GCP/Clinical Investigation in Japan
Industry perspective

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Agenda

- Clinical Regulations in Japan
- Global *Chiken* Pre-marketing Studies Experience
- Challenges of Clinical Infrastructure in Japan
- Global Regulatory Harmonization for Clinical Evidence

Clinical Regulations in Japan

Clinical Regulations in Japan

Clinical Trial Act was promulgated on 14th April, 2017 and enforced on April 1st, 2018 to regulate non-regulatory studies in Japan.

English translated Clinical Trial Act can be found at the below web page
https://www.mhlw.go.jp/file/06-Seisakujouhou-10800000-Iseikyoku/0000213334.pdf

Clinical Regulations in Japan

Until March 31st, 2018

Study Type	Regulatory Studies		Non-Regulatory Studies
	Chiken pre-marketing Study	Post-marketing Study	
Regulations	Pharmaceuticals and Medical Devices, etc. Act		-
	Good Clinical Practice (GCP)	Good Post-marketing Study Practice (GPSP)	Ethical Guidelines

Clinical Regulations in Japan

Since April 1st, 2018

Study Type	Regulatory Studies		Non-Regulatory Studies		
			Specified clinical studies		Others
	Chiken pre-marketing study	Post-marketing study	Clinical studies for unapproved products or off-label use	Clinical studies funded by a MAH company, etc.	
Regulations	Pharmaceuticals and Medical Devices, etc. Act		Clinical Study Act		
	Good Clinical Practice (GCP)	Good Post-marketing Study Practice (GPSP)	The Implementation Standards (Obligation to comply)		The Implementation Standards (Obligation to make efforts)

Global *Chiken* Pre-marketing Studies Experience

Medical Device Trials in Japan

Table: No. of Clinical Trial Notification (CTN) Submitted in Medical Devices v.s. Pharmaceuticals

		2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Medical Device	First CTN*	20 (1)	19 (0)	15 (0)	19 (2)	27 (3)	29 (0)	25 (3)	32 (2)	31 (4)	31 (7)	31 (8)	34 (8)
	Followed CTN*	2 (0)	7 (0)	2 (0)	2 (0)	7 (0)	6 (0)	4 (0)	11 (1)	14 (0)	6 (2)	10 (0)	20 (1)
	Total	22 (1)	26 (0)	17 (0)	21 (2)	29 (3)	35 (0)	29 (3)	43 (3)	45 (4)	37 (9)	41 (8)	54 (9)
Pharmaceutical	First CTN*	112 (5)	112 (0)	129 (1)	128 (0)	129 (1)	159 (5)	165 (3)	132 (13)	127 (6)	151 (20)	127 (10)	134 (10)
	Followed CTN*	422 (6)	387 (5)	379 (14)	396 (8)	431 (16)	473 (6)	524 (56)	424 (19)	474 (25)	450 (33)	530 (45)	511 (63)
	Total	544 (11)	499 (5)	508 (15)	524 (8)	560 (17)	632 (11)	689 (59)	556 (32)	601 (31)	601 (53)	657 (55)	645 (73)

1) *First CTN means clinical trial notification submitted for a product's first time in Japan while followed CTN means the product's second or later submission, e.g., for indication expansion, etc.
2) Number in () indicates one for investigator initiated pre-marketing study

Global Trials Experience

2003
- No Global Trials for Medical Devices
- PMDA Established in 2004
- New Japanese Medical Device GCP in 2005

2008
- A Few Global Medical Device Trials Started
- Faced Some Differences in Japan v.s. Outside Japan (Regulation, General Medical Treatment, Control Product, etc.)

