Efficiency of Product Review

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Pharmaceuticals and Medical Devices Agency (PMDA)

August 2nd, 2014

1st Brazil-Japan Seminar

Today's Topic

1. PMDA's achievements in review time reduction
2. Measures taken to achieve efficient review
3. Future projects to further enhance review efficiency
4. Conclusion

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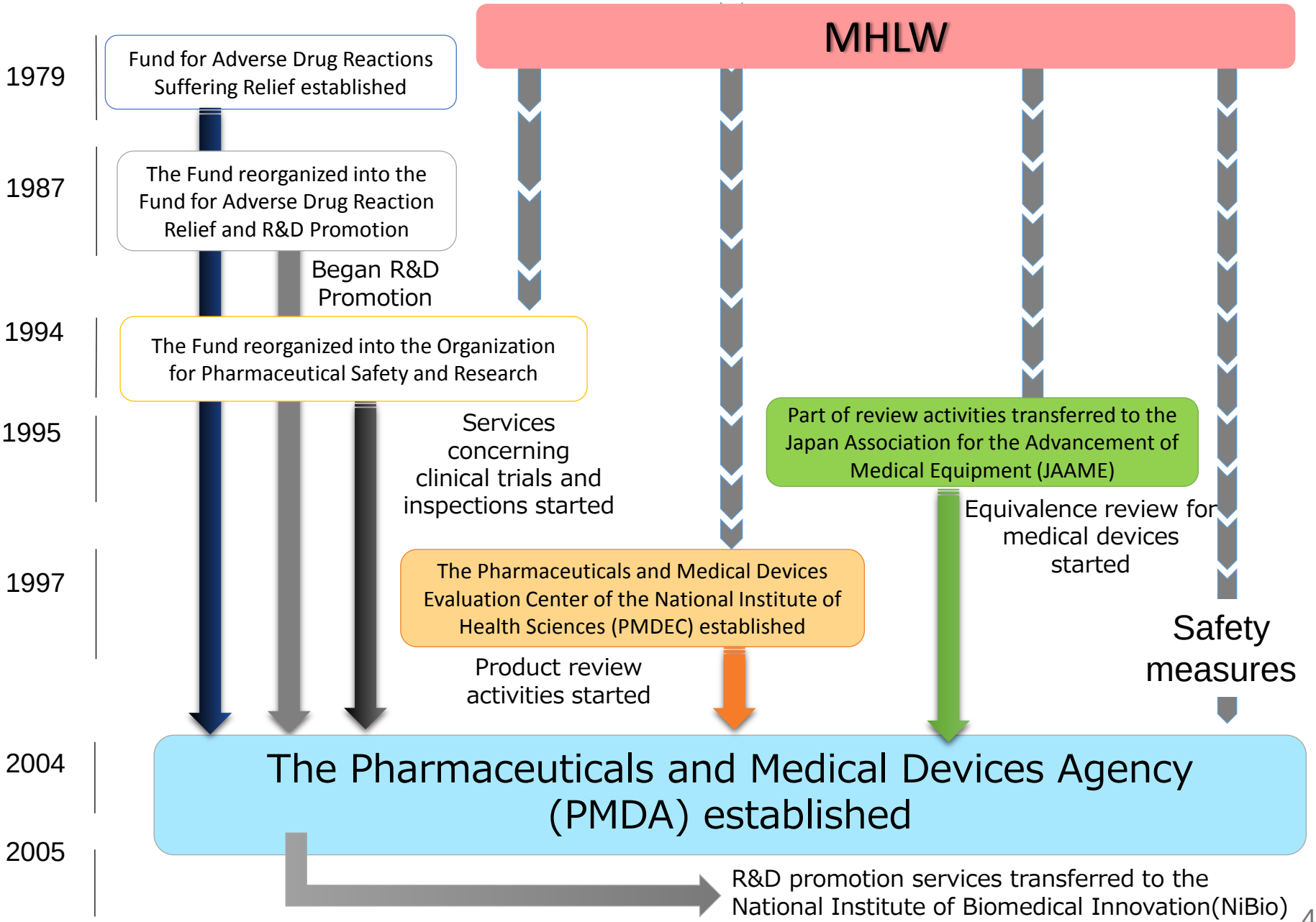
History of PMDA



Strategies and Measures for PMDA Innovation

Issues with PMDA (past 6 years)	Basic policies to address the issues
◆ **Shorten review time** ▪ **Reduce drug lag** ▪ **Reduce device lag** ◆ **Strengthen and enhance safety measures**	◆ **Philosophy** **(Mission Statement)** ◆ **Regulatory science** ◆ **Global partnership** **(Win-Win Relationship)**

