Regulatory progress for innovation/International trend on pharmaceutical regulatory convergence

Introduction of Horizon Scanning in ICMRA

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on Medical Products Regulation

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What is “ICMRA”?

ICMRA: International Coalition of Medicines Regulatory Authorities

[Mission]
A voluntary, executive-level, strategic coordinating, advocacy and leadership entity of regulatory authorities that work together to

- address current and emerging human medicine regulatory and safety challenges globally, strategically and in an on-going, transparent, authoritative and institutional manner
- provide direction for areas and activities common to many regulatory authorities’ missions
- identify areas for potential synergies
- wherever possible, leverage existing initiatives/enablers and resources

[Meeting]

- Face to face meeting; 2 times/year (started 2013)

[Participated regulators]

- Members/Associate Members; around 30 Regulators

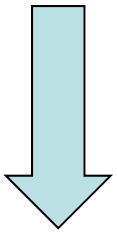
ICMRA Innovation Project
(started from 2017)

Major focus on “Horizon Scanning”

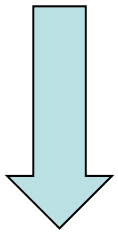
Interim report: Soon, 2018
Final report: by March, 2019

Relationship in each Project

Project 1 Seek best practices; methodologies on HS



Project 2 Find critical product and technology innovation for the future



Project 3 Novel approaches to licensing
+ Revise regulatory frame to adapt

Project 1

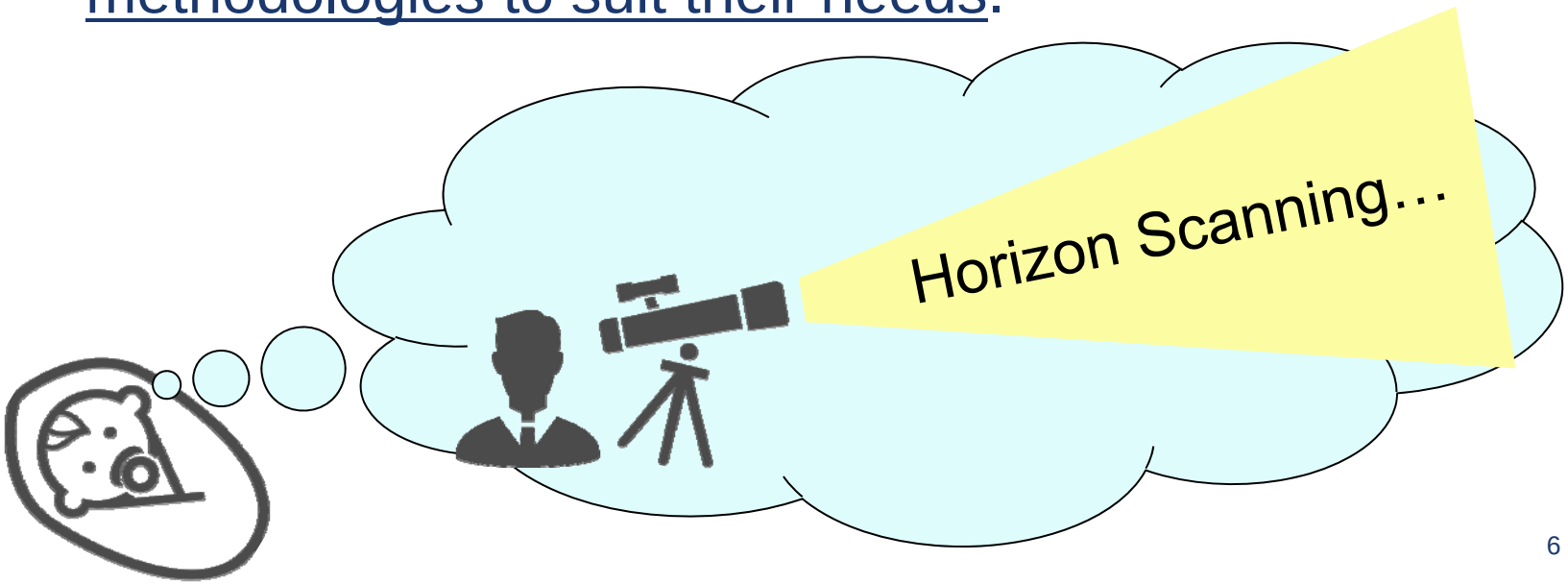
Analysis of global best practices in horizon scanning methodologies

Objectives

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.

HS for Regulators is Still Under Development

- HS is highly developed in other fields, but still in its infancy for regulators
  - Most HS programs studied were less than 3 years old, in a planning, pilot, or phased implementation stage.
  - Regulators are currently adapting and developing methodologies to suit their needs.

