Symposium for the draft ICH E8 (R1)
25 July, 2019, Yomiuri Holl, Tokyo, Japan

MHLW/PMDA international activities

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Pharmaceuticals and Medical Devices Agency (PMDA)

Outline

1. Multilateral Cooperation to Foster Regulatory Harmonization/Convergence

2. Initiatives toward Regulatory Harmonization/Convergence in Asia/Pacific Region

3. Next Step

MHLW/PMDA Multilateral Cooperation

World Health Organization

WHO (1948-) is the directing and coordinating authority on international health within the United Nations' system.

ICMRA
International Coalition of Medicines Regulatory Authorities

ICMRA (2012-) is a voluntary, executive-level, strategic coordinating, advocacy and leadership entity of regulatory authorities

ICH
harmonisation for better health

ICH (1990 renovation 2015-) unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration

IPRP
International Pharmaceutical Regulators Programme

IPRP (2018-) for **exchange of information** and **regulatory cooperation** for pharmaceuticals

Regulatory Harmonization Steering Committee
APEC
Life Sciences Innovation Forum

APEC-LSIF-RHSC (2009-) for **regulatory convergence** by promoting ICH and other international guidelines in the APEC region

PIC/S

PIC/S (1995-) for harmonizing **inspection procedures** and facilitating communication

GHTF

IMDRF International Medical Device Regulators Forum

GHTF (1992-)/ IMRDF (2012-) for harmonizing **medical device regulations**

etc.

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The International Coalition of Medicines Regulatory Authorities (ICMRA)

- ICMRA provides a global architecture to support enhanced communication, information sharing, crisis responses and address regulatory science issues.

- MHLW/PMDA lead ICMRA Innovation Work Stream 1

<Mission>

To identify best practices of horizon scanning (HS) through compiling and analyzing each regulator's scanning methods and to find solutions to common difficulties faced by the regulators.

