Efforts on the Japanese side

Session 1: Enhancing Review Efficiency of Pharmaceuticals and Medical Devices

4 October, 2016

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Office of International Programs
Pharmaceuticals and Medical Devices Agency

Today’s Content

1. Introduction

2. Promotion of Regulatory Science to the Global Level

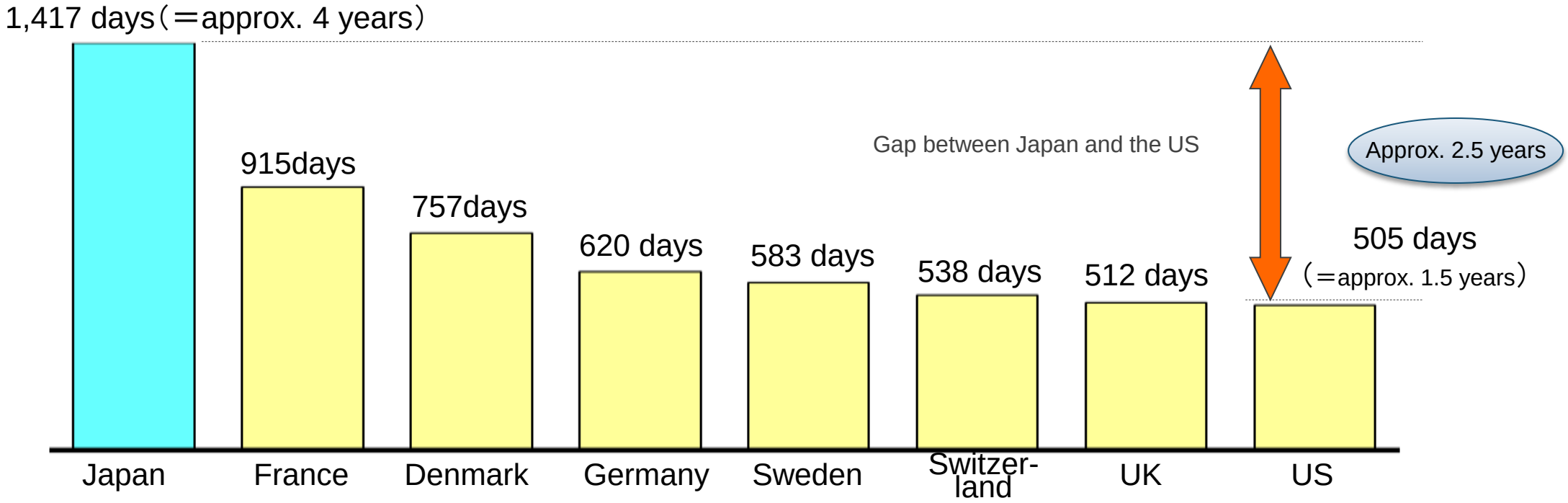
3. Promotion of Developing Innovative Products

Today’s Content

1. Introduction

Drug Lag – What did PMDA solve??

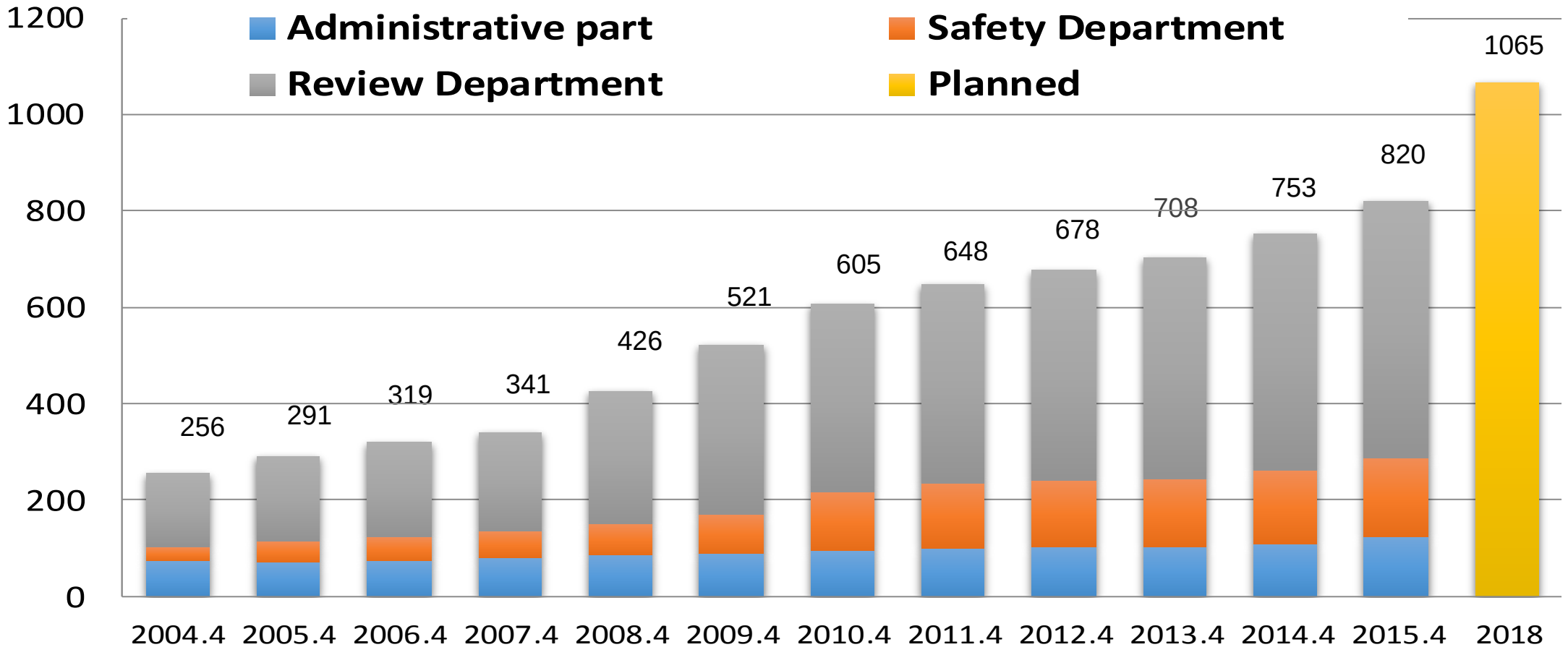
As at 2006, new drug marketing in Japan lagged on average 4 years behind the initial global launch, a gap of around 2.5 years over the US, the country with the smallest lag. *