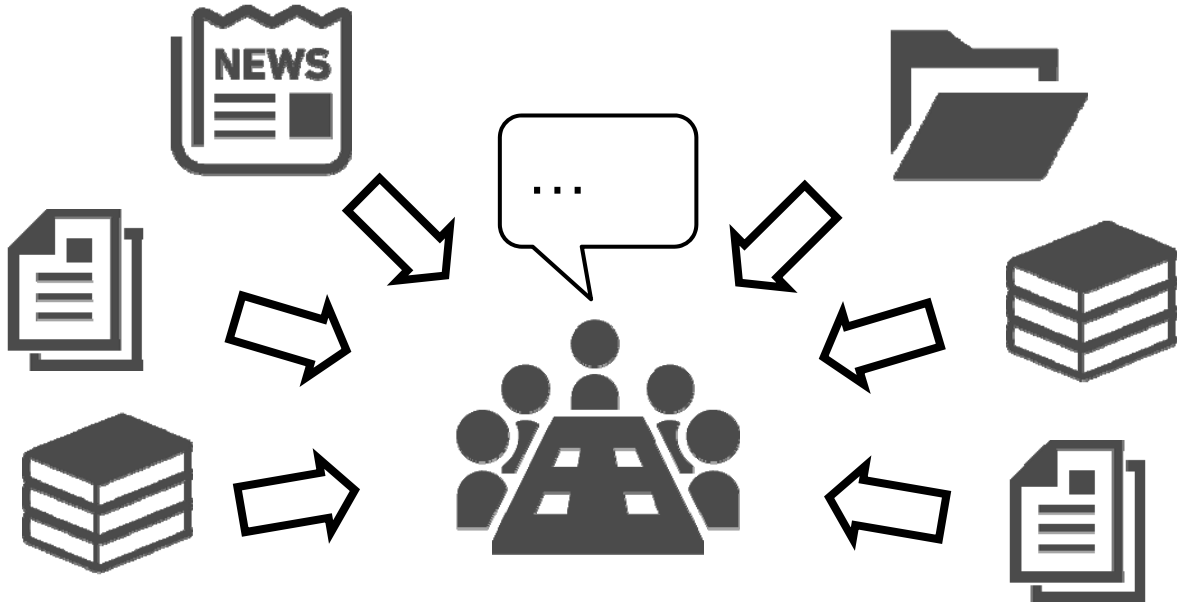


Resources Available for HS are Limited

Agency-wide buy-in/support for HS, especially from management, was important in carrying out recommended actions (e.g., hiring new expertise, establishing internal WG, modifying/developing new regulations)

[Reality]

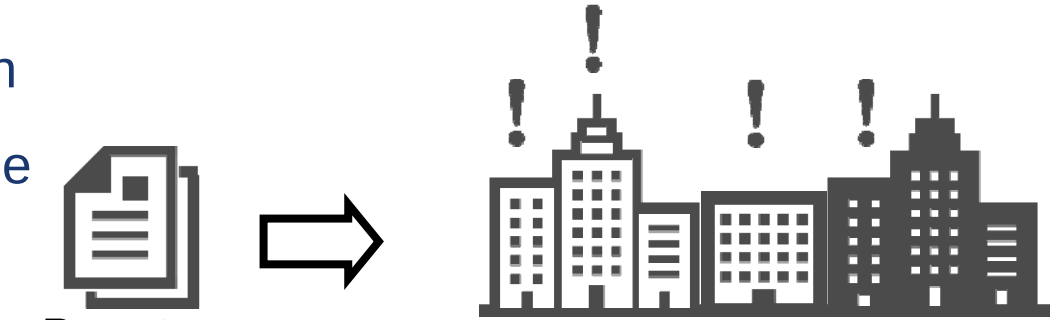
- Most agencies devote less than 5 FTEs to HS activities.
- High interest in digital and analytical tools to help scanning (e.g., Tools for Innovation Monitoring (TIM) used by EMA)
- Strong desire for international cooperation to pool resources.