<Members>

Leader

AIFA, DKMA, EMA, US.FDA, HC, HPRA, MFDS, MHRA, MPA, Swissmedic

What is Horizon Scanning?
~ General Overview ~

Without Horizon Scanning…

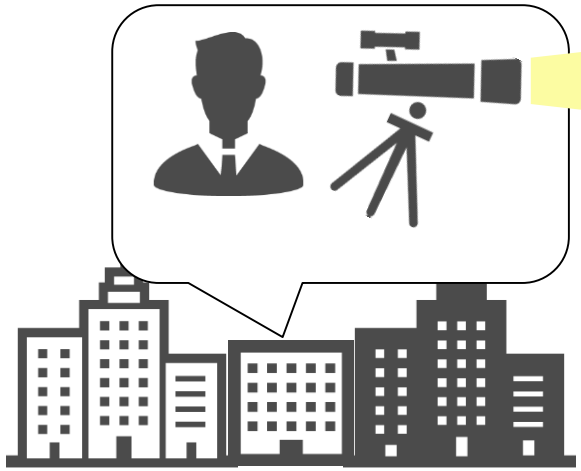
Stakeholders : *unsure of regulations…*

Report on Technology A

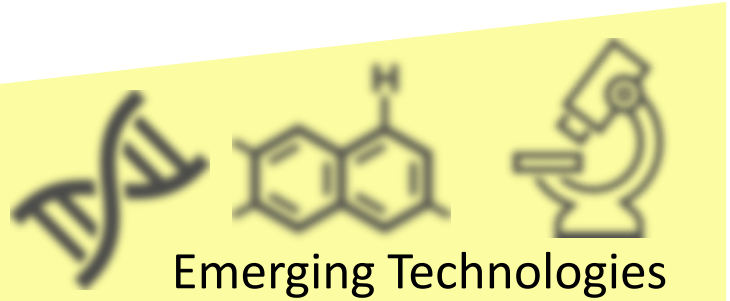
Regulator

Regulators : *cannot keep pace with accelerating innovation…*

With Horizon Scanning…



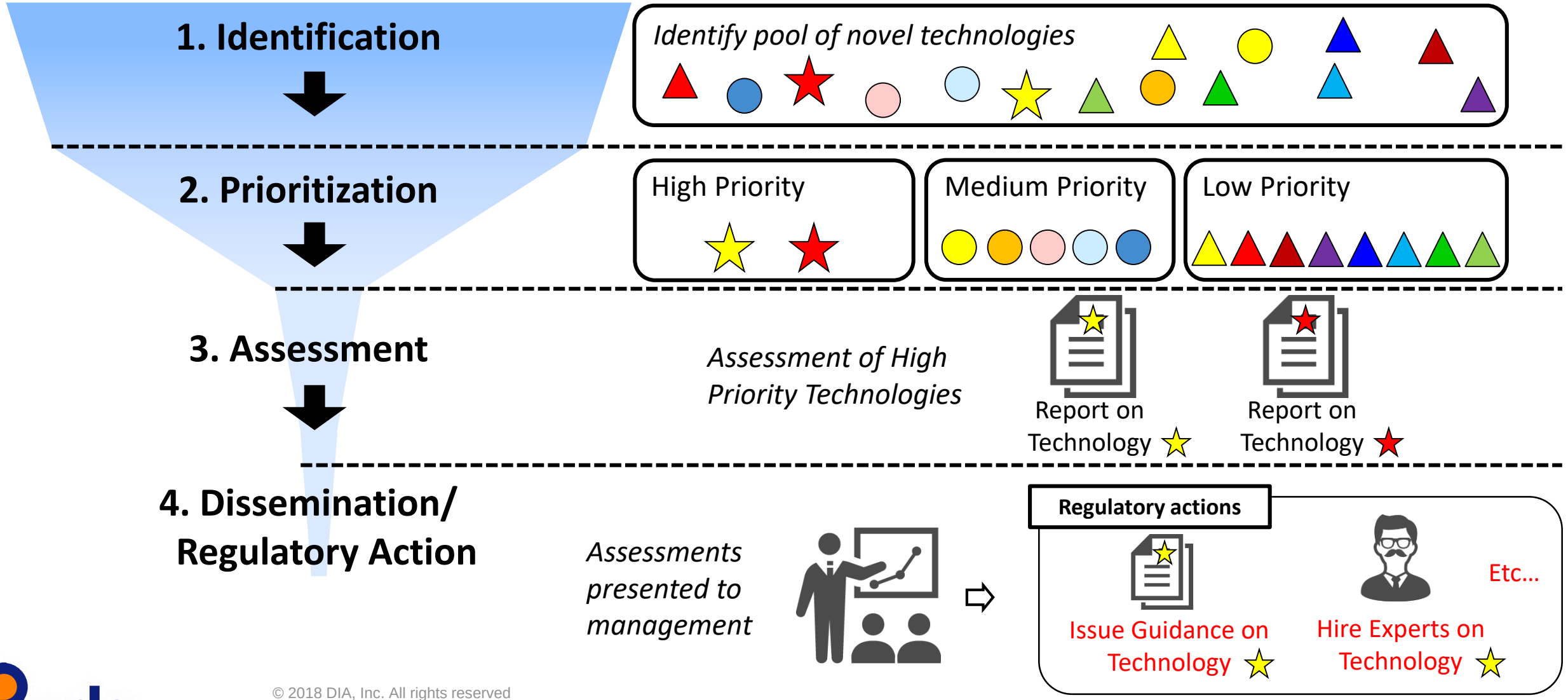
Regulator



Emerging Technologies

- ***Proactively scan the horizon***
  for emerging trends, technologies, etc.
- ***Make necessary regulatory preparations.***

What is Horizon Scanning?
~ Illustration of Horizon Scanning ~



ICMRA Innovation Project

Work Stream 1:

led by MHLW/PMDA

Analysis of global best practices in horizon scanning methodologies

- Survey of members to analyse existing HS methodologies and approaches
- Identification of HS best practices and development of a HS methodology framework

Work Stream 2:

Leveraging from outcomes of horizon scanning through critical innovation/ expertise and skills

led by EMA, HPRA

- Compilation of three case studies to identify and review products and technologies, where regulatory science approaches are required.
- Discussions regarding future expertise requirements and potential opportunities for collaboration and capacity building to support innovation

Work Stream 3:

led by Health Canada

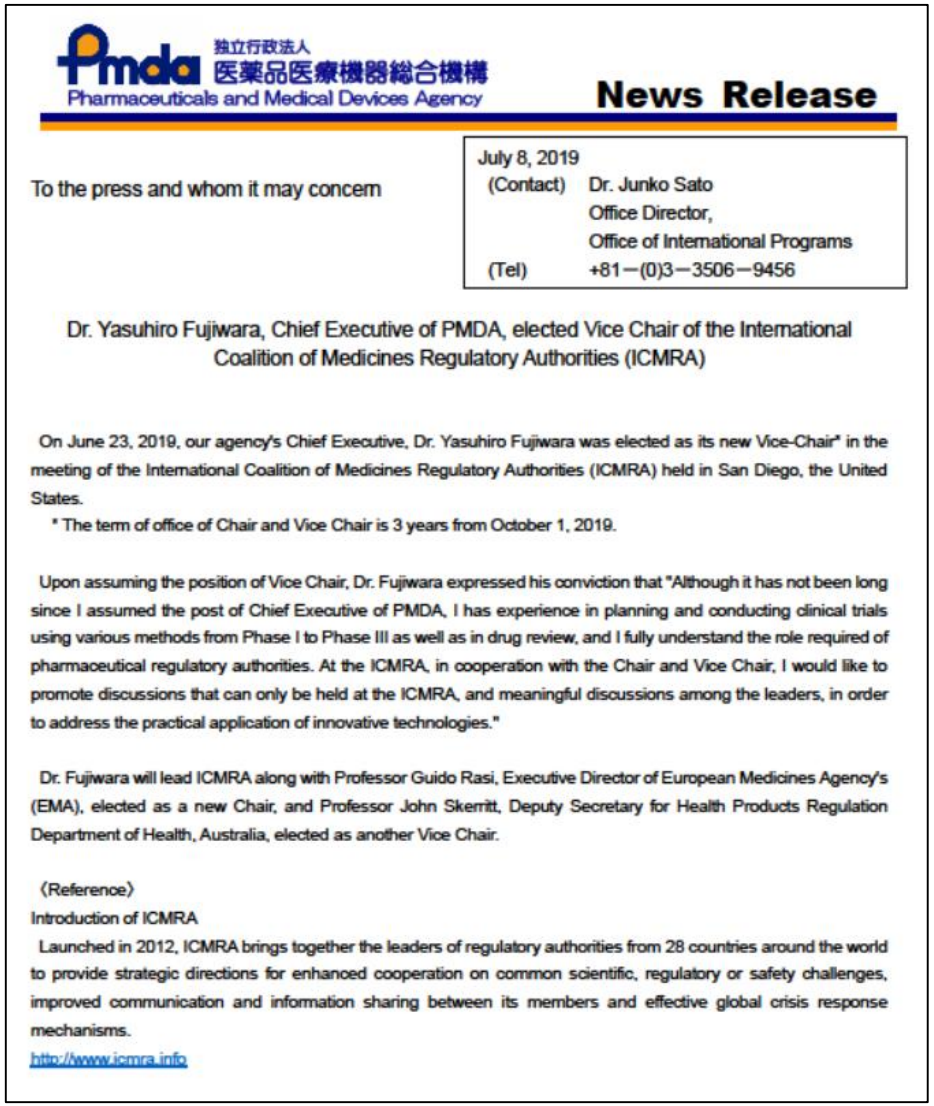
Novel Approaches to Licensing/ Early Access Schemes

- Review of various international regulatory approaches to licensing that aim to address the demand for timely access to innovative products.
- Questionnaire among ICMRA members regarding current novel regulatory pathways to licencing (NRPL) and which are implemented through legislation, regulation, and policy.

