regulatory Considerations for Companion Diagnostics", a staff member of PMDA delivered a presentation on the regulation of companion diagnostics in Japan and new regulatory approach to interchangeable companion diagnostics.

In a session titled "Interaction with Health Authorities", panelists from various regulatory agencies answered questions from audience. PMDA answered the questions on the process of product review and approval then discussed how to promote the development of medical devices. Vigorous discussion took place in each of the sessions, indicating a high level of interest in the Japanese regulations and relevant activities.

PMDA also ran an exhibition booth, where PMDA staff members actively communicated with the visitors to provide information on the current Japanese regulations and the services provided by PMDA, i.e. review, scientific advice, and safety measures. More than 160 visitors visited PMDA booth.

The next RAPS annual conference will be held in San Antonio, the U.S., from September 12 to 15, 2020.



Japan Updates session



Interaction with Health Authorities session

4. The 4th EMA-FDA-PMDA tripartite meeting to accelerate development of antimicrobial agents

The 4th EMA-FDA-PMDA tripartite meeting to accelerate development of antimicrobial agents was held from September 24 to 25, 2019 at PMDA. At the 4th tripartite meeting, taking into account the previous tripartite activities, the 3 agencies discussed further alignment on clinical trial designs for key indications for antibacterial drugs for which convergence has not yet been reached. The 3 Agencies plan to publish the outcome of the discussions e.g. in a scientific journal to inform stakeholders details of the work done so far. The meeting summary is available in the following PMDA website;

<https://www.pmda.go.jp/english/int-activities/outline/0018.html>

5. Call for application to PMDA-ATC Pharmacovigilance Seminar 2020 starts

PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) will hold the "PMDA-ATC Pharmacovigilance Seminar 2020" from February 3 to 6, 2020. This four-day seminar is designed for overseas regulatory authority officials who are engaged in pharmacovigilance activities. The Seminar includes lectures, group discussions with the training objective of acquainting the participants with knowledge that they could utilize in order to enhance the pharmacovigilance system in their countries/regions: The importance of regulatory harmonization in ICH and regulatory updates to ensure compliance with new pharmacovigilance, risk management, and adverse reaction reporting, etc.; The pharmacovigilance plan for each safety specification identified by signal detection and benefit-risk analysis; risk management tools for risk minimization; importance of collection and accumulation of adverse drug reaction reports and methodology of signal detection using such accumulated data, from the point of view of pharmacoepidemiology; and Benefit-Risk analysis through the life cycle of marketed medicinal products and the appropriate system for providing the

updated information to stakeholders using labeling and periodic reports such as Periodic Benefit Risk Evaluation Report (PBRER).

This seminar is offered as a Workshop of APEC-LSIF-RHSC (Asia-Pacific Economic Cooperation, Life Sciences Innovation Forum, Regulatory Harmonization Steering Committee), Center of Excellence (CoE), however, the seminar is open to non-APEC economies, as well.

Please refer to the following web site for the details of PMDA-ATC Pharmacovigilance Seminar 2020.

<http://www.pmda.go.jp/english/symposia/0159.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 | Non-proprietary Name | Posting date |
|--------------------------------|----------------------|--------------|
| Minnebro [Initial Approval] | esaxerenone | October 8 |

Medical Devices

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

| Brand Name | Non-proprietary Name | Posting date |
|---|-------------------------------|--------------|
| Absorb GT1 Bioresorbable Vascular Scaffold System [Initial Approval] | bio-absorbable coronary stent | September 24 |

Regenerative Medical Products

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

| Brand Name | Non-proprietary Name | Posting date |
|-----------------------------------|---|--------------|
| JACE [Partial Change Approval] | human (autologous) epidermal cell sheet | September 30 |
| Kymriah [Initial Approval] | tisagenlecleucel | September 30 |

Safety Information

Pharmaceuticals Revisions of PRECAUTIONS (September 24, 2019)

- Baricitinib
- Osimertinib mesilate
- Ofloxacin (oral dosage form)
- Garenoxacin mesilate hydrate
- Sitafloxacin hydrate
- Ciprofloxacin
- Ciprofloxacin hydrochloride hydrate
- Tosufloxacin tosilate hydrate (oral dosage form)
- Norfloxacin (oral dosage form)
- Pazufloxacin mesilate
- Pipemidic acid hydrate
- Prulifloxacin

- Moxifloxacin hydrochloride (oral dosage form)
- Levofloxacin hydrate (oral dosage form)
- Levofloxacin hydrate (injectable dosage form)
- Lomefloxacin hydrochloride (oral dosage form)
- Tocilizumab (genetical recombination)

<http://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0007.html>

Medical Devices Revisions of PRECAUTIONS (October 10, 2019)

- Revision of Precautions to the Package Inserts of Drug-eluting Coronary Stent or Drug-coated Balloon Dilatation Catheter for Coronary Angioplasty

<https://www.pmda.go.jp/english/safety/info-services/devices/0002.html>

Events

Conferences/Meetings PMDA hosts or participates in:

| Date | Title | Location |
|----------------|---|-----------|
| November 10-12 | DIA Japan Annual Meeting | Tokyo |
| November 11-15 | PIC/S Committee Meeting and Seminar 2019 | Toyama |
| November 12-15 | PMDA-ATC GMP Inspection Seminar 2019 | Toyama |
| November 16-21 | ICH week | Singapore |
| November 25-29 | PMDA-ATC Medical Devices Seminar 2019 | Tokyo |
| December 10-12 | PMDA-ATC Quality Control (Herbal Medicine) Seminar 2019 | Toyama |
| December 11 | Japan-US HBD East 2019 Think Tank Meeting | Tokyo |

Reports from overseas

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

USP's activity related to Performance Testing for finish products

The concept to focus on control of quality attribute important for assurance of efficacy and safety of pharmaceuticals is spreading in the US. The United States Pharmacopeia (USP) also works on testing methods for assessment of the performance of finish product *in vitro* and confirming bioequivalence through its lifecycle.

In current USP, the definitions of dosage forms are shown in <1151> Pharmaceutical Dosage Forms and quality testing for each dosage form is described in General Chapter <1> - <5>¹⁾. The testing methods for quality testing are implemented into General Chapter or General information Chapter, such as <711> Dissolution. Although USP covers many of typical dosage forms, there are dosage forms such as gastro-retentive tablets and liposomes for which *in vitro* performance testings have not been established. In order to catch up with these relatively new dosage forms, USP held Expert Panel meeting on October 4th, 2019, and started discussion related to their quality testing and performance testing²⁾.

To stimulate this discussion, USP will hold a Workshop on December 11th and 12th, 2019³⁾. The dissolution testing for products applied to the oral cavity and Inhalation products will also be discussed.

- 1) <1> Injections and Implanted Drug Products (Parenterals)—Product Quality Tests
- <2> Oral Drug Products—Product Quality Tests
- <3> Topical and Transdermal Drug Products—Product Quality Tests
- <4> Mucosal Drug Products—Product Quality Tests
- <5> Inhalation and Nasal Drug Products—General Information and Product Quality Tests
- 2) https://www.usp.org/events-training/search-past?aggregated_field=2019-10-04
- 3) USP Workshop: Advancements in In-Vitro Performance Testing of Drug Products
<https://www.usp.org/sites/default/files/usp/document/events-training/workshops/in-vitro-agenda-updated-072919.pdf>

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