Lesson and learn from Covid pandemic regulatory agility in Japan

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PMDA's Actions under COVID-19 pandemic

1. Speedy approvals of COVID-19 products
   - Special Approved for Emergency (SAE)
   - Close interaction with sponsors
   - Allowing quick start of clinical trial
2. Establishment of New regulations
   - Marketing Approval in Emergencies (MAE)
3. Maintain development/distribution of non-COVID-19 products
   - Q&A management of clinical trials
   - Remote inspections
   - Maintain manufacturing and distribution medical products

Special Approval for Emergency (SAE)

Under article 14-3 of the PMD Act, a certain medical product may be approved when

1. an emergency situation requires an unapproved medical product to be used to prevent damage to the public health caused by the spread of diseases

2. such emergency situation cannot be managed appropriately by any means other than the use of the unapproved product, and

3. such product is legally available in a country with a regulatory system for medical products that is equivalent to Japan

Example: Remdesivir (Special approval for emergency)

Timeline for SAE of Remdesivir

1st May 2020 The Emergency Use Authorization of Remdesivir by the U.S. FDA

2nd May 2020 Cabinet Order amendment

4th May 2020 Submission in Japan

3 days

7th May 2020 Special approval for emergency

Example: Remdesivir (Special approval for emergency)

Success factors

- **Close communication** with sponsor/applicant
- Rolling submission and rolling review

Marketing Approval in Emergencies

	Conventional Approval	Immediate approval in case of emergency	
		Special Approval for Emergency use Article 14-3	Emergent approval Article 14-2-2 (Enacted on 20 May 2022)
Target	All pharmaceuticals, etc.	Pharmaceutical, etc. distributed in foreign countries (countries that have a pharmaceutical system which level is equivalent to that of Japan)	All pharmaceuticals, etc.
Purpose of the system	Granted to pharmaceutical, etc. whose efficacy and safety have been confirmed based on scientific evidence	Granted to pharmaceutical, etc. that are approved for marketing in foreign countries in order to prevent the spread of health hazards in emergencies.	Granted to pharmaceutical, etc. whose **safety has been confirmed** and whose efficacy is **estimated to be effective**, in order to prevent the spread of health hazards in emergencies.
Efficacy /Safety	**Efficacy: Confirmed** **Safety: Confirmed**	**Efficacy: Confirmed** **Safety: Confirmed**	**Efficacy: Estimated** **Safety: Confirmed**
Special Exception	-	●GMP inspections (Submit later) ●National tests (Submit later) ●Regulations on containers and packaging of the pharmaceutical (possible to use foreign language), etc.	●GMP inspections (Submit later) ●National tests (Submit later) ●Regulations on containers and packaging of the pharmaceutical (possible to use foreign language), etc.

Vaccine Pharmacovigilance (PV) Network

Objectives

- Promote confidence in COVID-19 vaccines
- Share the COVID-19 Vaccine Safety Information in a timely manner

Activities

- ICMRA issued joint statements about the importance, safety and effectiveness of vaccines (June 2020)
- ICMRA developed a statement aimed to help healthcare professionals answer questions about the role of regulators in the oversight of COVID-19 vaccines