Future ICMRA Activities

- On June 23, PMDA's Chief Executive, Dr. Yasuhiro Fujiwara, was elected as ICMRA's New Vice Chair 2019 in ICMRA meeting held in San Diego.

- Dr. Fujiwara will lead ICMRA along with Prof. Guido Raji, Executive Director of European Medicines Agency, elected as new Chair, and Prof. John Skerritt, Deputy Secretary for Health Products Regulation Department of Health, Australia, elected another Vice Chair.



pmda 独立行政法人 医薬品医療機器総合機構 Pharmaceuticals and Medical Devices Agency

News Release

To the press and whom it may concern

July 8, 2019
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Office of International Programs
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Dr. Yasuhiro Fujiwara, Chief Executive of PMDA, elected Vice Chair of the International Coalition of Medicines Regulatory Authorities (ICMRA)

On June 23, 2019, our agency's Chief Executive, Dr. Yasuhiro Fujiwara was elected as its new Vice-Chair* in the meeting of the International Coalition of Medicines Regulatory Authorities (ICMRA) held in San Diego, the United States.

* The term of office of Chair and Vice Chair is 3 years from October 1, 2019.

Upon assuming the position of Vice Chair, Dr. Fujiwara expressed his conviction that "Although it has not been long since I assumed the post of Chief Executive of PMDA, I has experience in planning and conducting clinical trials using various methods from Phase I to Phase III as well as in drug review, and I fully understand the role required of pharmaceutical regulatory authorities. At the ICMRA, in cooperation with the Chair and Vice Chair, I would like to promote discussions that can only be held at the ICMRA, and meaningful discussions among the leaders, in order to address the practical application of innovative technologies."

Dr. Fujiwara will lead ICMRA along with Professor Guido Rasi, Executive Director of European Medicines Agency's (EMA), elected as a new Chair, and Professor John Skerritt, Deputy Secretary for Health Products Regulation Department of Health, Australia, elected as another Vice Chair.

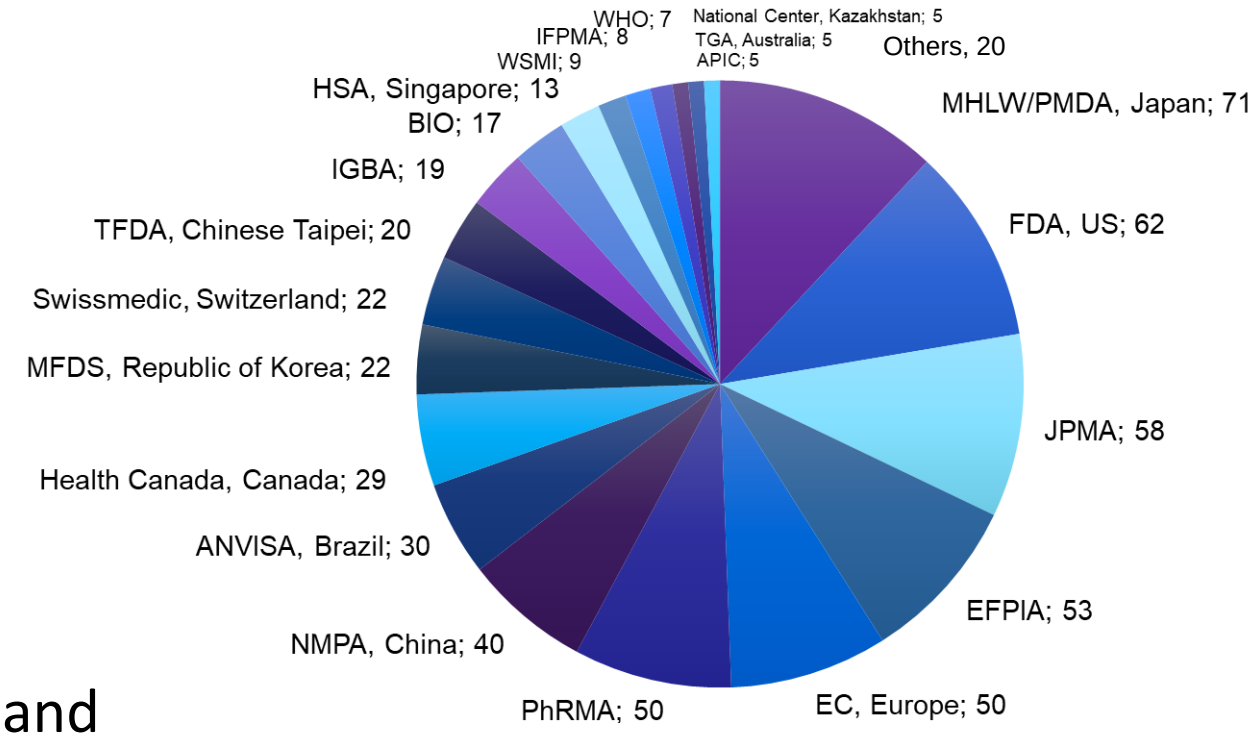
〈Reference〉
Introduction of ICMRA
Launched in 2012, ICMRA brings together the leaders of regulatory authorities from 28 countries around the world to provide strategic directions for enhanced cooperation on common scientific, regulatory or safety challenges, improved communication and information sharing between its members and effective global crisis response mechanisms.
http://www.icmra.info

International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)

ICH harmonisation for better health

- ICH is unique in bring together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration.

