PMDA Updates

April 2021

News

1. Further strengthening of alliances with Asian regulatory authorities

Mr. UZU
Senior Executive Director
and
Head of International Programs

Last April, in the PMDA Updates, I mentioned that this would be a year that would test the collaboration among regulatory authorities as we strive to contribute to the health of people around the world in the midst of the COVID-19 pandemic. Over the past year, regulatory authorities have overcome challenges and issues within a variety of frameworks, and we believe that we were able to demonstrate the importance of collaboration among regulatory authorities. With regards to international collaboration and cooperation, as Japan is located in Asia, collaborating with Asian regulatory authorities is one of the main activities of PMDA. Specific activities include the provision of training at the Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC), and cooperation with regards to reviews and safety measures.

Due to the COVID-19 pandemic, we were unable to offer in-person training at the PMDA-ATC. However, various training sessions on reviews of pharmaceuticals, medical devices, and regenerative medicine products, safety measures, and quality control were offered in the form of Webinars. Although there were challenges to overcome, there also was the advantage of being able to increase the number of participants with the Webinar format. We will continue to offer an enhanced array of training opportunities this year.

With regards to reviews, we offer support through the utilization of the PMDA review report. PMDA translates the review reports of the main products approved as new drugs into English, and releases. Some countries have a scheme in place that enables PMDA review reports to be used in the country's review process, and the scheme also enables PMDA to cooperate with their review process. For example, the Indonesian FDA clarified its scheme to utilize the review reports of regulatory authorities including PMDA. To facilitate the scheme, PMDA will cooperate with the Indonesian FDA by answering questions by the Indonesian FDA regarding PMDA review reports. This is expected to further enhance cooperation between PMDA and the Indonesian FDA with regards to the review process. PMDA intends to build similar cooperative relationships with other regulatory authorities utilizing PMDA review reports.

With regards to safety measures, when package inserts are revised to introduce new safety measures, PMDA provides the English translation of the information to registered regulatory authorities and responds to inquiries from regulatory authorities. It is our hope that by offering this form of cooperation, we will aid regulatory authorities in minimizing health damage in their countries.

Once again this year, PMDA will work closely with Asian regulatory authorities through the above activities to ensure the prompt delivery of necessary drugs and medical devices to the people of Asia.

2. Call for application to the MHLW/PMDA-USP Joint Workshop (June 2021)

The PMDA plans to organize a joint workshop on the role of quality in pharmaceuticals with the Ministry of Health, Labour, and Welfare (MHLW) and the United States Pharmacopeia (USP) on June 16 and 17, 2021. The MHLW/PMDA/Japanese Pharmacopeia and USP have a long history of collaboration and cooperation through the harmonization of pharmacopoeial standards and exchange of scientific and technical knowledge via visiting scientist and executive exchange programs. In our first joint workshop, we will introduce our collaborative activities that help ensure the quality of medicines and assist the development of new testing/manufacturing technology, and finally discuss the role we play in the midst of the ongoing crisis and challenges posed by the

COVID-19 pandemic. Our target audience for this workshop includes industry, academia, and regulators from Japan and East Asia. However, this workshop is open to other interested parties from all regions. It will be conducted as a free virtual meeting.

Please refer to the following website for details and registration.
https://www.pmda.go.jp/english/symposia/0196.html

3. 33rd DIA Europe Meeting (Virtual)

The 33rd DIA Europe Meeting was virtually held between March 15 and 19. Participants from the PMDA included Dr. FUJIWARA Yasuhiro (Chief Executive), Dr. SUZUKI Hiroshi (Director of the Center for Regulatory Science), Dr. NAKASHIMA Nobumasa (Associate Executive Director for International Programs), and Dr. SATO Junko (Director of the Office of International Programs). Additionally, from the Ministry of Health, Labour, and Welfare (MHLW), Ms. YAMAMOTO Fumi (Councilor for Pharmaceutical Affairs) and Mr. YASUDA Naoyuki (Director of the Office of International Regulatory Affairs) participated.

In this meeting, the PMDA mainly participated in the two sessions mentioned below.

A session titled "PMDA Updates" was chaired by Dr. NAKASHIMA. In this session, Ms. YAMAMOTO provided regulatory updates, such as implementation of the revised PMD Act. Dr. FUJIWARA delivered a presentation on the PMDA's recent efforts, including actions against COVID-19. Dr. SUZUKI spoke about the progress of the Center for Regulatory Science. Mr. YASUDA of the MHLW joined the panel discussion and took questions from viewers to provide the MHLW's views.

A session titled "Comparison of Emergency Use Pathways among Japan-the US-Europe – including post-marketing management –" was chaired by Dr. NAKASHIMA. In this session, Dr. SATO spoke about the Special Approval for Emergency in Japan.