Priority was Given to Disruptive Innovations

- Priority given to technologies that would:
  - Fall through the cracks of the regulatory framework
  - Affect multiple offices

- Common criteria for prioritization included the following:
  - Falls within remit of the agency
  - Regulatory impact
  - Timeframe to submission
  - Level of internal expertise



Project 2

Leveraging from outcomes of horizon scanning

through critical innovation/ expertise and skill

Objective

To identify critical product and technology innovation, which will benefit from or require regulatory science based approaches in terms of future regulations

Project 2 Discussion

- “Enquette” and extraction (potential technology influenced in the future)

- Overview and presentation/exchange of view (Case Study)
  - Additive manufacturing
  - Genome editing
  - Artificial intelligence

- Regulatory science consideration

- Technology and Expertise/Skill for regulator

Regulators of the 21st Century

Regulators as enablers — preparing for innovation

- Fostering a sustainable, international, collaborative Horizon Scanning system
- Building a regulatory system fit to support innovation in healthcare
- Collaborating to identify future expertise requirements and capacity building to support innovation

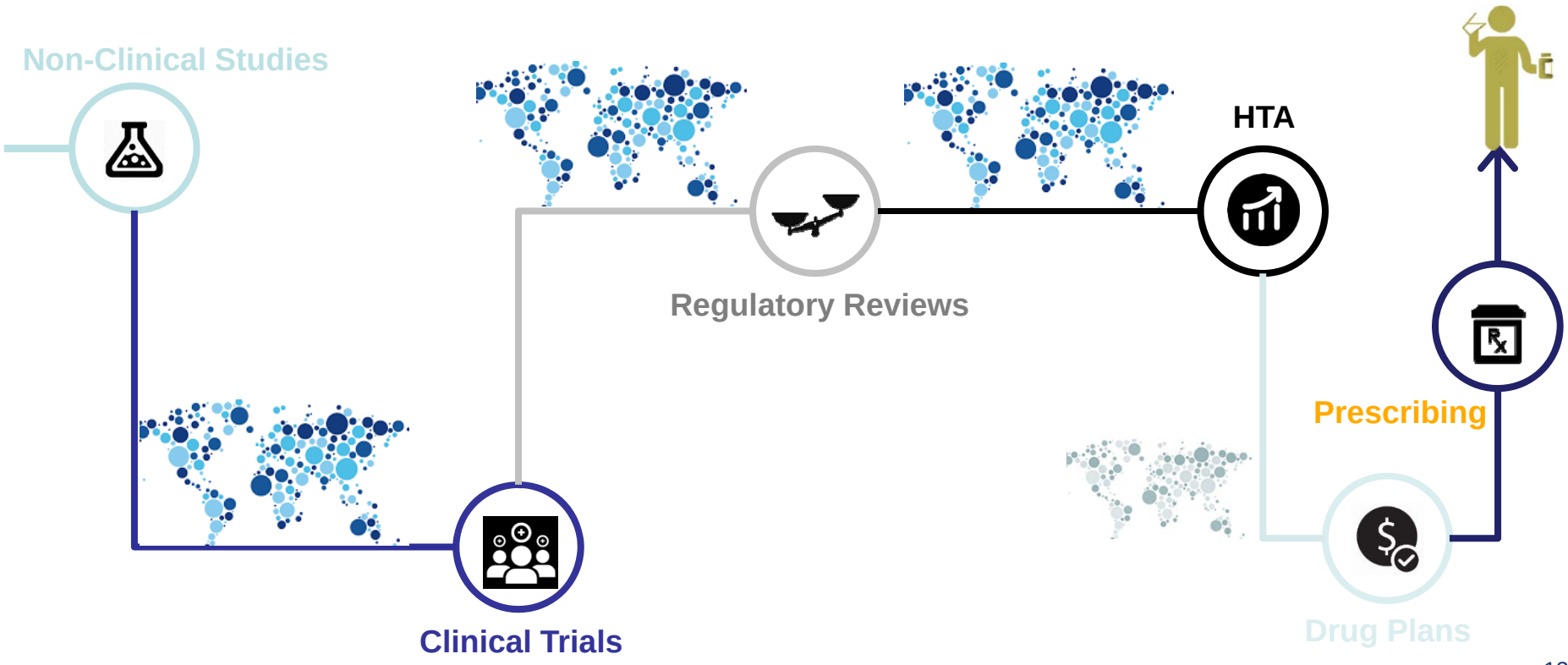
Project 3

Novel Approaches to Licensing/Early Access Scheme

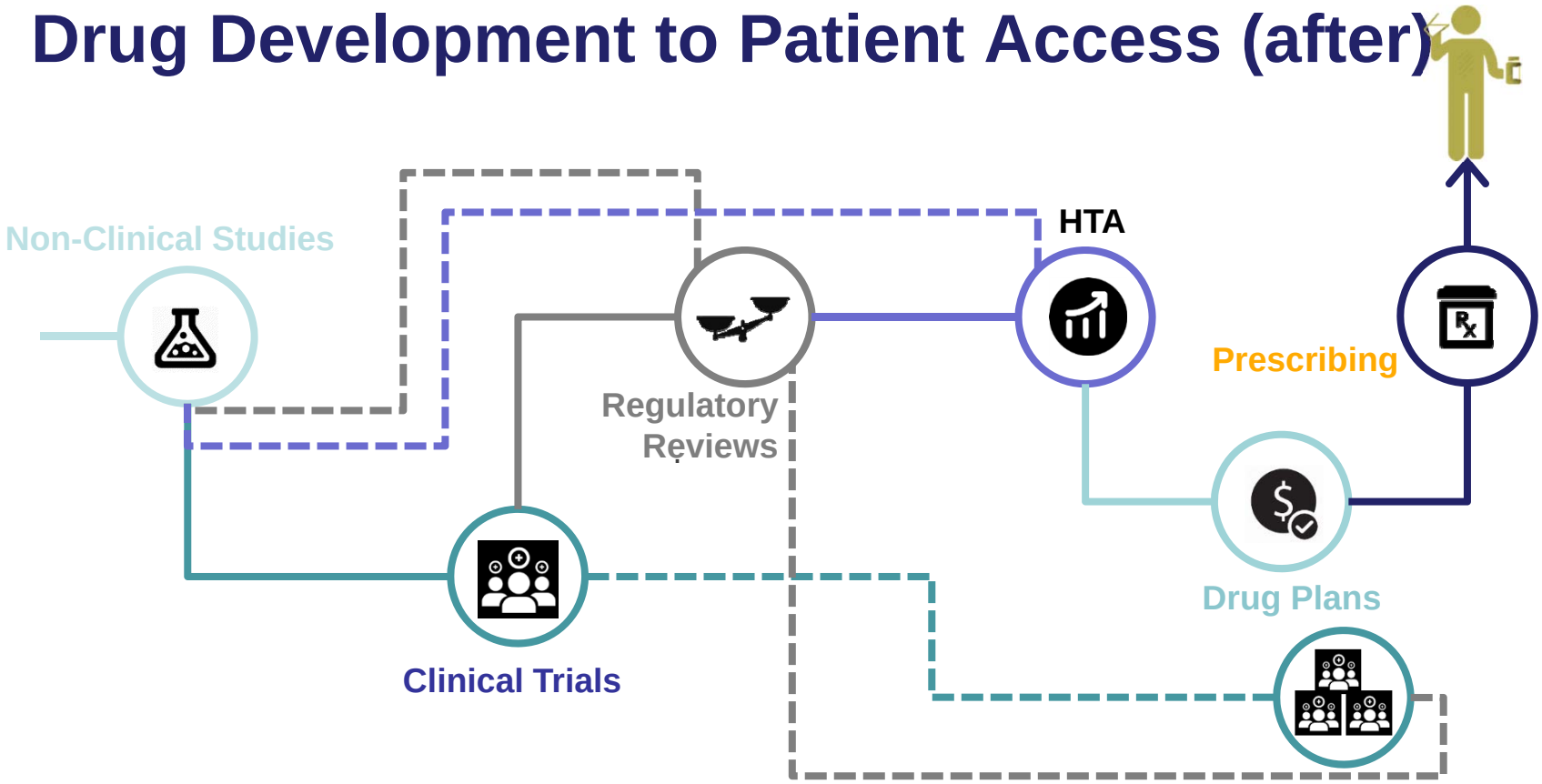
Objective

Tasked with mapping out novel approaches to licensing, identifying barriers and determining progressive approaches that might be used to address the identified challenges, with a focus on timely patient

Drug Development to Patient Access (before)



Drug Development to Patient Access (after)



Overview of Novel Approaches to Licensing

- Priority Review [12]
- Conditional Approvals [8]
- International Alignments [3]
- Use of Third Party [1]

Expedited

- Facilitated Schemes [3]
- Expedited Review with Enhanced Communications [2]
- Collaborated Facilitation by Health Authorities [6]
- Targeting Personalized ATMP [1]