- ICH aims to achieve harmonization through the development of ICH Guidelines with regulator and industry experts.
- ICH has produced over 60 Guidelines on technical requirement.
- Over 20 working groups are now ongoing.



<Number of experts in ICH>

ICH was created in 1990 and ***30th Anniversary*** in 2020.

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MedDRA

Med = Medical

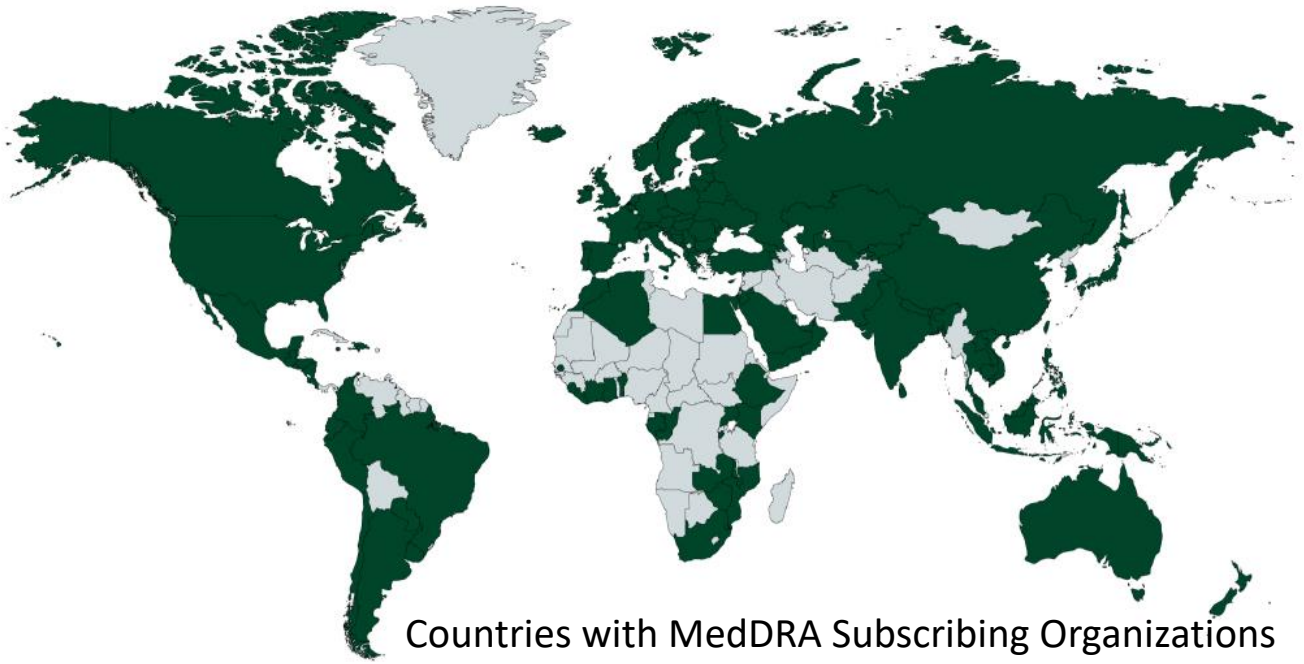
D = Dictionary for

R = Regulatory

A = Activities

- MedDRA – International standard for electronic safety data exchange, used through **the entire regulatory process**, from pre-marketing to post-marketing, and data entry, retrieval, evaluation and presentation.
- **2019 marks 20 years of MedDRA** which was first released in 1999.

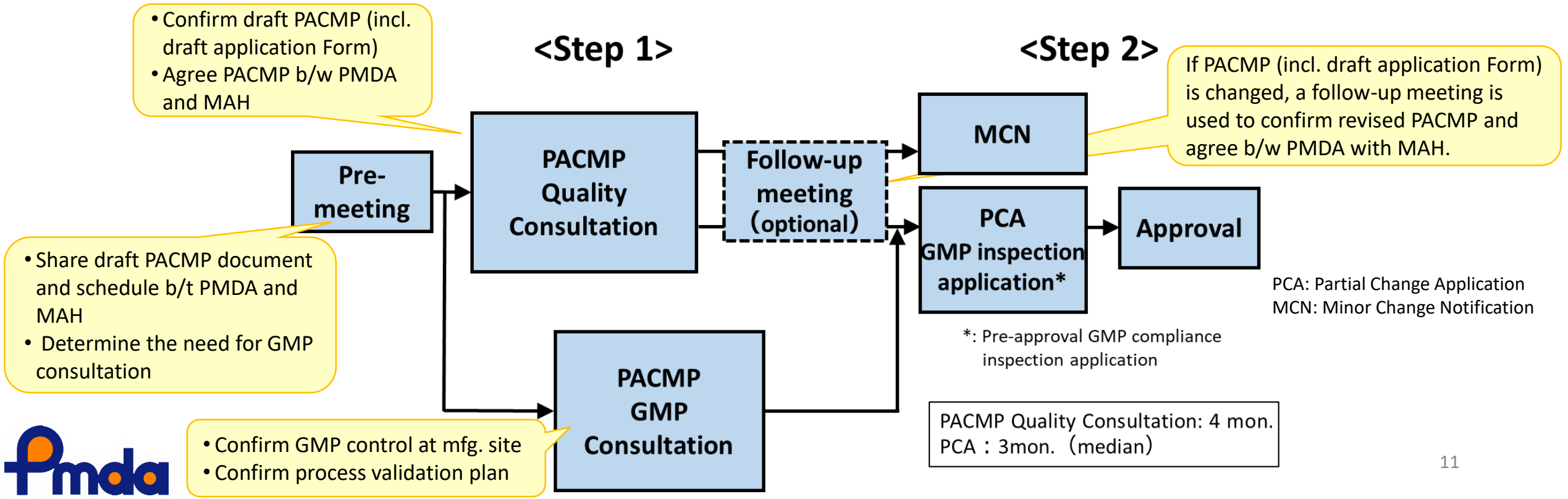
- **12 languages, Over 5,700 MedDRA Subscribing Organizations in 122 Countries**