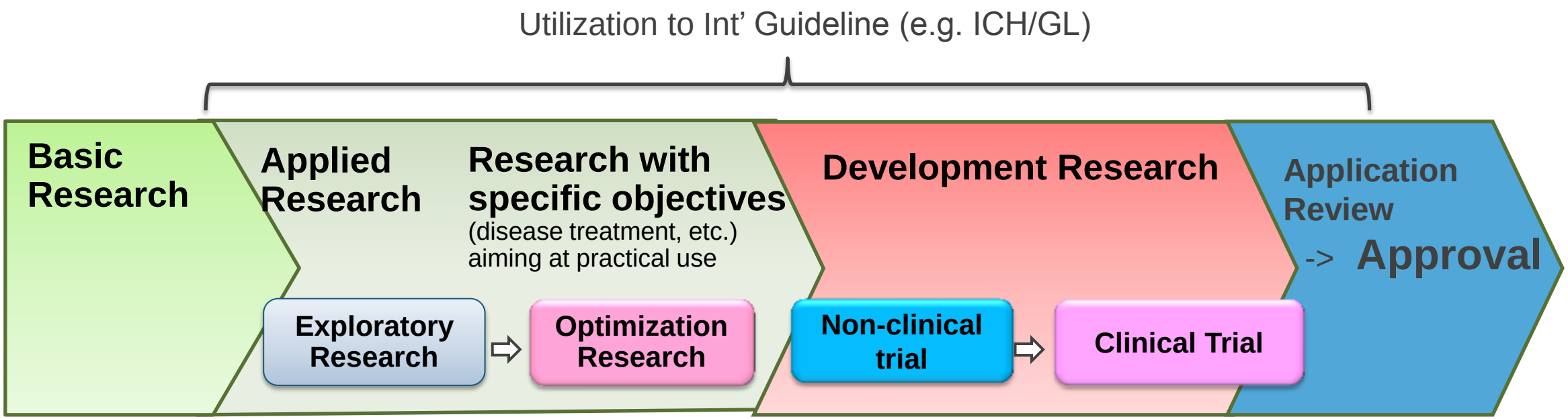
* The average of the number of days until marketing in the respective country following initial launch of the global top 100 products. Since the number of the top 100 products available varies with the country, the marketing lag has been calculated using only the number of products marketed in the respective country. For example, for the US where all drugs are available it was calculated using 88 of the 100 best-selling drugs after deduction of duplicate ingredients and those launched prior to 1981.

Source: OPIR Research Paper No. 31 (May 2006)

PMDA Staff Size



Enhancement of Consultation from earlier stage



[Old Model]