Each session had a panel discussion and an active exchange of opinions among the speakers. The questions from viewers were answered by session speakers, which led to a greater understanding of Japan's latest regulations pertaining to pharmaceuticals.

The 34th DIA Europe Meeting will be held in Brussels, Belgium, from March 29 to 31, 2022.

「PMDA Updates」Session
Top row, from left: Dr. NAKASHIMA Nobumasa (Associate Executive Director for International Programs of PMDA), Mr. YASUDA Naoyuki (Director of Office of International Regulatory Affairs of MHLW)
Bottom row, from left: Dr. SUZUKI Hiroshi (Director of Center for Regulatory Science of PMDA) and Dr. FUJIWARA Yasuhiro (Chief Executive of PMDA)

「Comparison of Emergency Use Pathways among Japan-the US-Europe – including post-marketing management –」Session
Top row, on the right: Dr. NAKASHIMA Nobumasa (Associate Executive Director for International Programs of PMDA)
Bottom row, on the left: Dr. SATO Junko (Director of Office of International Programs of PMDA)

4. PMDA-ATC Regenerative Medicinal Products Review Webinar 2021 for NPRA, Malaysia

On March 19, the PMDA held a webinar titled "PMDA-ATC Regenerative Medicinal Products Review Webinar 2021 for NPRA, Malaysia." A total of 53 regulators of the National Pharmaceutical Regulatory Agency (NPRA), who reviewed, inspected, and surveyed pharmaceutical products, including regenerative medicinal products, participated in the webinar.

The webinar opened with remarks by Mr. UZU Shinobu, Director of Asia Training Centre for Pharmaceuticals and Medical Devices Regulatory Affairs of the PMDA, in a video message and by Dr. Azizah Ab Ghani, Head of Biologics Section, Center for Product and Cosmetic Evaluation, NPRA, covering topics related to the regulation and review process of pharmaceuticals, especially focusing on regenerative medicinal products, aiming to provide deeper insight into the present challenges in these areas.

In the webinar, lecturers from the PMDA and NPRA shared information about the regulatory framework for regenerative medicinal products, and lecturers from the PMDA shared their experiences in the review of human somatic cell-processed products and plasmid vector products.

At the end of the webinar, Dr. FUJIWARA Yasuhiro, Chief Executive of PMDA, awarded the course completion certificate virtually in a recorded video, and Dr. Azizah provided the closing remarks.

Please refer to the following website for details of the PMDA-ATC Regenerative Medicinal Products Review Webinar 2021 for NPRA, Malaysia.

https://www.pmda.go.jp/english/symposia/0202.html

Top row, from left: Mr. UZU Shinobu, Director of Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA), Dr. Azizah Ab Ghani, Head of Biologics Section, Centre for Product and Cosmetic Evaluation (NPRA), Dr. FUJIWARA Yasuhiro, Chief Executive (PMDA)
Middle row: Lecturers
Bottom row: some of the NPRA participants

5. The 19th IMDRF Management Committee Meeting

The 19th International Medical Device Regulators Forum (IMDRF) Management Committee (MC) meetings were held on March 16, 18, 23, and 25, and Dr. KUSAKABE Tetsuya (International Coordination Officer) and two staff members from the Office of International Programs of the PMDA along with a staff member from the MHLW attended them. The meetings were conducted virtually, as in the previous year, because of the pandemic. The IMDRF members take turns to lead the IMDRF meetings each year, and the MFDS in Korea chaired this year.

On March 16, a joint workshop between the IMDRF and DITTA (The Global Diagnostic Imaging, Healthcare IT & Radiation Therapy Trade Association), an industry group, was held. The theme was "WHAT TO LEARN FROM COVID-19?"; 446 stakeholders registered. Regulators and industry groups shared their efforts toward combating COVID-19, and Japan introduced regulatory actions, including regulatory agilities, during the COVID-19 pandemic.

On September 18, an open meeting was held to exchange views on the IMDRF's activities for regulatory members, observers (official and invited), industry, and other related groups.

The IMDRF Stakeholder Forum was held on March 23, and 545 participants, including IMDRF MC members and industry stakeholders, attended. The presentations about the latest information from each IMDRF country, progress reports of each WG, the interests and concerns from industry groups, etc. were published on the IMDRF website in advance, and on the day of the forum each speaker responded to the questions submitted before the meeting. Dr. KUSAKABE, PMDA, provided an outline of the amendment of the Pharmaceuticals and Medical Devices Act (PMD Act) and its enforcement; the AE WG Chair provided a progress report of the Adverse Event Terminology (AE) WG. There were questions and answers regarding the post-market data required to submit after the early approval under the system, such as the SAKIGAKE designation in the amended PMD Act and the Adverse Event reporting and signal detection in the AE WG.