Countries with MedDRA Subscribing Organizations

Preparation for ICH Guideline Implementation
~ Introduction of PACMP pilot program in Japan ~

- ICH Q12 will introduce PACMP (Post-Approval Change Management Protocol), a mechanism enables planning and implementation of future CMC changes in an efficient and predictable manner.
- MHLW/PMDA started the pilot program for future implementation since April 1, 2018 (before ICH Q12 reaches Step4/5).



Preparation for ICH Guideline full-Implementation
~ Review of PMD Act.* ~

*: Pharmaceuticals and Medical Devices Act

Theme 1: Ensuring early access to innovative pharmaceuticals & medical devices, and enhancing the safety measures

(1) Streamline of Approval Process for early patient access

① "Conditional Early Approval System" and "SAKIGAKE Review Designation" should be legislated to clarify process and raise transparency.

② New Approval system for Medical Devices to reflect the characteristics of medical devices (considering innovative technologies; Big Data, AI etc.,)

③ Clarification of Clinical Trials Process

(2) Introduction of new Quality Management System

① Introduction of GMP and GCTP inspection per manufactory

② Revision of current QMS inspection

③ **Introduction of PACMP**

MHLW will introduce PACMP in the regulation for full-implementation of ICH Q12.

(3) Strengthen Safety Measures

① Provide electronic information of Package Inserts

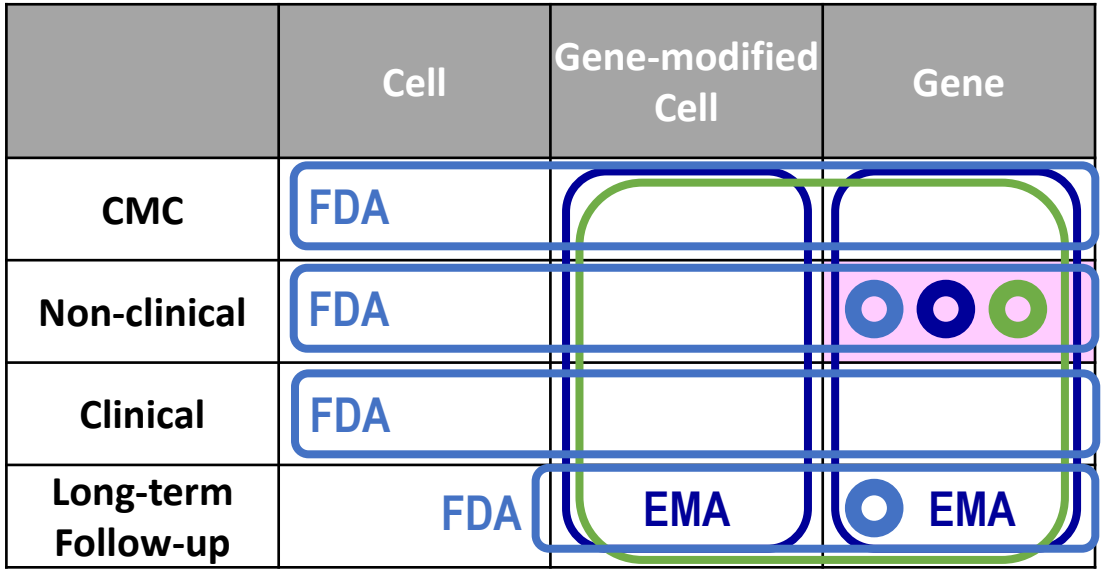
② Increase traceability of pharmaceuticals and medical devices

③ Utilize Patient Registry Data For safety measure

S12 – Non-clinical Biodistribution Studies for Gene Therapy

- Based on the outcome from the IPRP discussion, ICH will initiate new ICH guideline preparation for Non-clinical BD studies for gene therapy products.

Current guideline for Gene Therapy Products in the Founding Regions



- Scope of Guideline
- Timing and design of BD study to support early human clinical trials
- Design of BD studies and collection of BD data, etc.

: where BD consideration is described in each guideline

➡ Streamlined development of the gene therapy products with higher scientific rigor while minimizing the unnecessary use of animals.

***This slide is provided by Mr. Yokota, JPMA**

Synergetic Activities

ICH harmonisation for better health

ICH Assembly endorsed proposed "Non-clinical Biodistribution Studies for Gene Therapy Products" as a new ICH topic at ICH Assembly in Amsterdam (5-6 June 2019).