Consultation

LATER SATGE

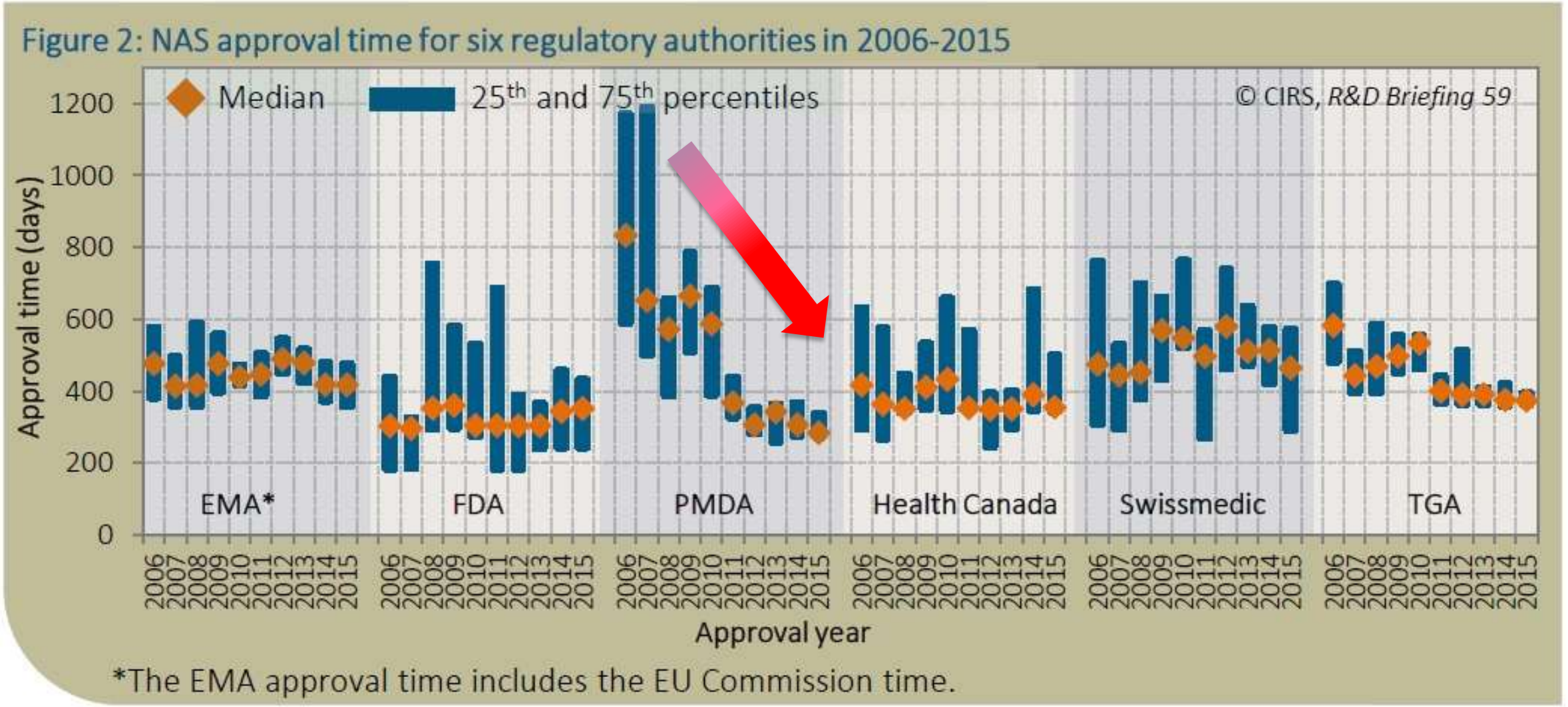
[New Model]

Consultation

EARLIER SATGE

Accelerate the application & approval period

PMDA achieved shorting approval time of new drug



R&D Briefing 59, May 2016, © Centre for Innovation in Regulatory Science, Ltd.
http://www.cirsci.org/wp-content/uploads/2016/05/CIRS_RD_-Briefing_59_23052016.pdf

Today’s Content

2. Promote Regulatory Science to the Global Level

Science Board

Basic Research

Seeds of new drug / medical devices

Quality Tests → Non-clinical tests → Clinical Trial → Review → Approve → Post Marketing

Practical use

Innovative medical products

Pharmaceutical consultation on R&D Strategy | Clinical Trial Consultation | Review | Post Marketing Safety Measure

Offices of Review (Drugs & Medical Devices), Office of Safety

Science Board

Established in May 2012 ;
to discuss how PMDA can better cope with products with advanced science & technology, in each developmental stage
(basic research, development support, product review, and PMS).

Board members

Communication

Academia (Knowledge of the Latest Innovative Technologies)

Outcome of the Science Board

1st term (FY2012 - 2013)

- Summary of discussion on the assessment of the current status of personalized medicine related to development and regulatory review (2014)
- **Summary of discussion on non-clinical pharmacological studies on anticancer drugs (2013)**
- Current perspective on evaluation of tumorigenicity of cellular and tissue-based products derived from induced pluripotent stem cells (iPSCs) and iPSCs as their starting materials (2013)

2nd term (FY2014 - 2015)

- Discussion on Evaluation of Medical Devices in Pediatric Use (2015)
- Proposal on Basic Principle to Quality Assurance of Cell Therapy (CT) Products (2015)
- Report on the use of non-clinical studies in the regulatory evaluation of oncology drugs (2016)
- Current Status and Perspectives of Placebo-Controlled Studies (2016)
- Report on the Use of Numerical Analysis for Evaluating the Strength of Orthopedic Implants (2016)

3rd term (FY2016 - 2017)

- Topics are now in discussion (rare diseases, bottle neck of medical development, and artificial intelligence)

Harmonization to International Guideline/Standards

[Pharmaceutical area]

- Participation to ICH
- Participation to PIC/S
- Bilateral talking with US/Europe on each area & GCP inspection

[Medical Devices area]

- Participation to IMDRF (GHTF)
- Participation to ISO/IEC standard setting (horizontal)

