Symposium 6
Establishment and Future of the National Consortium for Regenerative Medicine

NRMD & REAP

JSRM's Clinical Databases for Regenerative Medicine

Yoji Sato, Ph.D.
Division of Drugs, National Institute of Health Sciences
Database Committee, Japanese Society for Regenerative Medicine

DISCLAMER

NRMD & REAP：日本再生医療学会の再生医療等臨床データベース

佐藤陽治
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薬品部

筆頭演者は、過去１年間（1月～12z月）において、本演題の発表に関して開示すべきCOIはありません。

本発表で述べられた見解・意見は発表者のものであり、必ずしも国立医薬品食品衛生研究所、厚生労働省、日本再生医療学会の公式な方針や見解を示すものではありません。

NRMD & REAP: The Japanese Society for Regenerative Medicine's Clinical Databases for Regenerative Therapies

Yoji Sato, Ph.D.,
Division of Drugs,
National Institute of Health Sciences

For the past year (January–December), the speaker has no COI to disclose for this presentation

The views and opinions expressed in this presentation are those of the presenter and do not necessarily represent official policy or position of the National Institute of Health Sciences, the Ministry of Health, Labour & Welfare, or the Japanese Society for Regenerative Medicine.

1. What are NRMD and REAP?

NRMD and REAP: Features of the two databases

JSRM

Regenerative Medicine Patient Data Registration Systems Established and Operated by the Japanese Society for Regenerative Medicine

NRMD *(National Regenerative Medicine Database)*

NRMD/CR Platform for registering
non-commercial clinical research on specified processed cells,
certified advanced medical care using specified processed cells, and
commercial clinical trials of regenerative medical products

NRMD/PMS Platform for registering
post-marketing surveillance of regenerative medical products

REAP *(Regenerative Medicine Evidence Accumulation Platform)*

Platform for registering
therapies based on physician's discretion using specified processed cells

There is no particular difference in the electronic data capture (EDC) system used.

NRMD and REAP: Features of the two databases

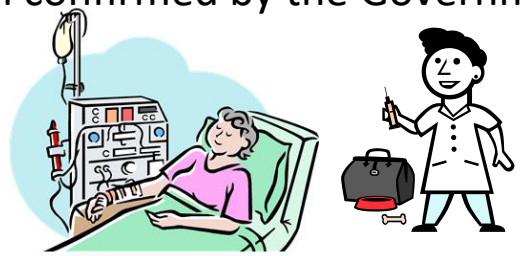
JSRM

Name	Patient Data Registration System for Regenerative Medicine (RM)		
	REAP (RM Evidence Accumulation Platform)	**NRMD** (National Regenerative Medicine Database)	
Main Purpose	Verification of RM	Development & Evaluation of RM	Commercial Development of Regenerative Medical Products
Relevant Law	Act on the Safety of RM (**RM Safety Act**)		Pharmaceuticals & Medical Devices Act (**PMD Act**)
Target	[RM Safety Act] Therapies based on physician's discretion using specified processed cells (= cell processed products not yet approved by the MHLW)	NRMD/CR [RM Safety Act] Non-commercial clinical research on specified processed cells or certified advanced medical care using them	[PMD Act] Commercial clinical trials for regenerative medical products
			NRMD/PMS [PMD Act] Post-marketing surveillance (PMS) for regenerative medical products (= cell processed products or gene therapeutics)
Determination of Input Items	Joint WG of Regenerative Medicine-Related Societies	WG of the Registry Committee of the Japanese Association of Medical Sciences	

Two Acts Regulating RM/CT

Regenerative Medicine (RM)
Cell Therapy (CT)

Medical practices using processed cells, whose safety and efficacy have not yet been confirmed by the Government



Manufacturing and marketing of **products for RM/CT** by firms

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- Clinical researches using processed cells (non-commercial)

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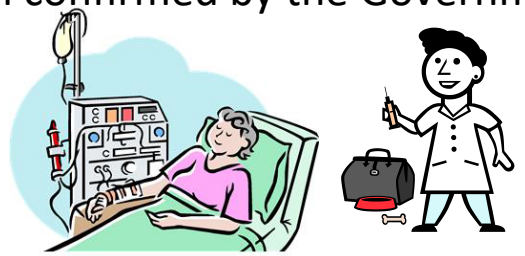