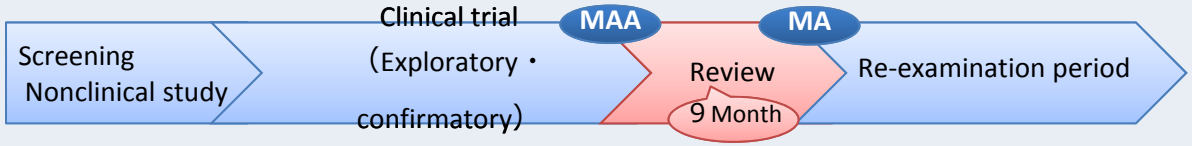
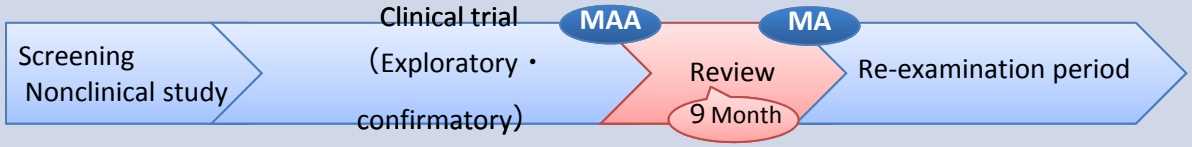
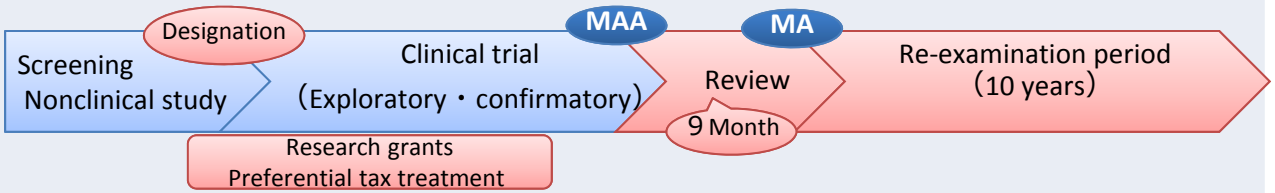
Facilitated

Introduction of regulations in Japan

Year	Regulatory system
At the latest 1960 -	Condition on approval*
1980 -	Re-examination period*
1993 -	Priority review*
1993 -	Orphan designation*
2014 -	**Conditional time-limited authorization***
2015 -	**SAKIGAKE designation**
2017 -	**Conditional early approval**

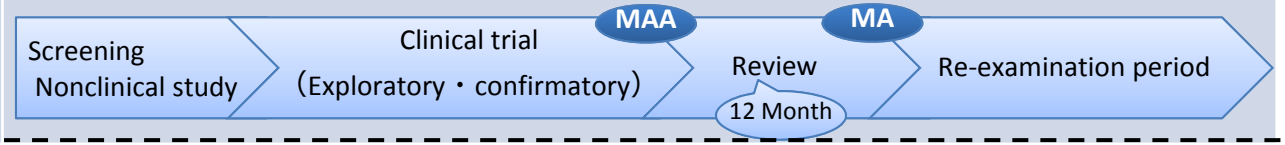
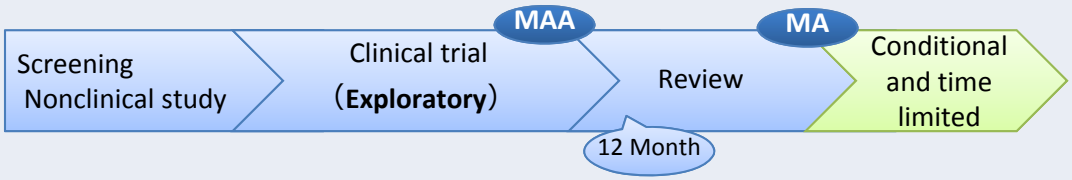
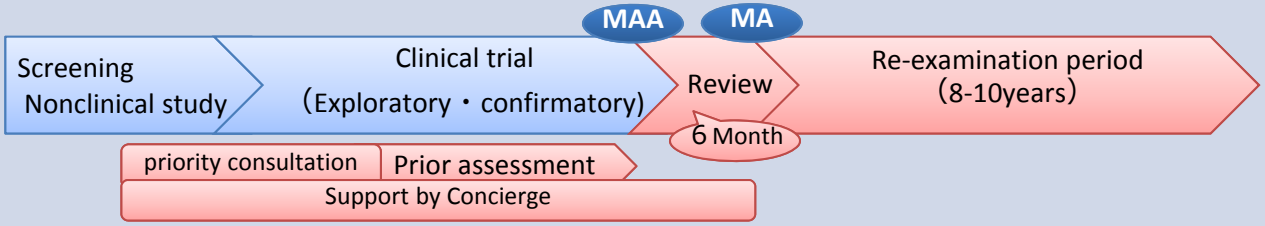
* stipulated in Pharmaceuticals and Medical Devices Act

Summary of the Accelerated review system in Japan (1/2)

Type/Designation requirement	Outline
Basic	
Expedited review 1. Needed to expedite the review	
Priority review 1. For severe diseases 2. Apparent improvement of medical care	
Orphan Disease product's Designation * In addition to priority review 1. No. of patients is less than 50,000 or intractable diseases designated based on a law 2. Possibility of development	