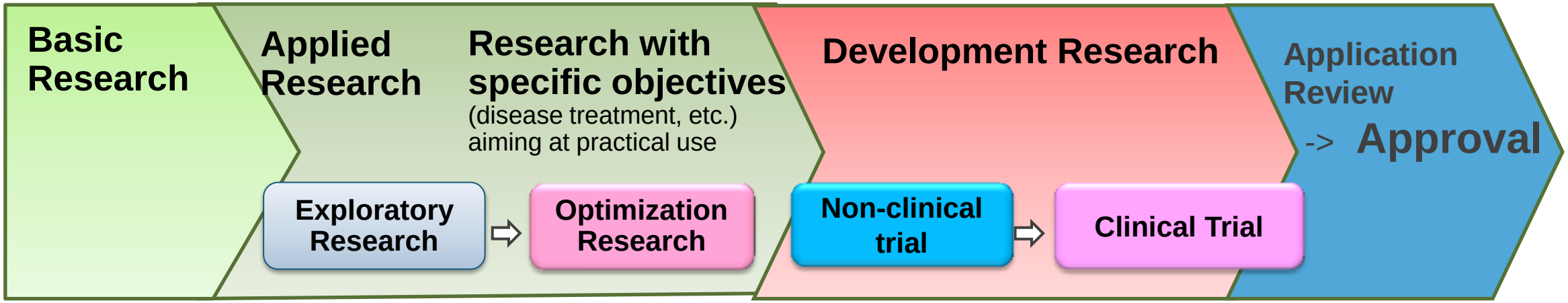
Can avoid duplicative works and seek common data utilization Under the harmonization

Today’s Content

3. Promotion of Developing Innovative Products

- Pharmaceutical Affairs Consultation on R&D Strategy
- SAKIGAKE Designation
- Conditional and Time-limited Authorization of Regenerative Medical Products
- Utilization to International Standards on Medical Devices

(1) Pharmaceutical Affairs Consultation on R&D Strategy



[Old Model]

Consultation

LATER SATGE

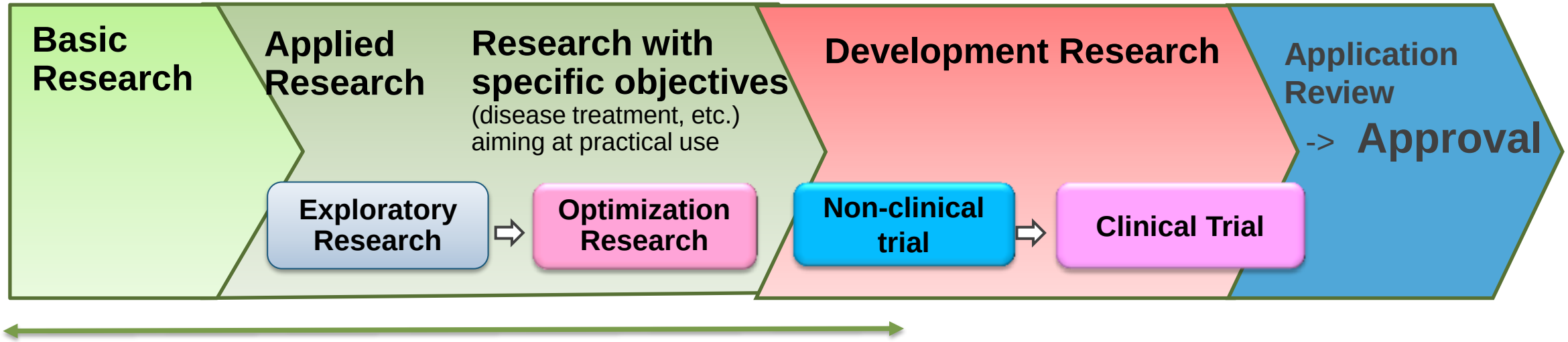
[New Model]

Consultation

EARLIER SATGE

Communication from the early development

Seamless Activity from Research to Approval
- Collaboration PMDA & AMED -



AMED* ⟷ **PMDA**

Close Collaboration

- Japan Agency for Medical Research and Development

Partnership Agreement with AMED

(August 19, 2015)

1. Utilizing Pharmaceutical Affairs Consultations on R&D Strategy
2. Support AMED to evaluate projects
3. Mutual cooperation to improve clinical research infrastructures
4. Sharing information

Japan Agency for Medical Research and Development (AMED) was established on 1 April, 2015, with following missions

1. Research and Development on Medical issues
2. Foundation of Clinical Study
3. Support towards commercialization
4. Promotion of International Strategy

Collaboration with other Organizations

Joint Graduate School Agreement（December 2009-）

with 19 graduate schools in medicine: Personnel Exchanges

Expansion and Improvement

Comprehensive Partnership Agreements since FY 2015

NCC (National Cancer Center) (February 2, 2016)

Hiroshima University (March 4, 2016)

Keio University (March 11, 2016)

University of Tsukuba (March 30, 2016)

National Center of Neurology and Psychiatry (July 11, 2016)

- Joint Research
- Human Resources Development
- Information Dissemination

(2) SAKIGAKE Designation

Designation Criteria

- New mechanisms compared to existing approved products
- Medical products for diseases in dire need of innovative therapy
- Applied for approval firstly or simultaneously in Japan
- Prominent effectiveness can be expected based on non-clinical study and early phase of clinical trials

Advantage for Designated Products

Prioritized Consultation
[Waiting time:
2 →1 month]