On September 25, a closed meeting was held for regulatory members and observers (official) to discuss guidance documents and future new work items developed by each WG. At the plenary session, guidance for post-market clinical follow-up from medical device clinical evaluation WG was approved as the final document. The new work items were approved to create a template to implement a table of contents for in vitro diagnostics and non-in vitro diagnostics devices market authorization, as well as develop a reporting model for medical device regulatory reviews conducted by conformity assessment bodies, submitted by the Regulated Product Submission WG and the Good Regulatory Review Practice WG, respectively.

The next IMDRF MC meeting will be held in September 2021.

The details of the outcome for the IMDRF MC Meeting will be available on the following website.

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

6. MDSAP Regulatory Authority Council

On March 9, the Medical Device Single Audit Program (MDSAP) Regulatory Authority Council (RAC) was held, and Japanese delegates attended, representing Japan as a member country. At the meeting, the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) and Singapore's Health Sciences Authority (HSA) were approved as an official observer and an affiliate member, respectively.

The date of the next MDSAP RAC meeting is yet to be confirmed.

7. PMDA-ATC E-learning Course on Quality Control (Herbal Medicine) newly released Call for application to PMDA-ATC Quality Control (Herbal Medicine) WEBINAR 2021 starts

PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) is pleased to announce that PMDA-ATC Quality Control (Herbal Medicine) E-learning Course is newly released. This course will provide you with PMDA review process, Approval standards for OTC Kampo medicines, Japanese Pharmacopoeia, and Evaluation processes/GMP inspection by prefectural authorities through videos and quizzes, which take about 120 min in total.

Person who wishes to take this course has to register him/herself to the PMDA-ATC E-learning system in advance. Please refer to the following website for details.

https://www.pmda.go.jp/english/int-activities/training-center/0006.html

PMDA-ATC is also pleased to inform you of the "Quality Control (Herbal Medicine) Webinar 2021" to be held from June 22 to 24, 2021 through web conference system. This webinar is designed for officials from overseas regulatory authorities.

The objective of the webinar is to provide the participants with opportunities to share the knowledge and experiences of approval review, quality control and manufacturing control of crude drugs and herbal medicine through on-line lectures and case-study based group discussion as well as a video-taped tour of the manufacturing site. All participants of the Webinar should take the PMDA-ATC Quality Control (Herbal Medicine) E-learning Course prior to attending the live sessions.

Please refer to the following website for entry details of PMDA-ATC Quality Control (Herbal Medicine) Webinar 2021.

https://www.pmda.go.jp/english/symposia/0204.html

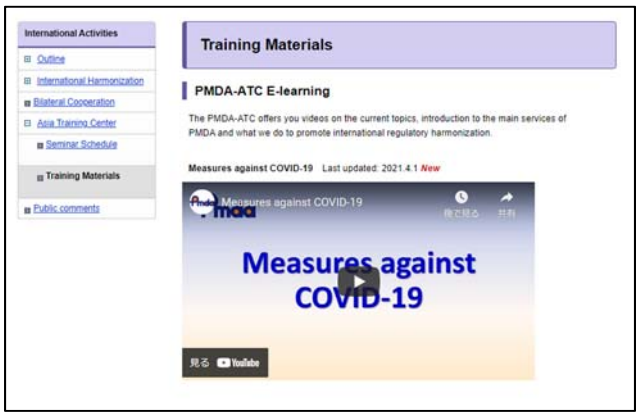
8. PMDA-ATC E-learning Content on COVID-19 released

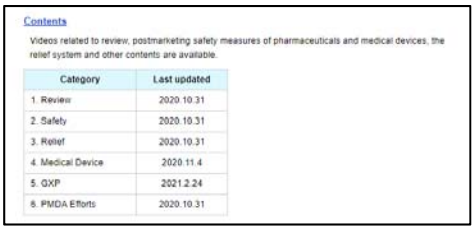
The PMDA has been providing the PMDA-ATC E-learning system since January 2020.

Since April, the PMDA-ATC E-learning content has been made available on YouTube for easier access instead of the previous system. The content on "Measures against COVID-19" was newly released in addition to all the existing content.

The e-learning website can be accessed through the following link.

https://www.pmda.go.jp/english/int-activities/training-center/0003.html





9. ICH E6(R3) Guideline

The ICH E6(R3) Expert Working Group(EWG) has been working on the revision of the ICH E6 (Guidance for Good Clinical Practice) guideline for the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The draft Principles of ICH E6(R3) guideline is now available on the ICH website. The current progress of the ICH E6(R3) EWG, including the concept of the proposed Principles and Annexes under revision, will be explained at the public web conference on 18th and 19th May 2021. For more information, please refer to the following website.