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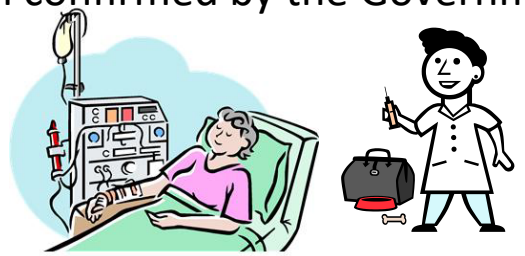

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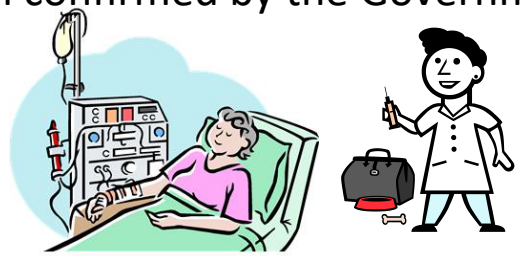

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Current status of NRMD/REAP (as of March 2024)

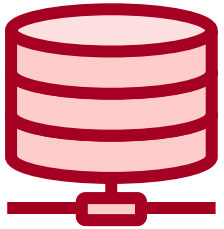
REAP (Mar 2023～)

Already in Use	Under Develop-ment	Under Consid-eration
3	0	3

NRMD/CR (Oct 2017～)

Already in Use	Under Develop-ment	Under Consid-eration
4	2	2

NRMD/PMS (Mar 2018～)



Already in Use	Under Develop-ment	Under Consid-eration
6	0	1

2. Overview of NRMD

Two Acts Regulating RM/CT

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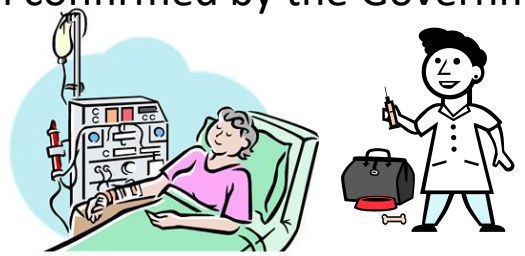

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Two Major Regulatory Challenges for the Development of Regenerative Medical Products

JSRM

☐ Conventional approval process

☐ New approval process that accommodates early practical application of RM products

- If data from the clinical trial are likely predict efficacy and confirming safety, conditional/term-limited marketing authorization for RM products might be granted to timely provide the products to patients.
- The PMD Act requires further confirmation of safety and efficacy during the post-marketing phase.

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Real world data are quite important!

Non-commercial Clinical Research → Clinical Trial (confirmation of efficacy and safety) → Approval → Marketing

☐ New approval process that accommodates early practical application of RM products

Non-commercial Clinical Research → Clinical Trial (likely to predict efficacy, and confirming safety) → Conditional/ Term-limited Approval → Marketing (Further confirmation of efficacy and safety) → Approval (or Revocation) → Marketing Continues

Post-marketing safety measures must be taken, including prior informed consent of risk to patients

RM Safety Act

PMD Act

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Challenge

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Background of NRMD Construction

Report of the Study Group on the Ideal Patient Registration System for Regenerative Medical Products and the Study Group on the Ideal Patient Registration System for *In-Vitro* Implantable Medical Devices (MHLW, July 4, 2014)

"Considering that a wide variety of products are expected for regenerative medical products and implantable medical devices and that the number of patients using each product is not necessarily large, it is efficient for medical institutions, academic societies, manufacturing/marketing authorization holders, and the government to cooperate to establish and utilize a cross-sectional patient registration system, rather than for manufacturing/marketing authorization holders to establish a patient registration system for each product."

History of NRMD

PMDA

Constructed a post-marketing surveillance EDC (with the reliability assured by CSV)

2015

AMED

Outsourced the development of RMed-Japan (mainly for non-commercial clinical research) to JSRM as a contract R&D project

The RM National Consortium

2016

JSRM

Integrated PMDA-built EDC and RMeD-Japan services, adopted Viedoc as platform, and renamed NRMD.

2016
2017

NRMD

NRMD operation started **by JSRM**

2017

EDC employed for NRMD/CR and NRMD/PMS

JSRM

Clinic/PMS

Study Registration and Reference
Compliant with the GPSP Ordinance

Reports

Diverse reporting services

Me

ePRO/eCOA Services

TMF

Document management of related documents

Connect

Video Calling Service

Logistics

Common Management System for Regenerative Medicine Product

In addition to Viedoc EDC, there are several other services available.