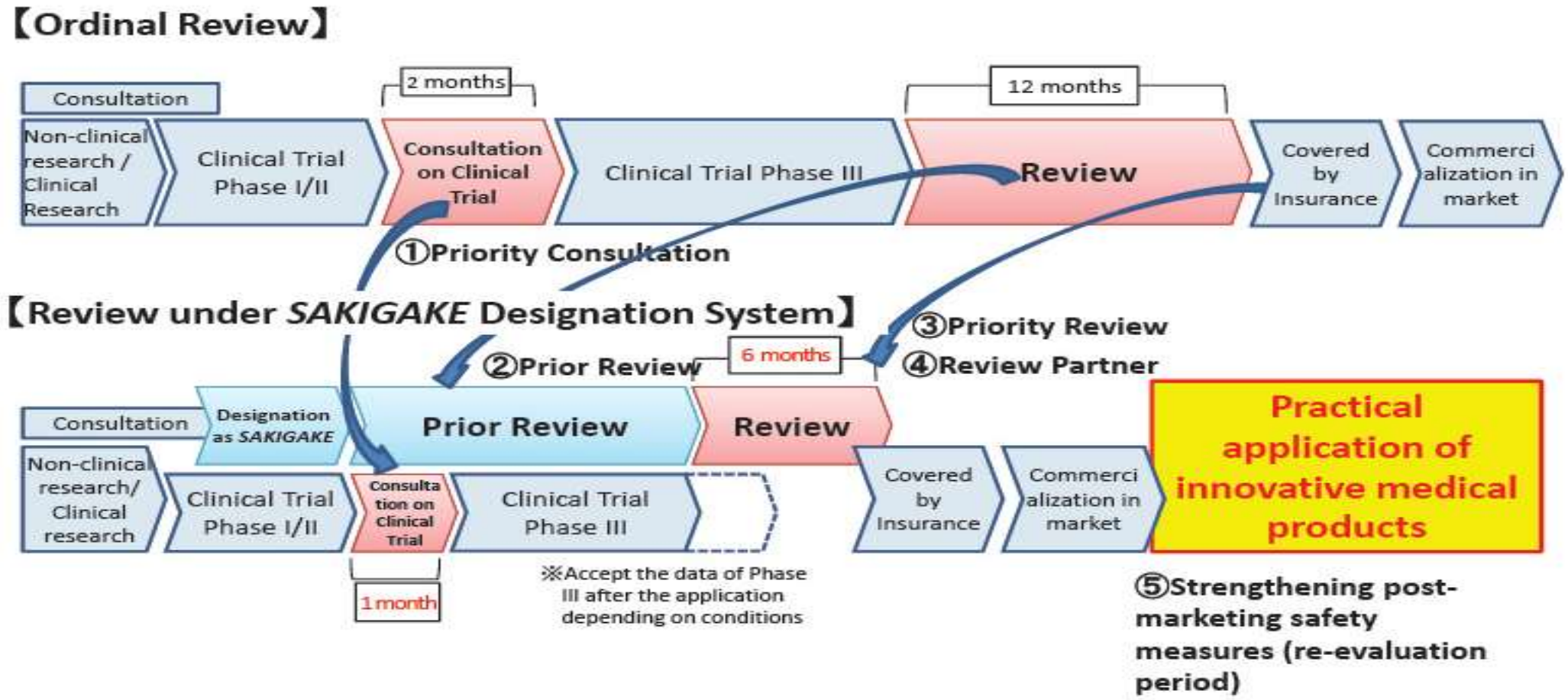
Prior-Review Consul.
(Rolling Review)

Prioritized Review
[12 → 6 months]

Review Partner
[PMDA manager as concierge]

Post Market Measures
[Extension of re-examination period considered]