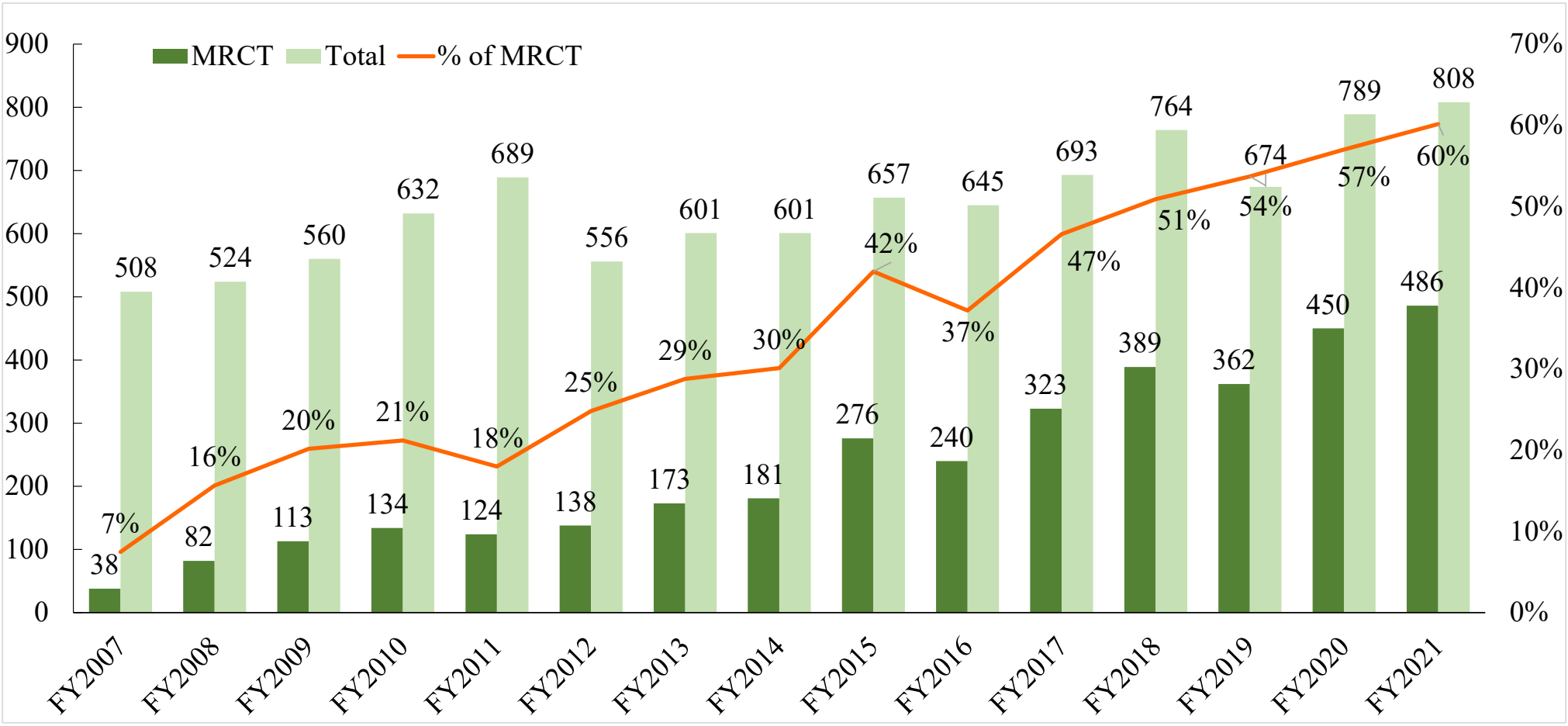
Statement for healthcare professionals: How COVID-19 vaccines are regulated for safety and effectiveness (Revised 17 May 2022)

ICMRA
International Coalition of Medicines Regulatory Authorities

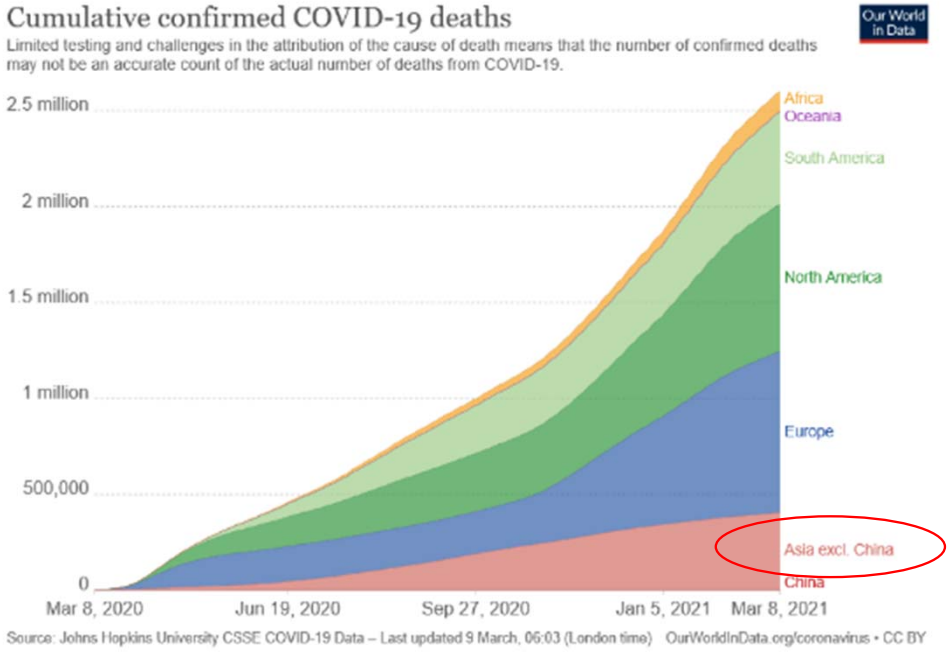
Joint Statement from the International Coalition of Medicines Regulatory Authorities and World Health Organization

Healthcare professionals and public health authorities have a central role in discussing vaccination against COVID-19 with their patients. Vaccines play a critical role in preventing deaths, and hospitalisation caused by infectious diseases, and are contributing to controlling the spread of the disease, thus their impact on infection and serious illness is significant. Both vaccinated and unvaccinated people also need to be aware of the additional protective behaviours required to control the pandemic locally.