Outline of NRMD

JSRM

※To be discussed in the future

Manufacturing Management System

Quality/Mfg Data

Application Programming Interface (API)

Mfg/Res Support Systems

Clinical Data

WGs of Registry Council for Regenerative Medicine
The Japanese Association of Medical Sciences

Determination of input items

	NRMD/CR				NRMD/PMS			
	Items specific to each clinical study				Items specific to each product			
2F	PRP Study #1	PRP Study #2	Cornea Study	Heart Study	PRP Product	Heart Product	Cornea Product #1	Cornea Product #2
	Common items for PRP		Common items for ophthalmo-logy/corneal diseases	Common items for cardiology	Common items for PRP	Common items for cardiology	Common items for ophthalmology/corneal diseases	
1F	Common basic items (established by PMDA) e.g., basic patient information, consent information, adverse events, clinical conditions, study discontinuation, study termination, etc.							

Product Development

Reverse Translational Research (Product Verification/Improvement)

CSV (Computerized System Validation) is applied to the clinical research database to ensure the data quality and to realize seamless utilization of real-world data for product development and reverse translational research. (CR has been operational since October 2017, and PMS since March 2018)

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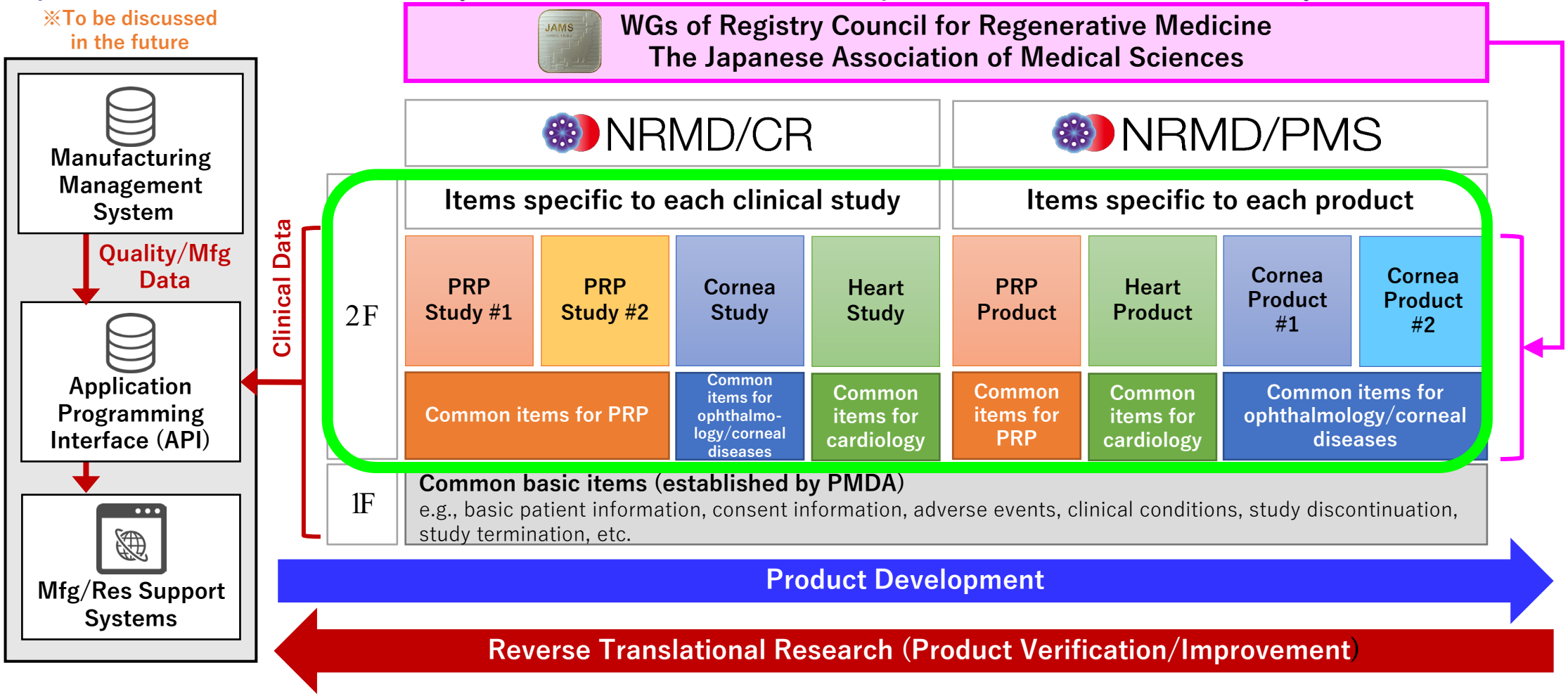
1F: Common basic items (general items determined in consultation with PMDA)