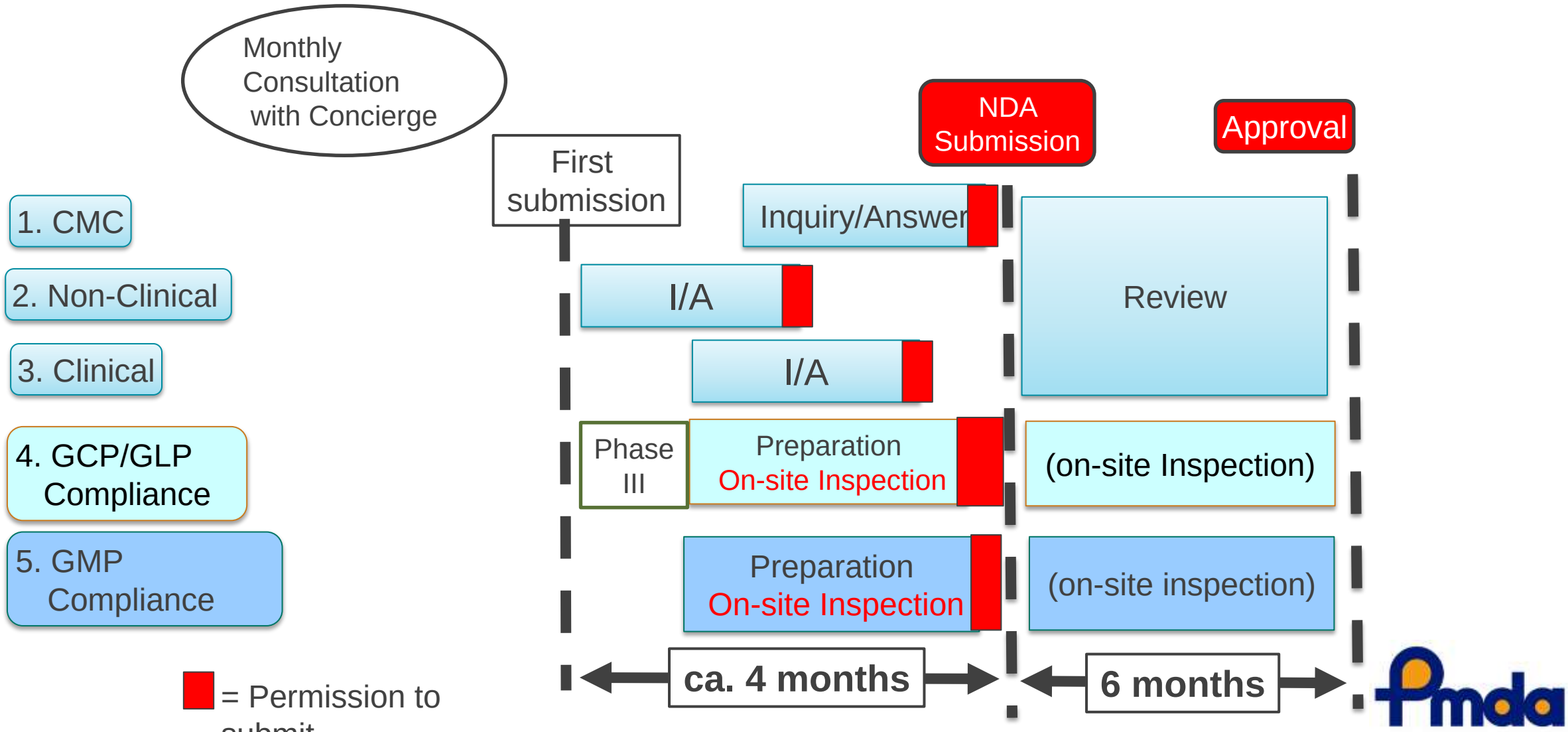
SAKIGAKE - General Timeframe



Designated:
6 Pharmaceuticals, 2Medical Devices, 3 Regenerative Products

Progress of *SAKIGAKE* Designation System

Comprehensive Evaluation Consultations in *SAKIGAKE* System



SAKIGAKE Designated Products
(Drugs, as of Oct. 2015)

Name of drug	Proposed indication	Name of applicant
Sirolimus (NPC-12G)	Angiofibroma associated with tuberous sclerosis	Nobelpharma Co., Ltd.
NS-065/NCNP-01	Duchenne muscular dystrophy (DMD)	Nippon Shinyaku Co., Ltd
S-033188	Influenza A or B virus infection	Shionogi & Co., Ltd.
BCX7353	Management of angioedema attacks in patients with hereditary angioedema (HAE)	Integrated Development Associates Co., Ltd.
ASP2215	First-relapsed or treatment-resistant FLT3 mutation-positive acute myeloid leukaemia	Astellas Pharma Inc.
Pembrolizumab (genetical recombination)	Unresectable, advanced and recurrent gastric cancer	MSD K.K.

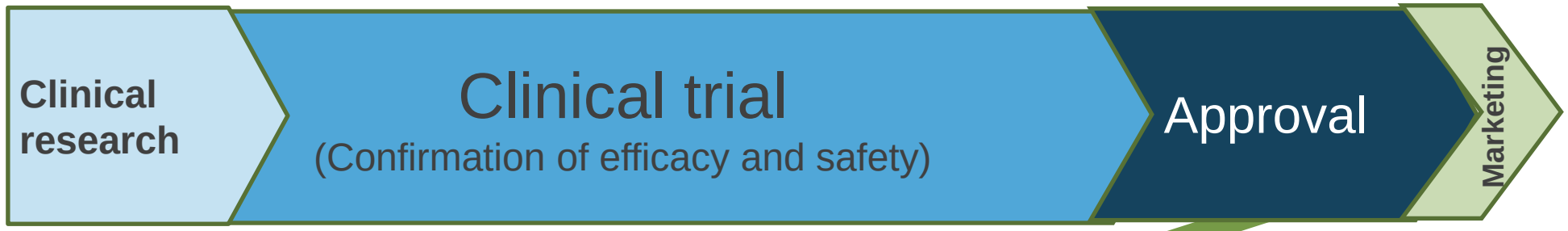
SAKIGAKE Designated Products

(Medical Devices and Regenerative Medical Products, as of Feb. 2016)

Name of medical products	Proposed indication	Name of applicant
Titanium Bridge (Hinge-type plate with titanium)	Adduction-type spasmodic dysphonia	Nobelpharma Co., Ltd.
Bioresorbable adhesion barrier (THN-01: Trehalose solution)	Postoperative adhesion prevention	Otsuka Pharmaceutical Factory, Inc.
STR01 (Autologous bone marrow-derived mesenchymal stem cell)	Nerve syndrome and dysfunction caused by spinal cord injury	NIPRO Medical Co., Ltd.
G47Δ (Growth-controlled oncolytic herpes simplex virus type 1)	Malignant glioma	Daiichi Sankyo Co., Ltd. The University of Tokyo, Institute of Medical Sciences
Autologous cardiac progenitor/stem cells	Pediatric congenital heart disease (single ventricle physiology)	Japan Regenerative Medicine Co., Ltd.