Trends of MRCT-related Clinical Trial Notifications in Japan



Similarity in Asian region



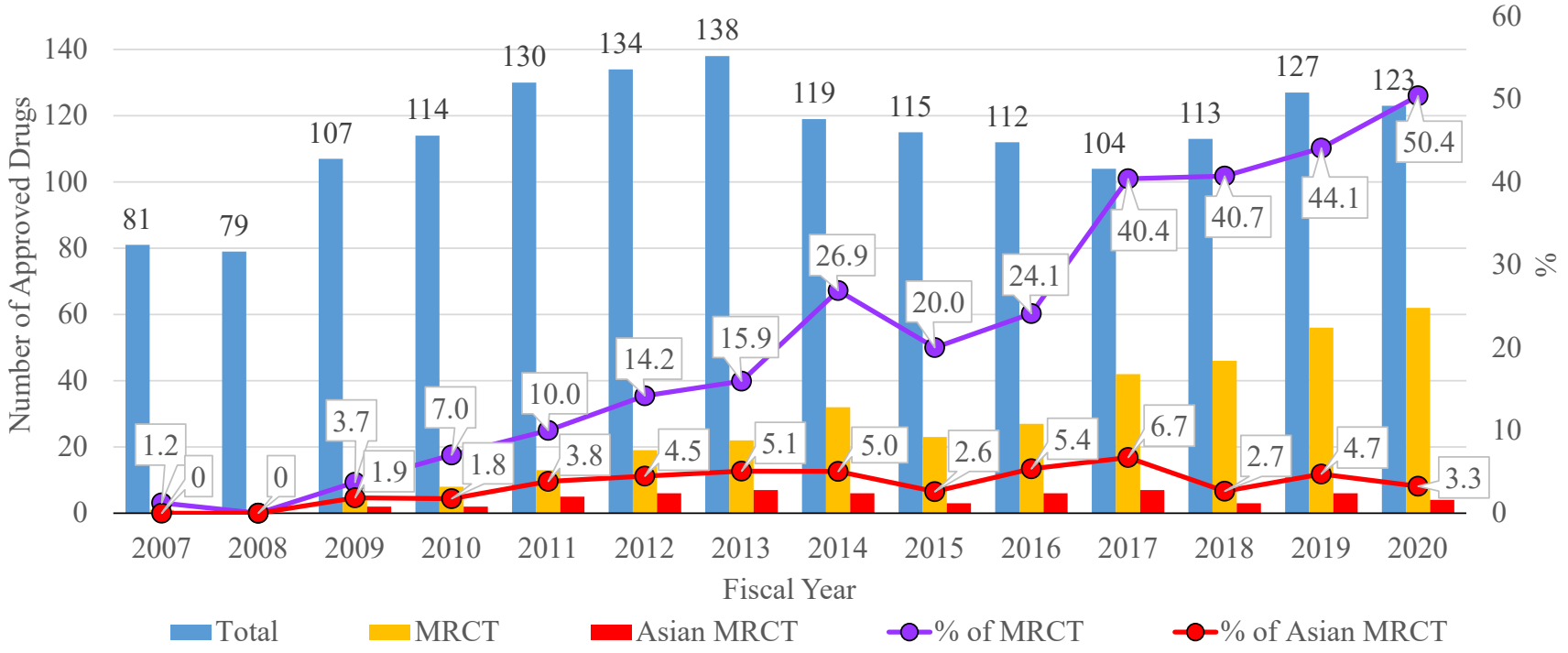
https://ourworldindata.org/grapher/cumulative-covid-deaths-region