IPRP International Pharmaceutical Regulators Programme

ICMRA International Coalition of Medicines Regulatory Authorities

12th Summit Heads of Medicines Regulatory Agencies 2017 (**ICMRA** Summit)

Main Theme: Innovation
Regulatory convergence on regenerative medicines

IPRP Reflection Paper
Expectations for Biodistribution Assessments for Gene Therapy Products (June 2018)

proposed as new ICH topic based on the IPRP Reflection Paper

MHLW/PMDA

pmda Kyoto, Japan

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1. Multilateral Cooperation to Foster Regulatory Harmonization/Convergence

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2nd Asian Network Meeting in Tokyo on April 10, 2019

- Co-chaired by Japan, China, India and Singapore
- Participants; top-level executives of regulatory agencies from 10 countries
  (Japan, China, India, Singapore, Indonesia, Malaysia, Myanmar, Philippines, Thailand and Vietnam)
- Confirmed the following points;
  - The importance of the opinion exchange from a high-level perspective on the common issues across Asian region
  - Fostering trusting relationships
  - Sharing best practices
  - Periodical meeting in the future

Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs

- Plan, design and coordinate training for Regulatory Authority staffs (established in 2016)
- Provide **training opportunities** including **on-site training**

- Help raise the level of Regulations in Asia and the world.
- **In FY2018, 267 regulators from 31 countries/regions participated.** (Numbers are growing)

Training seminar seminars to Regulatory Authority members by PMDA

Outside Japan

APEC regions

Lectures, case studies, and on-site training

Establishing a centralised training center for multi-regional clinical trials

PMDA-ATC Training Seminars held in FY 2018

	Contents	Date	Location	Participants
1	Pediatric Review*1	Jun. 11-14, 2018	Tokyo (PMDA)	24 (12 countries/regions)
2	Pharmaceuticals Review	Jun. 18-22, 2018	Tokyo (PMDA) and Toyama Prefecture	30 (16 countries/regions)
3	Good Registration Management	Sep. 26-28, 2018	Taipei	29 (11 countries/regions)
4	Pharmaceuticals Review	Oct. 15-16, 2018	Nay Pyi Taw, Myanmar	32 (Myanmar)
5	Quality Control (Herbal Medicine)	Oct. 22-24, 2018	Toyama, Toyama Prefecture	15 (14 countries/regions)
6	Medical Devices Review	Nov. 12-16, 2018	Tokyo (PMDA)	25 (17 countries/regions)
7	Good Manufacturing Practice (GMP) *2	Nov. 26-30, 2018	Utsunomiya, Tochigi Prefecture	14 (14 countries/regions)
8	Multi-Regional Clinical Trial (MRCT)*3	Jan. 21-24, 2019	Tokyo (PMDA)	21 (13 countries/regions)
9	Pharmaceuticals Review	Jan. 28-31, 2019	Jakarta, Indonesia	48 (Indonesia)
10	Pharmacovigilance*3	Feb. 4-7, 2019	Tokyo (PMDA)	29 (15 countries/regions)

*1 Joint Seminar with U.S.FDA, *2 With the support of PIC/S, *3 APEC-LSIF-RHSC CoE Workshop

PMDA-ATC Training Seminars held/planned in FY 2019

	Contents	Date	Location
1	Pediatric Review*[1]	Jul. 8-11, 2019	Tokyo (PMDA)
2	Pharmaceuticals Review*[2]	Jul. 22-26, 2019	Tokyo (PMDA) and Toyama Prefecture
3	Good Registration Management (GRM)	Sep. 2019	Taipei
4	Good Manufacturing Practice (GMP) *[3]	Nov. 11-15, 2019	Toyama Prefecture
5	Medical Devices Review *[4]	Nov. 25-29, 2019	Tokyo (PMDA)
6	Quality Control (Herbal Medicine)	Dec. 10-12, 2019	Toyama, Toyama Prefecture
7	Multi-Regional Clinical Trial (MRCT)*[5]	Jan. 20-23, 2020	Tokyo (PMDA)
8	Pharmacovigilance*[5]	Feb. 3-6, 2020	Tokyo (PMDA)

*[1] Joint Seminar with U.S.FDA, *[2] Joint Seminar with WHO, *[3] With the support of PIC/S, *[4] APEC-LSIF-RHSC pilot CoE Workshop, *[5] APEC-LSIF-RHSC CoE Workshop

- Increased cooperation with other organizations (FY2018: 4/10, FY2019: 6/8).
- PMDA contributes to the capacity building for partner regulatory agencies through these training seminars.

Achievement of PMDA-ATC Training Seminars

Excerpt from

Joint Statement of ASEAN-JAPAN Health Ministers Meetings: Universal Health Coverage and Population Ageing

15 July, 2017, Tokyo, Japan

22. We commit to improve and harmonize the national regulatory system of pharmaceutical products and medical devices in ASEAN Member States through fostering collaboration and advancing regulatory science platforms such as the ASEAN harmonization systems and **“Asian Training Center for Pharmaceutical and Medical Devices"** by the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan with technical assistance by the WHO.

APEC-LSIF-RHSC

(Asia-Pacific Economic Cooperation – Life Sciences Innovation Forum – Regulatory Harmonization Steering Committee)

Regulatory Harmonization Steering Committee

APEC

Life Sciences Innovation Forum

- APEC-LSIF-RHSC aims to promote a more ***strategic***, ***effective*** and ***sustainable*** approach to pharmaceuticals and medical devices regulatory harmonization.
- Japan serves as co-Chair of APEC-LSIF-RHSC with the United States.

Champion economies lead several activities for Priority Work Areas (PWAs).

PWAs	Champion Economies
MRCT/GCP inspection	Japan, Thailand
Pharmacovigilance	Republic of Korea
Biotherapeutics	Republic of Korea
Advanced Therapies	Singapore
Good Registration Management	Chinese Taipei, Japan
Global Supply Chain Integrity	the United States
Medical Devices	Japan, the United States, Republic of Korea

APEC-LSIF-RHSC

(Asia-Pacific Economic Cooperation – Life Sciences Innovation Forum – Regulatory Harmonization Steering Committee)

Center of Excellences (CoEs) provide the training seminars for promoting regulatory convergence, capacity and cooperation in PWAs.