MAA: Marketing Authorization Application MA: Marketing Authorization

Summary of the Accelerated review system in Japan (2/2)

Type/Designation requirement	Outline
Basic	
Conditional and Time-limited Authorization Regenerative Medical Products 1.The product is not homogeneous 2.The clinical data on the products are likely to predict efficacy 3.The product does not exhibit remarkably adverse results in efficacy, effectiveness or performance.	
SAKIGAKE (Forerunner designation) 1. Innovative medical products 2. For serious diseases 3. Development & NDA in Japan: being world's first or simultaneous with other countries 4. Prominent effectiveness expected on non-clinical and early phase clinical studies	
Conditional Early Approval Pharmaceuticals Medical devices * In addition to priority review 1. Confirmatory clinical trials don't have sufficient feasibility. 2. Confirmation of a certain degree of efficacy and safety through clinical trials other than confirmatory clinical trials.	

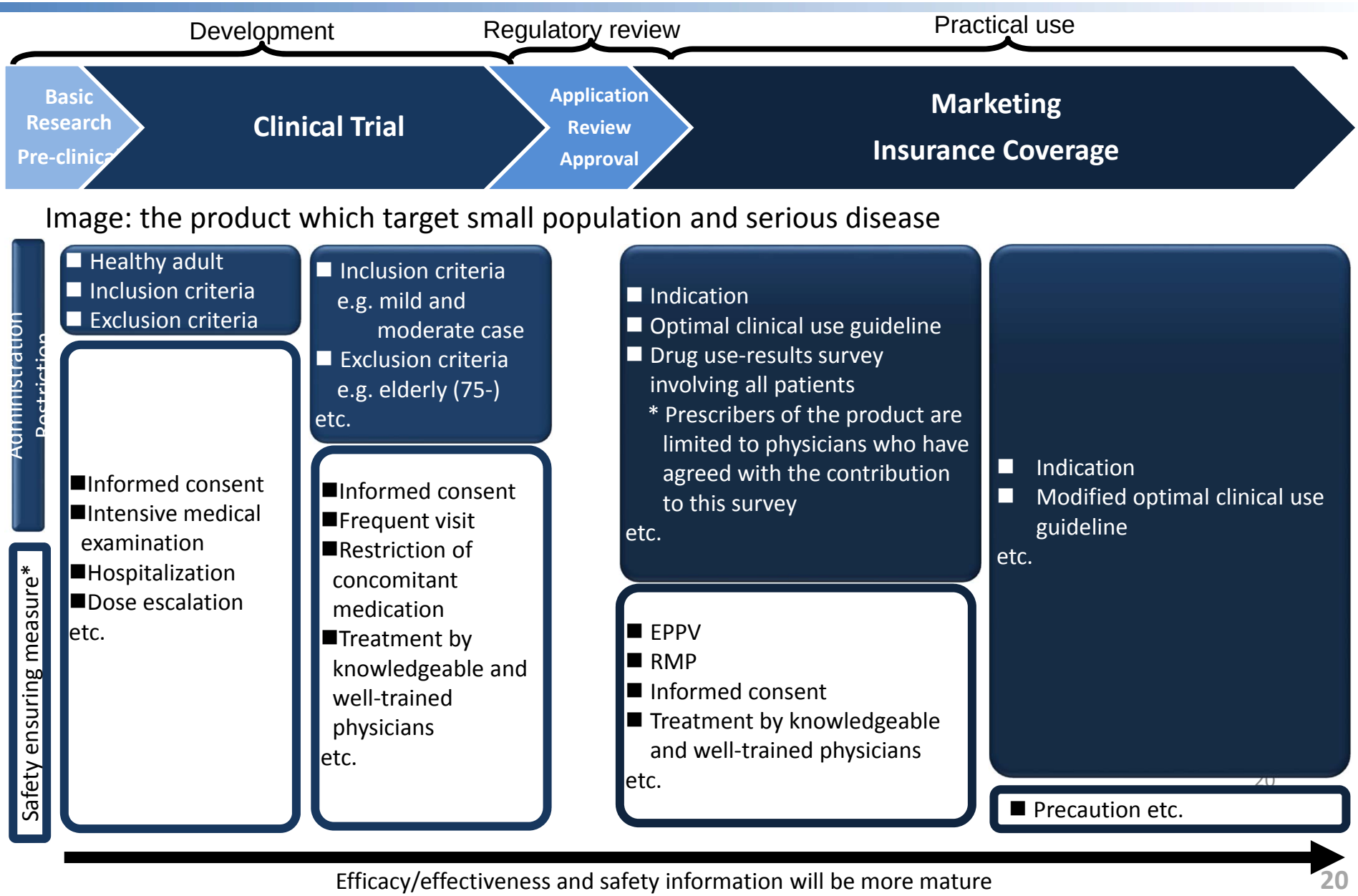
MAA: Marketing Authorization Application MA: Marketing Authorization