Category	Items
General Information	consent, date of consent, post-marketing survey flag, date of birth, and gender, date of use or start of use, time of use or start of use, height, weight, primary disease, disease history, complications, allergies, specific allergies
Periodic Survey	survey conducted or not, date of observation
Adverse Events /Defects Information	whether or not an adverse event occurred, type of the adverse event, date of onset, severity, treatment or other measures for the adverse event, specific details, date of outcome, outcome, detailed status, causal evaluation, opinion on the adverse event, whether or not a defect occurred, type of the defect, date of occurrence
Survey Completion	Date of survey completion, reason for survey completion, detailed status

https://www.pmda.go.jp/safety/surveillance-analysis/0036.html

Outline of NRMD



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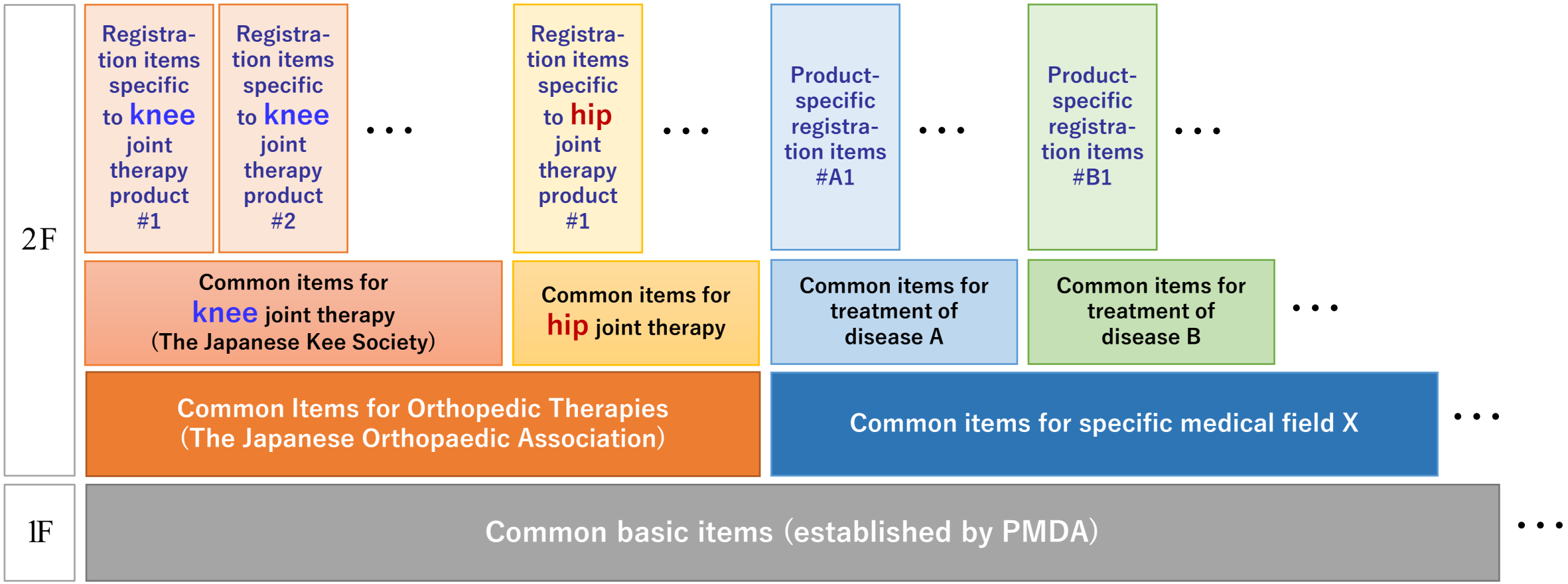
2F: Hierarchy of product/disease-specific items (examples)