(3) Conditional and Time-limited Authorization of Regenerative Medical Products

Conventional Regulatory Approval Process



Regulatory System that Facilitate Early Patient Access

Regenerative Medical Products Approval

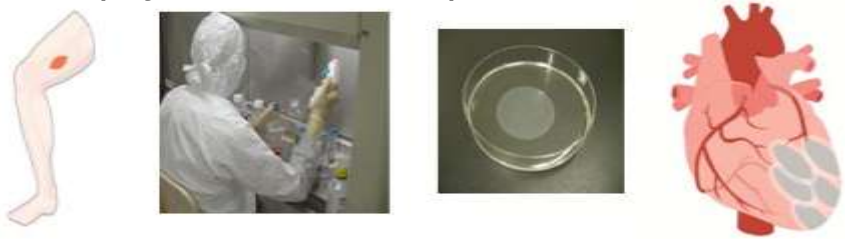
1 Product approved on 18 September 2015

Note: application in September/in October 2014

HeartSheet® for serious heart failure due to ischemic heart disease **(conditional and time-limited authorization –** 5 years, conducting post-marketing efficacy studies**)**

[Conditional and time-limited authorization(HeartSheet®)]

- Target: Serious heart failure due to Ischemic Heart Disease
- Product: Autologous skeletal myoblast
- Manufacturing Process
  - Biopsy from Quadriceps -> manufactured at company CPF -> sheet culture in hospital CPF



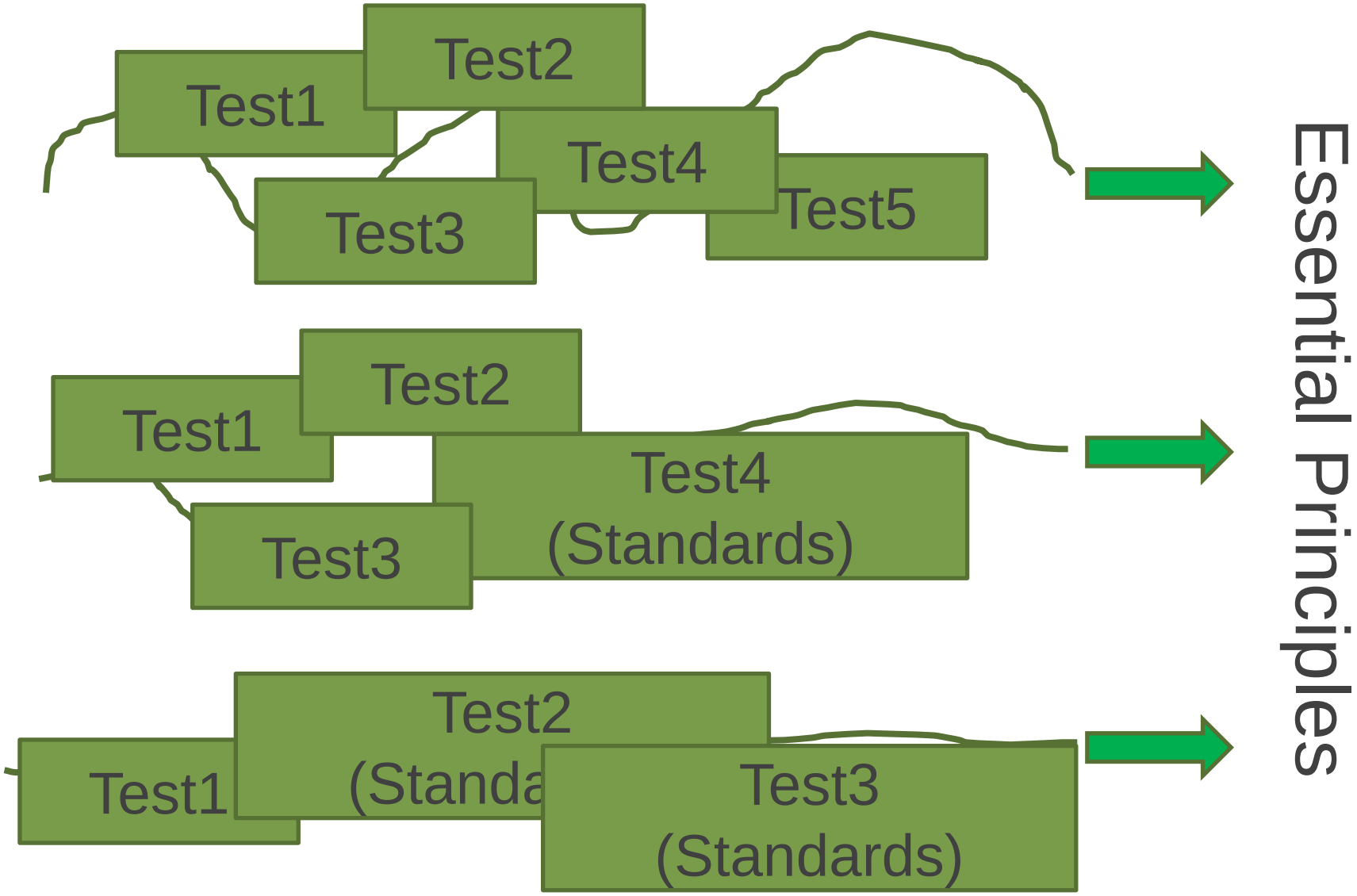
Figures quoted from the company press release docs