ICH-E5

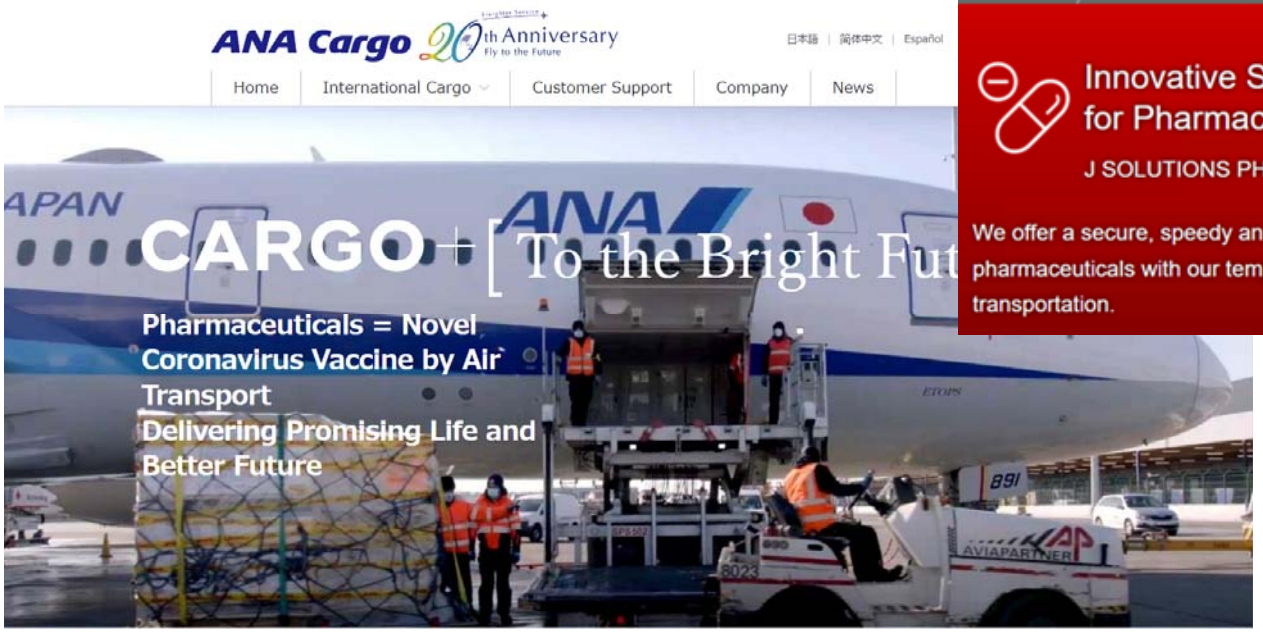
INTRINSIC		EXTRINSIC
Genetic	Physiological and pathological condition	Environmental
Gender		Climate
	Height	Sunlight
	Body weight	Pollution
	Liver	Culture
	Kidney	Socioeconomic status
	Cardiovascular functions	Educational status
		Language
	ADME	
	Receptor sensitivity	Medical practice
		Disease definition/Diagnostic
Race		Therapeutic approach
		Drug compliance
		Smoking
		Alcohol
Genetic polymorphism of the drug metabolism		
		Food habit
		Stress
Genetic diseases	Diseases	Regulatory practice/GCP
		Methodology/Endpoints

Trend of Asian Study

- Regarding several diseases such as liver cancer, gastric cancer and infectious diseases like malaria, medical needs in Asia are higher than that in other regions.
- A question whether Asian MRCTs are conducted sufficiently or not is raised.



Direct flights specific for pharmaceuticals from/to oversea countries



Innovative Solutions for Pharmaceutical Shipments - JAL International Cargo

Cargo + [To the Bright Future] | ANA Cargo

Pharmaceutical Quality Knowledge Management System (PQKMS)

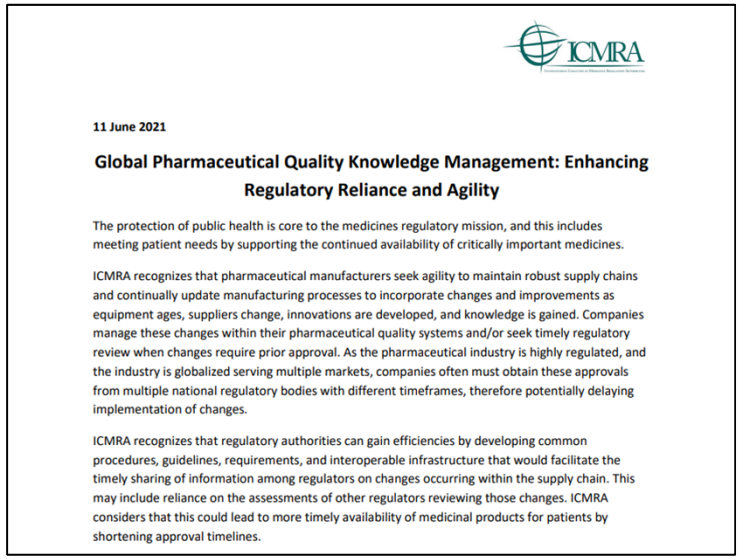
Objectives

- Support the development of a collective Pharmaceutical Quality Knowledge Management System (PQ KMS) capability