3. Overview of REAP

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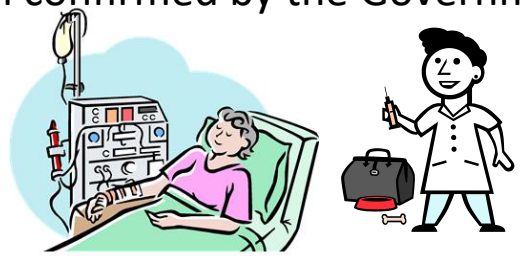

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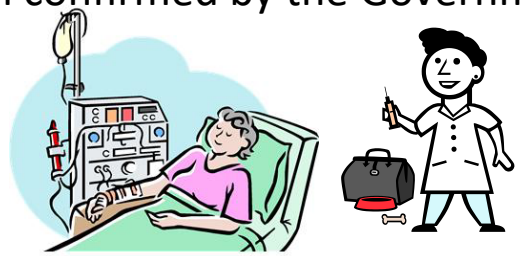

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The Establishment of REAP

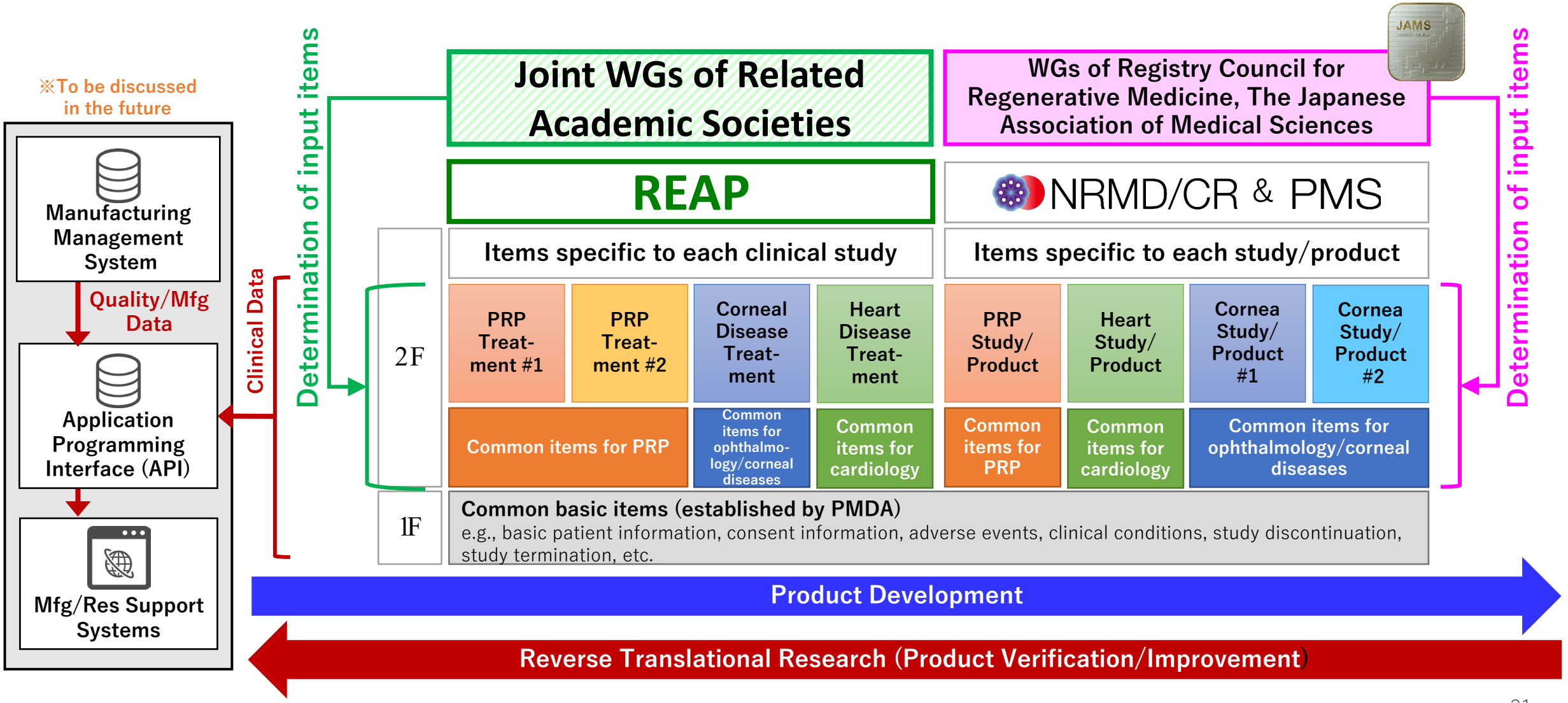
Background

- From the viewpoints of public health and new product development, **a registry should be established for therapies using unapproved cell processed products**, which is legal in Japan **as medical practices at the discretion of physicians**, and **information on their safety and validity (efficacy) should be accumulated**.
- Asking for cooperation of the Japanese Association of Medical Sciences in the development of input items for their clinical results may give rise to the misunderstanding that the JAMS is promoting unproved medical treatment.