Conditional approval requirement (part)

I. Confirmation of efficacy (survival) with 60 HeartSheet cases vs 120 existing treatment cases

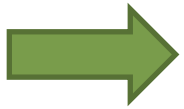
II. Time limitation of approval: 5 years

Demonstrating Conformity Assessment



Merits of Standards

- Enhance transparency
- Reduce duplication
- Reduce Oversight

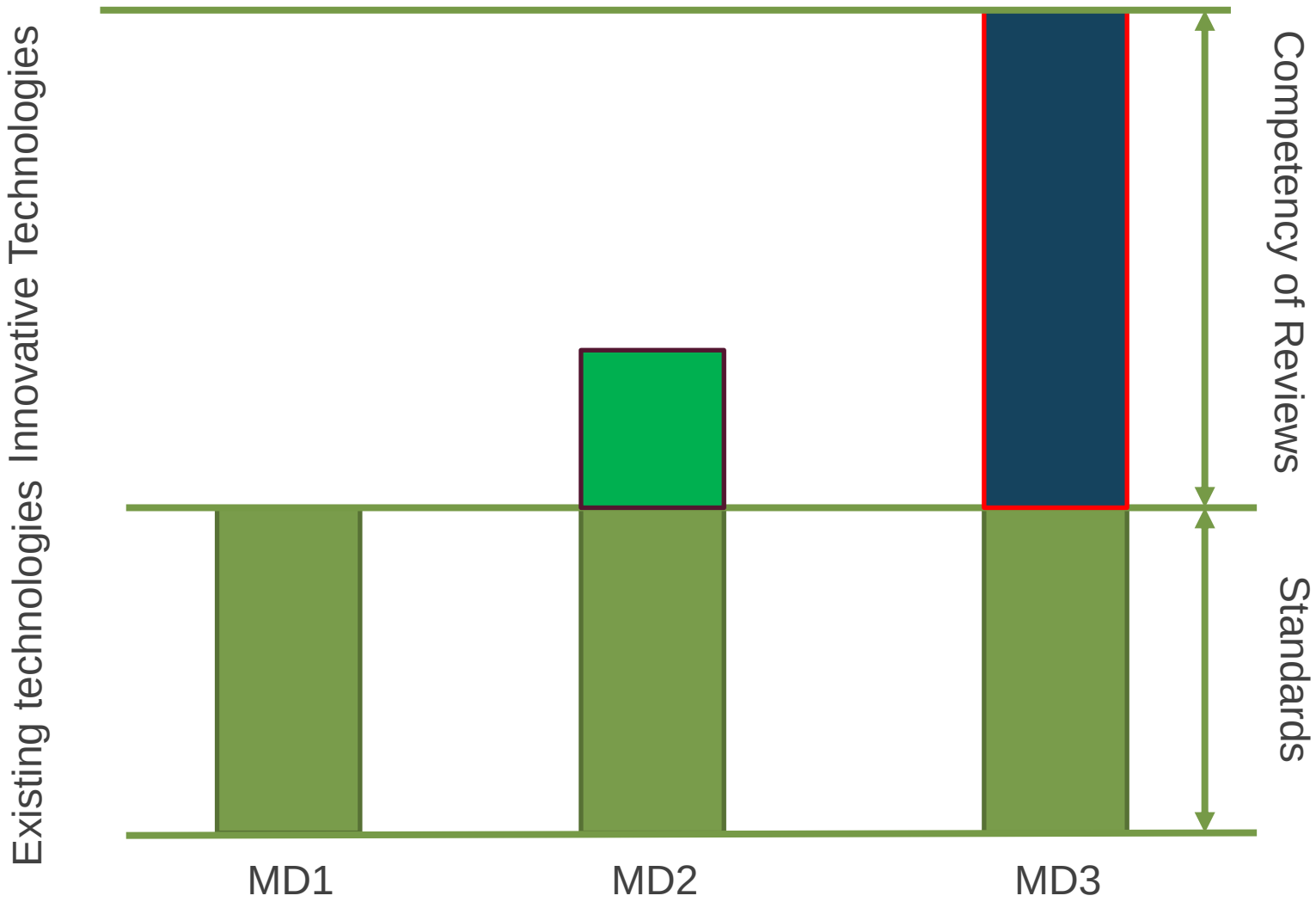


Enhancing Safety and Efficacy

Time saving

Cost saving

Technologies beyond Standards



IMDRF Strategic Priority

- The MC will select further New Work Items (NWIs) to improve the effectiveness and efficiency of premarket review. These may include assuring the reliability of data submitted to regulatory bodies, improving quantity and quality of clinical data, developing Good Review Practices for premarket reviews/evaluations which includes competence and training for pre-market reviewers, developing guidance on benefit-risk determinations, and **improving the suitability of international standards for regulatory authorities** and **effective regulatory authority involvement at each stage in standards development**.

Thank you for your attention!!