Activities

Published…

- Statement in June 2021
- ICMRA-ICH-PIC/S-IPRP Joint Reflection Paper in August 2022
- Collaborative Pilot Information and Application Forms in June 2022



ICMRA

11 June 2021

Global Pharmaceutical Quality Knowledge Management: Enhancing Regulatory Reliance and Agility

The protection of public health is core to the medicines regulatory mission, and this includes meeting patient needs by supporting the continued availability of critically important medicines.

ICMRA recognizes that pharmaceutical manufacturers seek agility to maintain robust supply chains and continually update manufacturing processes to incorporate changes and improvements as equipment ages, suppliers change, innovations are developed, and knowledge is gained. Companies manage these changes within their pharmaceutical quality systems and/or seek timely regulatory review when changes require prior approval. As the pharmaceutical industry is highly regulated, and the industry is globalized serving multiple markets, companies often must obtain these approvals from multiple national regulatory bodies with different timeframes, therefore potentially delaying implementation of changes.

ICMRA recognizes that regulatory authorities can gain efficiencies by developing common procedures, guidelines, requirements, and interoperable infrastructure that would facilitate the timely sharing of information among regulators on changes occurring within the supply chain. This may include reliance on the assessments of other regulators reviewing those changes. ICMRA considers that this could lead to more timely availability of medicinal products for patients by shortening approval timelines.

PIC/S

(The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme)

- ✓ **Established in 1995, as an extension to the Pharmaceutical Inspection Convention (PIC) of 1970.**
- ✓ **Currently 54 participating authorities**

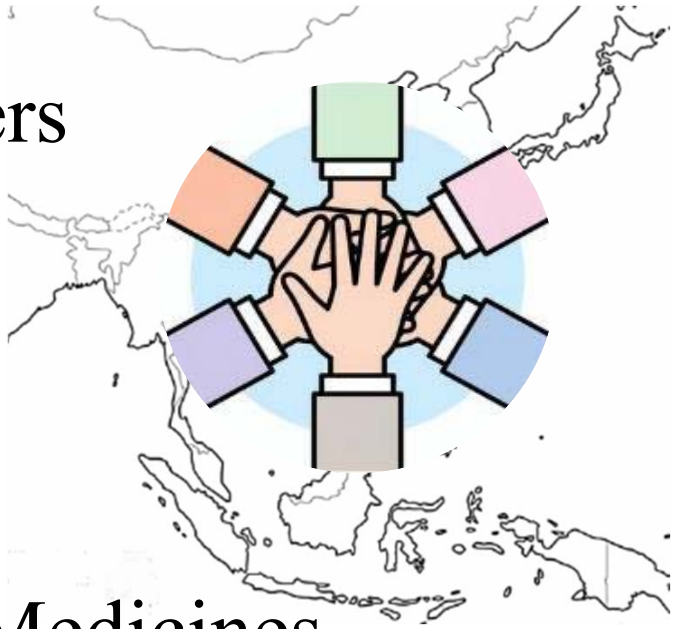
PIC/S aims to **increase mutual confidence in the field of GMP** through by;

- ➢ Harmonized GMP standards
- ➢ Training to inspectors
- ➢ Quality systems of inspectorates
- ➢ Co-operation and networking among competent authorities and international organizations. [ex.inspection reports sharing] etc...

- ✓ **MHLW/PMDA joined in 2014**
- ✓ **MHLW/PMDA hosted in 2019;**
  - **The 48th PIC/S Committee Meeting**
  - **PIC/S Seminar (Training for GMP inspectors)**

Working as “Team Asia” toward Asian people

1. Well communications with stakeholders
2. Regulatory Agility
3. International collaborations
   - Especially in Asia
4. Maintain distribution of high quality Medicines



Collaboration with India is the Key!

Work together with transparency for patients/citizens needs in own country and globally