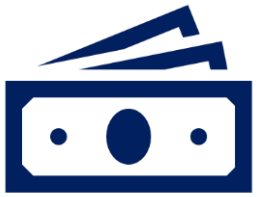
2013
- Found out Solutions to Challenges (e.g.,Comparing GCP requirements in Japan and the US. http://www.jfmda.gr.jp/hbd/pdf/GCP_en.pdf
- Discussion Started on Japanese Trial Costs

2018
- More Experienced with Cardiovascular Area
- Solutions Needed for Effective Trial Execution, and Rebalancing of Pre and Post Marketing Clinical Data

Challenges of Clinical Infrastructure in Japan

Challenges in Japan

- Clinical Trial Costs
- Less number of medical device trials
- Less experienced clinical staffs (i.e., CRO and SMO)
- English Operations



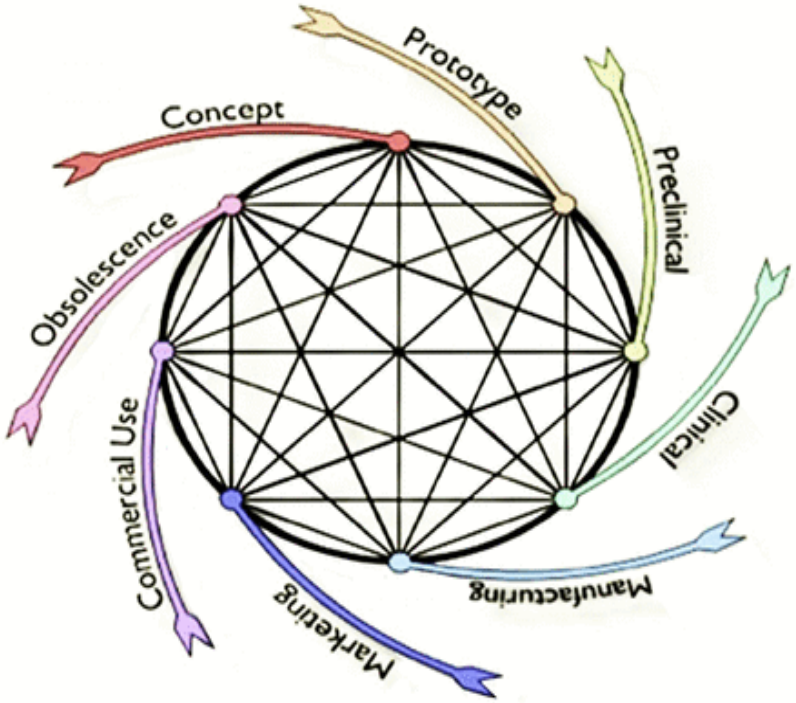
Advantages:

- High quality clinical data
- Fast subjects enrollment

Global Regulatory Harmonization for Clinical Evaluation

The Total Product Life Cycle

Not only focusing on pre-marketing clinical data, but rebalancing between pre-marketing clinical data and post-marketing clinical data