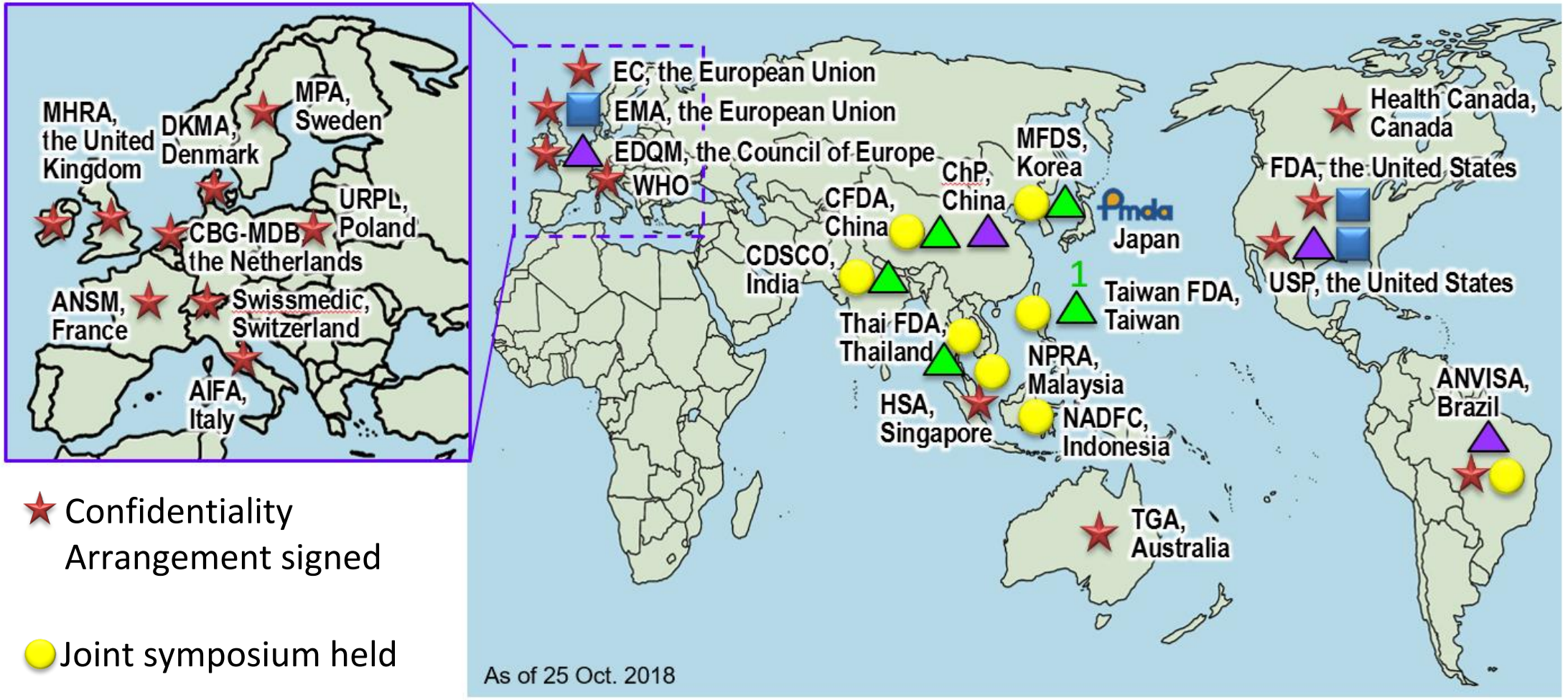
CoEs (As March 22, 2019)*

- Duke-NUS Singapore (MRCT/GCP)
- Korea Institute of Drug Safety & Risk Management(Pharmacovigilance)
- MRCT Center of Brigham and Woman's Hospital and Harvard (MRCT/GCP)
- Northeastern University (Biotherapeutics)
- Peking University (MRCT/GCP)
- PMDA (MRCT/GCP), (Pharmacovigilance)
- RAPS in cooperation with TFDA (GRM)
- University of Tennessee HSC (Supply Chain)
- USP (Supply Chain)

*12 institutes were endorsed as Pilot CoEs by APEC-LSIF-RHSC.

- Thai FDA(GRM PWA) <CoE Pilot program : Oct. 2019>
- PMDA (Medical Device PWA) <CoE Pilot program : Nov. 2019>

MHLW/PMDA Bilateral Cooperation



★ Confidentiality Arrangement signed

● Joint symposium held

■ PMDA staff stationed at the agency

▲ Cooperative Arrangement on cooperation of pharmacopoeia signed

▲ Cooperative Arrangement signed

Example. The history of Thailand-Japan cooperation for pharmaceuticals and medical devices regulation

Year	Cooperation
2013	The First Thailand-Japan Symposium and the bilateral-meeting (24th-25th Oct.) ➢ The symposium takes place every year since 2013. This is the 6th symposium. ➢ The bilateral-meeting between Thailand and Japan takes place almost twice every year since 2013
2014	The PMDA training programs for staff members in Thai FDA starts ➢ The PMDA training programs take place every year since 2014. Total numbers of conducted programs : **9** • **Pharmaceuticals ×7** (Japanese Pharmacopeia ×2, clinical evaluation, etc ×5) • **Medical devices ×2**
2015	The abridged evaluation of New drug in Thailand was issued. ➢ PMDA was regarded as one of “benchmark / reference agencies” in “Priority review ”which was the one of channels for new drugs registration.
2016	PMDA-ATC seminar was conducted for the first time in Thailand.
2017	An expert from JICA was dispatched to Thai FDA.
2018	Thai FDA and MHLW signed the MOC between Thailand and Japan.
2019	Thai FDA was endorsed becoming a Pilot CoE of APEC-LSIF-RHAC GRM PWA by APEC-LSIF-RHSC (Champion economies; Japan and Taiwan) in Feb. 2019.