Examples of Conditions for Approval

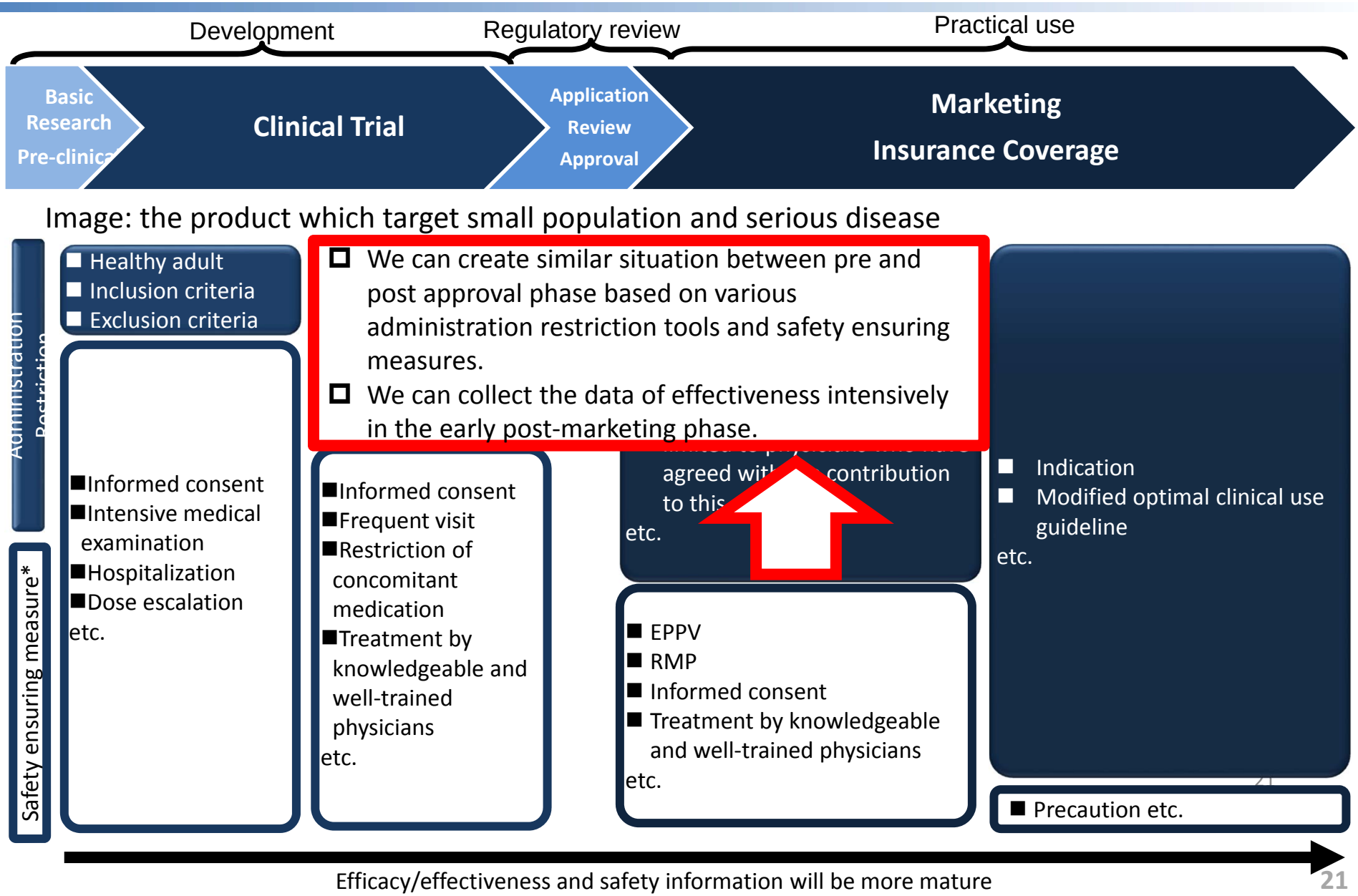
Several conditions are imposed to MAH on a case by case basis.