PMDA website:

https://www.pmda.go.jp/english/symposia/0044.html

ICH website:

https://www.ich.org/news/draft-principles-ich-e6-good-clinical-practice-gcp-now-available

The draft principles of ICH E6(R3):

https://database.ich.org/sites/default/files/ICH_E6-R3_GCP-Principles_Draft_2021_0419.pdf

English Translations of Review Reports

The followings is the current information about the English version of 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
Inavir [Partial Change Approval]	laninamivir octanoate hydrate	March 18
Akalux [Initial Approval]	cetuximab sarotalocan sodium (genetical recombination)	March 23
Vanflyta [Initial Approval]	quizartinib hydrochloride	April 7

Safety Information

Pharmaceuticals and Medical Devices Safety Information No. 381 (March 23, 2021)

1. Digitization of Package Inserts
2. Safety in Co-administration of Sildenafil (indicated for pulmonary arterial hypertension) and Amiodarone (oral dosage form)
3. Important Safety Information
   (1) Salbutamol sulfate
4. Revision of Precautions (No. 321)
   Aspirin (preparations indicated for antipyresis, analgesia, anti-inflammation, prevention of thrombus/embolus formation, Kawasaki disease) (and 22 others)
5. List of Products Subject to Early Post-marketing Phase Vigilance

https://www.pmda.go.jp/english/safety/info-services/drugs/medical-safety-information/0018.html

Pharmaceuticals Revisions of PRECAUTIONS (March 30, 2021)

- Magnesium sulfate hydrate/glucose (preparations indicated for prophylaxis and treatment of eclampsia in severe hypertensive disorders of pregnancy)
- Magnesium sulfate hydrate (preparations indicated for eclampsia)
- Ritodrine hydrochloride (oral dosage form)
- Ritodrine hydrochloride (injections)
- Magnesium sulfate hydrate/glucose (preparations indicated for inhibition of uterine contractions in threatened premature labour, and prophylaxis and treatment of eclampsia in severe hypertensive disorders of pregnancy)
- Cetuximab (genetical recombination)
- Durvalumab (genetical recombination)
- Iopamidol

https://www.pmda.go.jp/english/safety/info-services/drugs/revision-of-precautions/0008.html

Partial Correction to Pharmaceuticals Revision of PRECAUTIONS (February 25, 2021) (March 30, 2021)

- Salicylamide/acetaminophen/anhydrous caffeine/chlorpheniramine maleate, salicylamide/acetaminophen/anhydrous caffeine/promethazine methylenedisalicylate

Events

Conferences/Meetings the PMDA hosts or participates in:

Date	Title	Location
May 20-23	13th DIA China Annual Meeting	Suzhou
May 25, 31-June 3	ICH virtual meeting	Virtual
May 27-28	5th Japan-India Medical Products Regulatory Symposium	Virtual
June 22-24	PMDA-ATC Quality Control (Herbal Medicine) Webinar 2021	Virtual
June 27-July 1	57th DIA 2021 Global Annual Meeting	Virtual

Reports from Overseas

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

Pharmaceutical strategy for Europe

This report addresses upcoming topics in the EU although some important discussions around COVID-19 vaccines are currently ongoing [1, 2]. As briefly introduced in PMDA Updates July 2020, some mid-/long-term measures in the field of health have been recently developed in the EU, and one of which is "Pharmaceutical strategy for Europe" [3].

Since the publication of the strategy roadmap in June 2020, the European Commission has conducted a series of consultations and meetings to inform the designing of the strategy. The most recent public consultation in relation to the strategy is the one for the roadmap on the revision of the general pharmaceutical legislation [4]. It was published on 30 March 2021 and will be open until 27 April 2021. In addition, some evaluations such as the revision of the legislation for medicines for rare diseases and for children are already under way [5]. In parallel, the discussion on the extension of the mandate of EMA, introduced in PMDA Updates November 2020, has been progressing steadily [6]. As these may eventually have an impact on our activities in Japan, attention should be paid to these trends as well as things right before our eyes.

1) https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-provide-further-context-risk-very-rare-blood-clots-low-blood
2) https://www.ema.europa.eu/en/news/covid-19-vaccine-janssen-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood
3) https://ec.europa.eu/health/human-use/strategy_en
4) https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12963-Evaluation-and-revision-of-the-general-pharmaceutical-legislation
5) https://ec.europa.eu/health/human-use/paediatric-medicines/evaluation_en
6) https://www.europarl.europa.eu/doceo/document/ENVI-PR-680818_EN.pdf

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