…what kind of cooperation we will be able to do…

Outline

1. Multilateral Cooperation to Foster Regulatory Harmonization/Convergence

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3. Next Step

The Future of PMDA

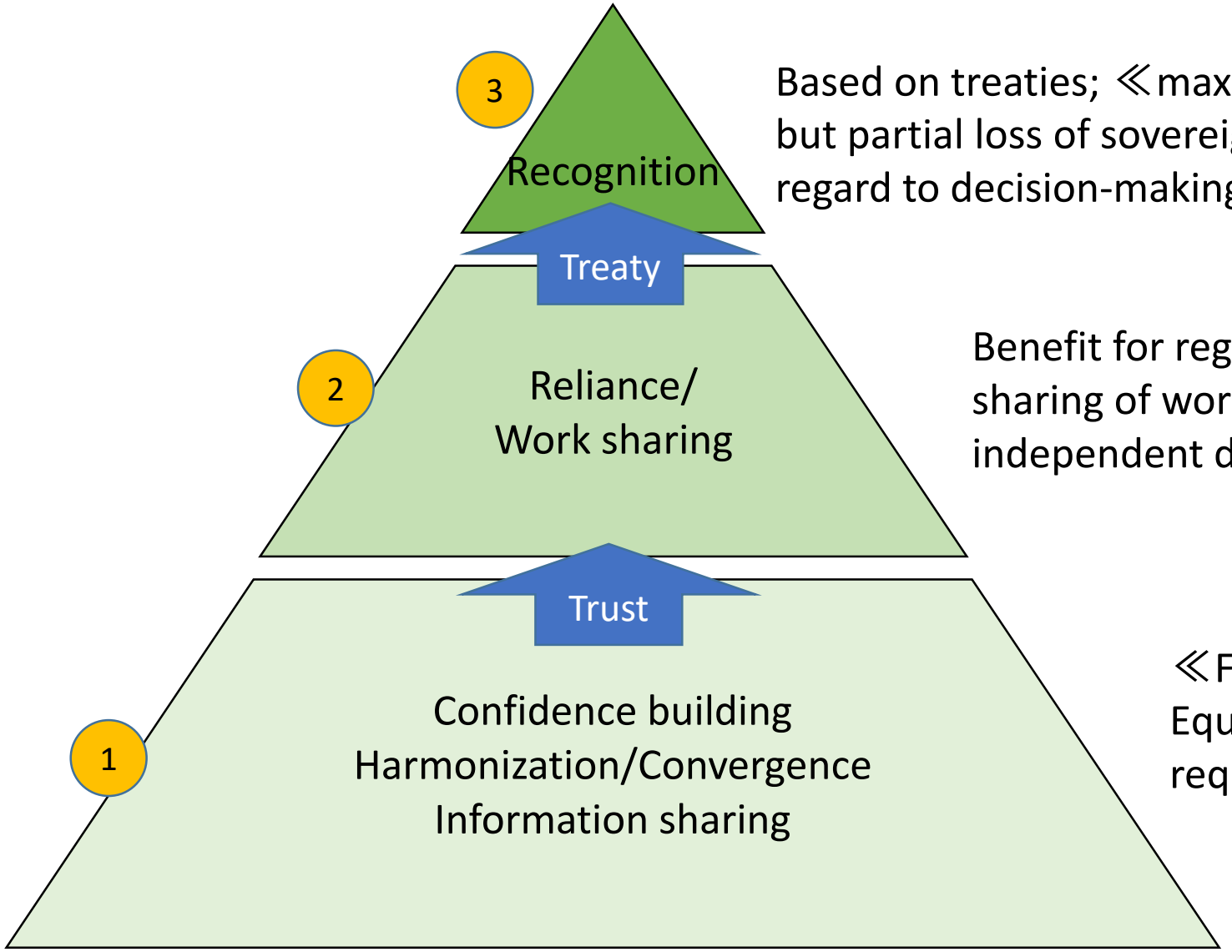
Patient First

Safety First

Asia First

Access First

Views on Reliance and Recognition in WHO



Based on treaties; ≪maximal benefit≫ but partial loss of sovereignty with regard to decision-making

Benefit for regulators; sharing of workload, but independent decisions

≪Foundation≫ Equivalence of requirements

Essential points of the Grand Design

Basic Policy for Asian Human Well-Being Initiative (determined by Headquarters for Healthcare Policy in July 2016, revised in July 2018)

・In order to contribute to the elimination of drug lags between Japan and Asia, **harmonization will be promoted so that the pharmaceutical approval and safety regulations in Asia will become more effective and reasonable**, such as securing the interoperability of data used for drug approval in Asian countries.

1. Promote regulatory harmonization

- **Capacity building** including PMDA Asia Training Center
- **Reliance**
- **Support** to embrace international standards and to participate in international activity

2. Establish high quality clinical trial systems

- **The use of highly innovative pharmaceuticals and medical devices in the post-market phase is spread from clinical trial sites** to other facilities.
- Establishing clinical trial sites for pharmaceuticals/medical devices result not only **in accumulating useful evidence based on clinical trials**, but also **in improving access to post-market** pharmaceuticals/medical devices.
- To build the necessary infrastructure, Japanese government **examine the options available for financing other Asian partners**.

Publicity Papers on PMDA International Activity

http://www.pmda.go.jp/int-activities/outline/0007.html
http://www.pmda.go.jp/english/int-activities/outline/0006.html

Work Together for patients!!

All the players in good harmony

Thank you for your attention!