- Conduct **early post-marketing phase vigilance (EPPV)**
- Prepare a **Risk Management Plan (RMP)**, and implement it appropriately.
- Conduct a **drug use-results survey involving all patients treated with the product** after the market launch until data from a certain number of patients have been gathered in order to grasp the characteristics of treated patients
- Take necessary measures to **ensure that the product is used only by qualified physicians** who have completed a training course on the product.
- **Request physicians to obtain patients' informed consent** to the use of the product after having thoroughly informed them that additional data on the efficacy and safety of the product are still being collected.
- **Submit the results and analyses of ongoing or planned clinical studies** promptly after the study completion.

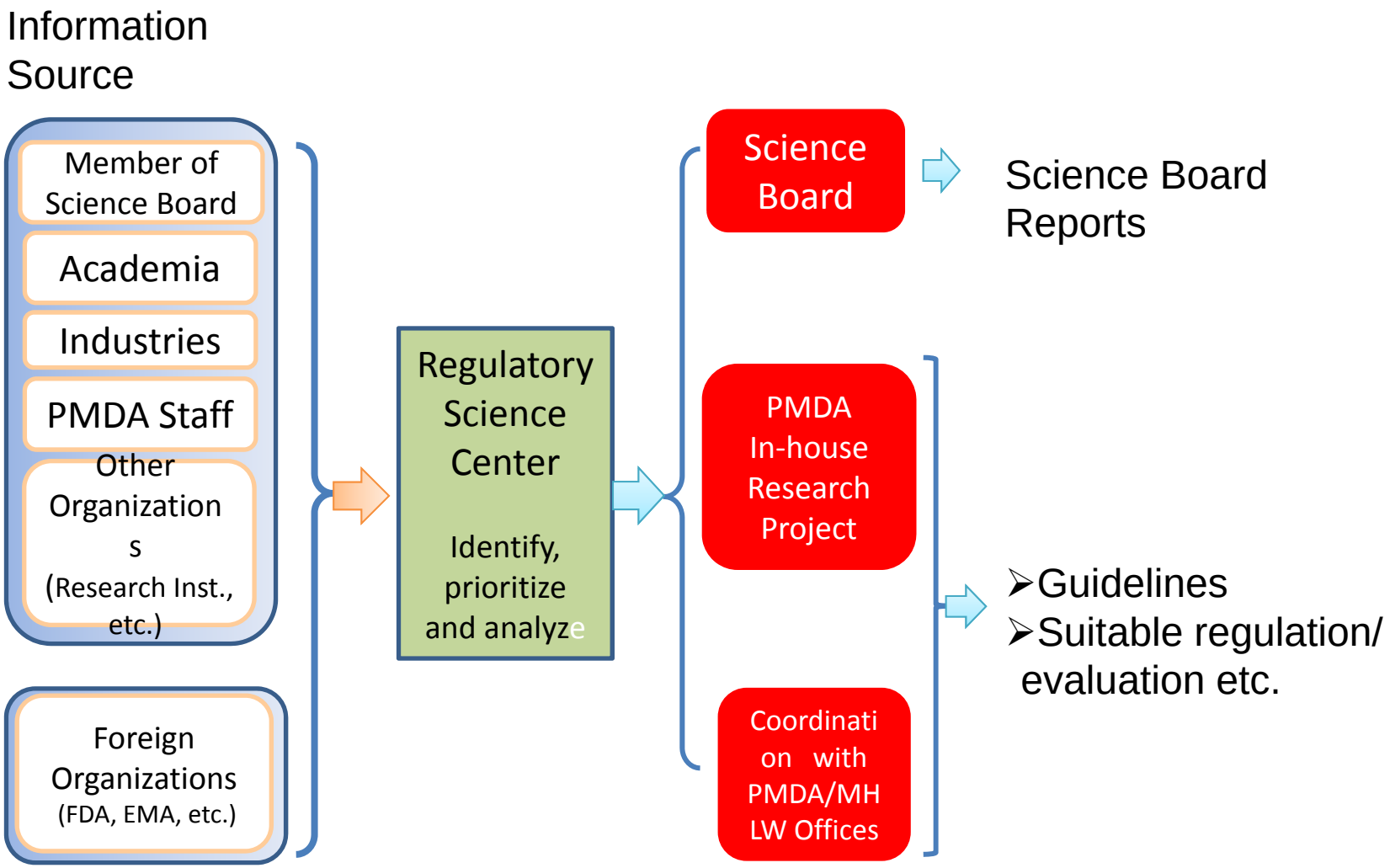
Concept of gradual drug administration expanding



Concept of gradual drug administration expanding



PMDA's Horizon Scanning -Process-



MHLW/PMDA make continuous efforts to identify further approaches to address innovation through practical experience.