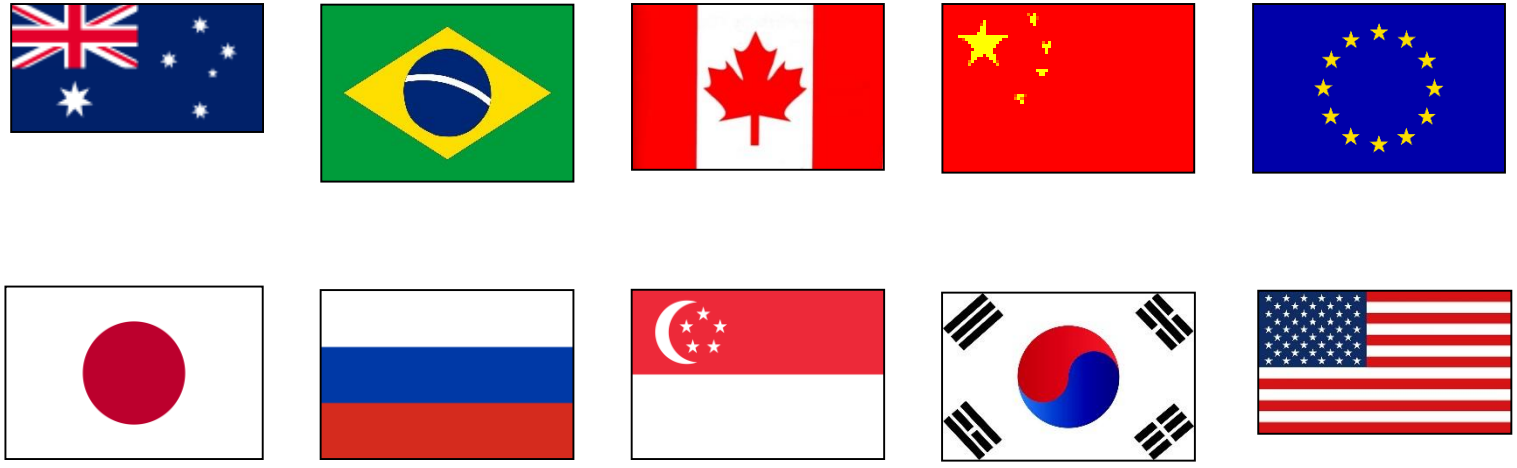


Source of Figure: CDRH INNOVATION INITIATIVE. February 2011. downloaded from https://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHInnovation/UCM242528.PDF on 15th August, 2018

IMDRF

International Medical Device Regulators Forum is a voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF) and aims to accelerate international medical device regulatory harmonization and convergence.

IMDRF was born in October 2011, when representatives from the medical device regulatory authorities of Australia, Brazil, Canada, China, European Union, Japan and the United States, as well as the World Health Organization (WHO) met in Ottawa to address the establishment and operation of this new Forum. A copy of the outcome statement from this meeting is available from the Meetings page. (source: http://www.imdrf.org/index.asp)



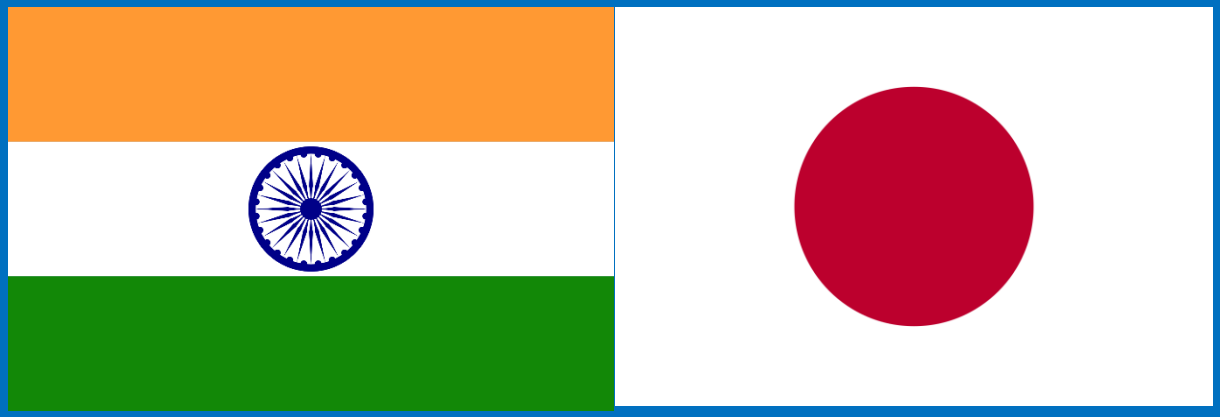
IMDRF – Registry WG

Table: Released Technical Documents from IMDRF Registry Working Group

Title	Link to the technical documents	Date
Principles of International System of Registries Linked to Other Data Sources and Tools	http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-160930-principles-system-registries.pdf	30 September 2016
Methodological Principles in the Use of International Medical Device Registry Data	http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-methodological-principles.pdf	16 March 2017
Tools for Assessing the Usability of Registries in Support of Regulatory Decision-Making	http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-180327-usability-tools-n46.pdf	27 March 2018

IMDRF – Clinical Evaluation WG

- The New Work Item Proposal “Medical device clinical evaluation” was just approved by the IMDRF Management Committee.
  http://www.imdrf.org/docs/imdrf/final/meetings/imdrf-meet-180320-china-meeting-outcome-statement.pdf
- Look forward to learning from upcoming technical documents



Thank you for your kind attention