Solution

- **REAP (Regenerative medicine Evidence Accumulation Platform)** was established in 2023 as a registry service for such treatments, independent of NRMD.
- Related academic societies other than the Japan Medical Association are in charge of input items.

Outlines of NRMD & REAP



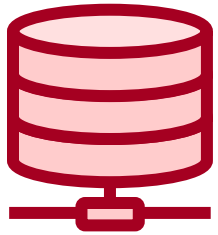
4. Operation and utilization of NRMD/REAP

Utilization of registration data

REAP

NRMD/CR

NRMD/PMS



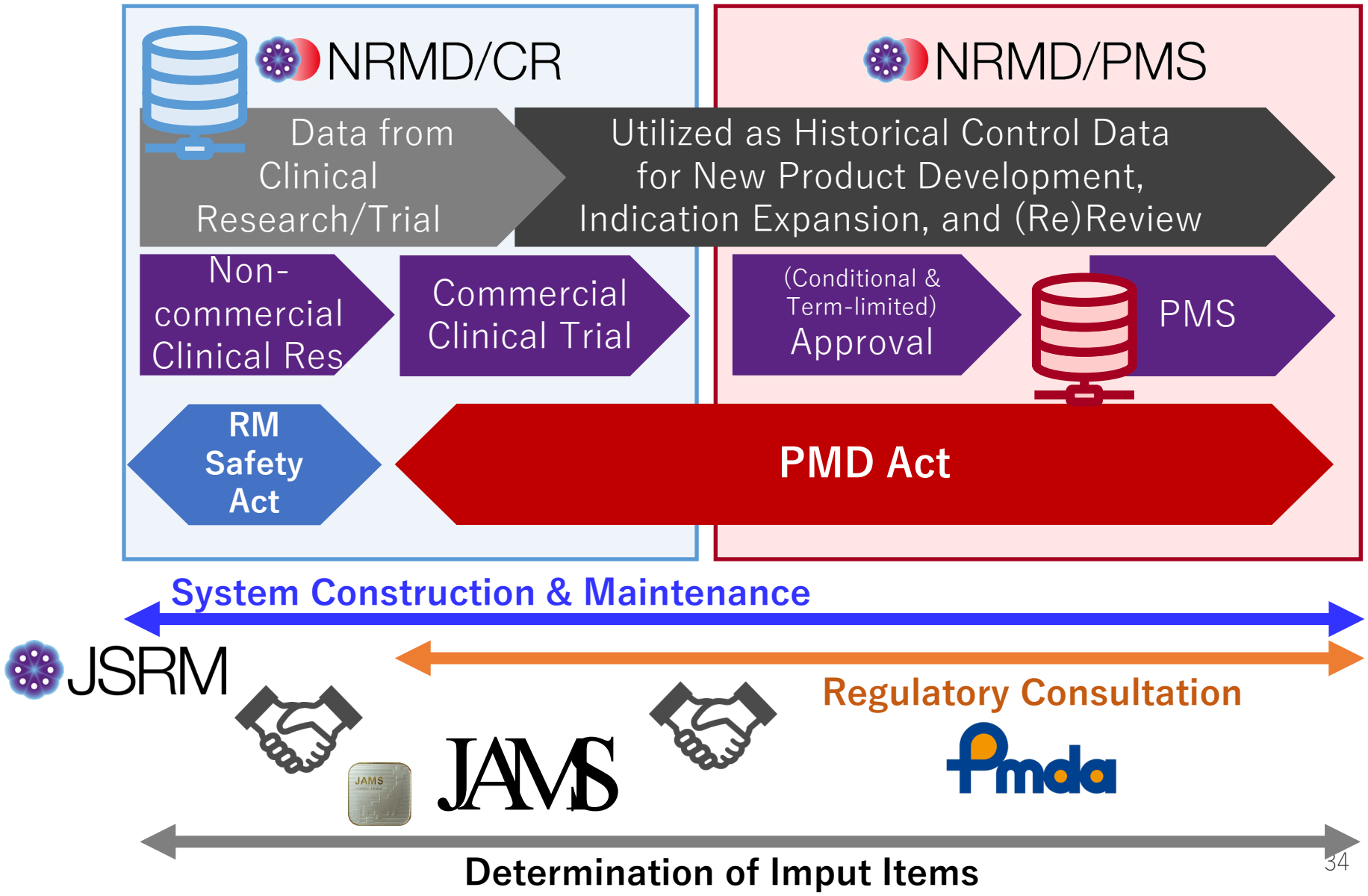
1. Data quality is assured for **REAP** and **NRMD/CR** by using CSV (Computerized System Validation), which conforms to **the Good Post-marketing Study Practice (GPSP) under the Pharmaceuticals and Medical Devices Act**.
(→ Certified Advanced Medical Care, Tech Transfer to Industry, *etc.*)

1. For **non-commercial clinical research** that allows for a control group, **data from the control group can be registered with the same quality**.

2. **Data from previous control groups may be used as historical controls** in subsequent non-commercial clinical research or post-marketing studies (PMS).

3. For products for which it is difficult to establish a control group, **a PMS-focused R&D design** could support smooth commercialization without reliance on randomized controlled trials (RCTs).

Integrated use of NRMD/CR, and NRMD/PMS



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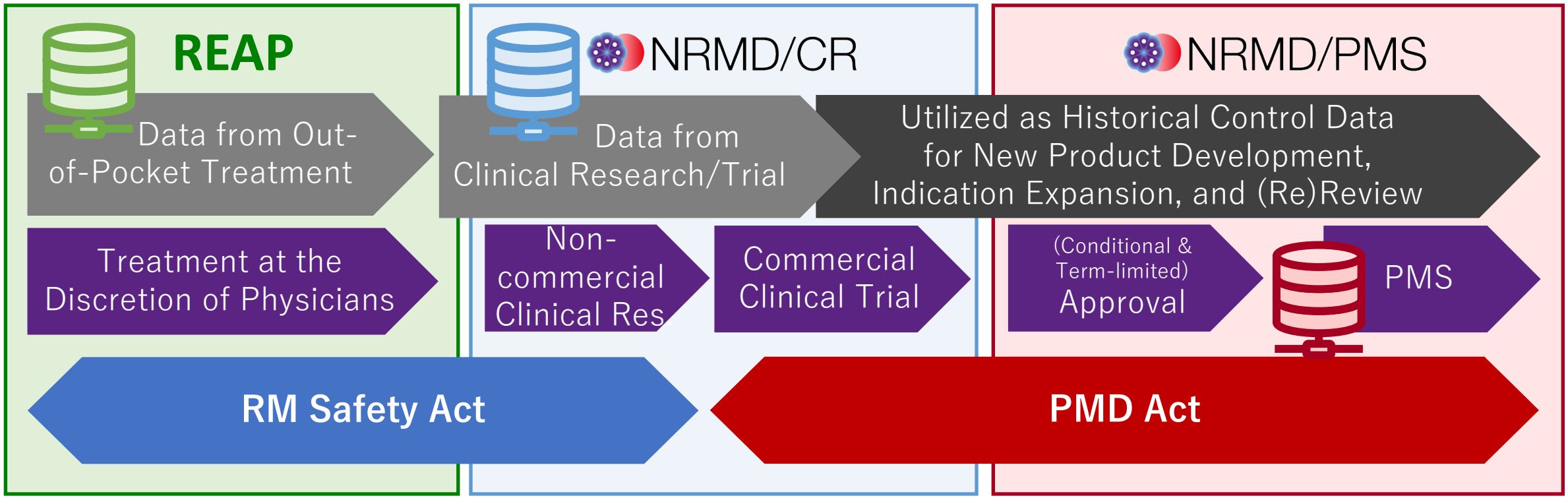

For more information about NRMD

For more information about REAP

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Visit
https://www.reap.jp