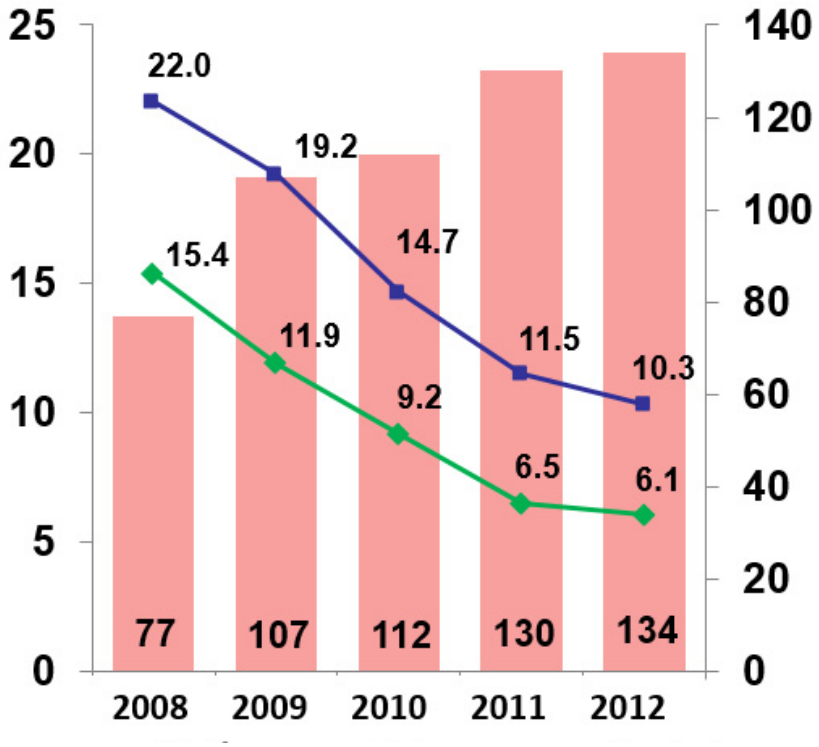
Pharmaceutical affairs are the ultimate medical ethics, and regulatory science is the underlying science.

Efforts made so far

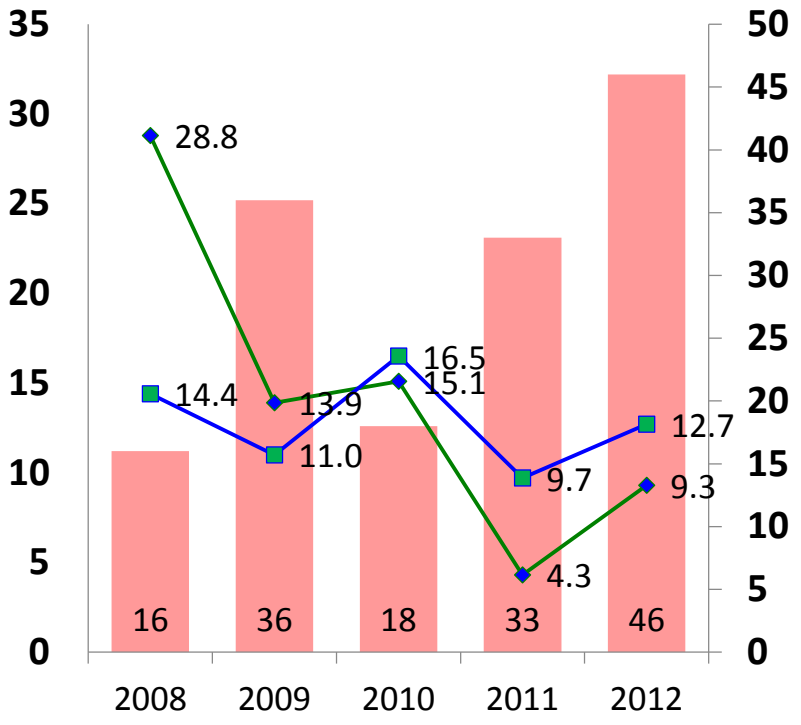
- Increase staffs
- Enhance training program
- Academic cooperation
  - Science Board
  - Joint Graduate School Program
  - Human resource exchange program
- Industry-Government-Academia collaboration
- Pharmaceutical affairs consultation
- Cross-sectional project within PMDA
- IT-based safety measures
  - MIHARI Project
  - Project for developing medical information database infrastructure
- Risk Manager（RM）
- Risk Management Plan（RMP）
- GLP, GCP, GMP ,QMS inspection programs
- Adverse health effect relief system
- International strategic plan
- International liaison officers to US and EU
- Global partnership with US, EU and Asian countries（ICH, IMDRF, PIC/S, etc.）

Number of Approvals and Review Time

New Drugs



Medical Devices



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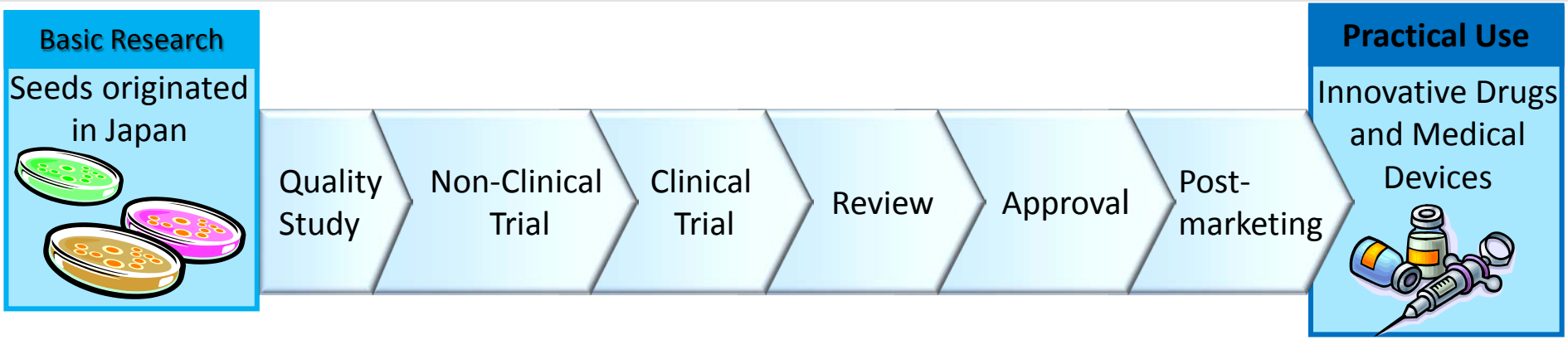
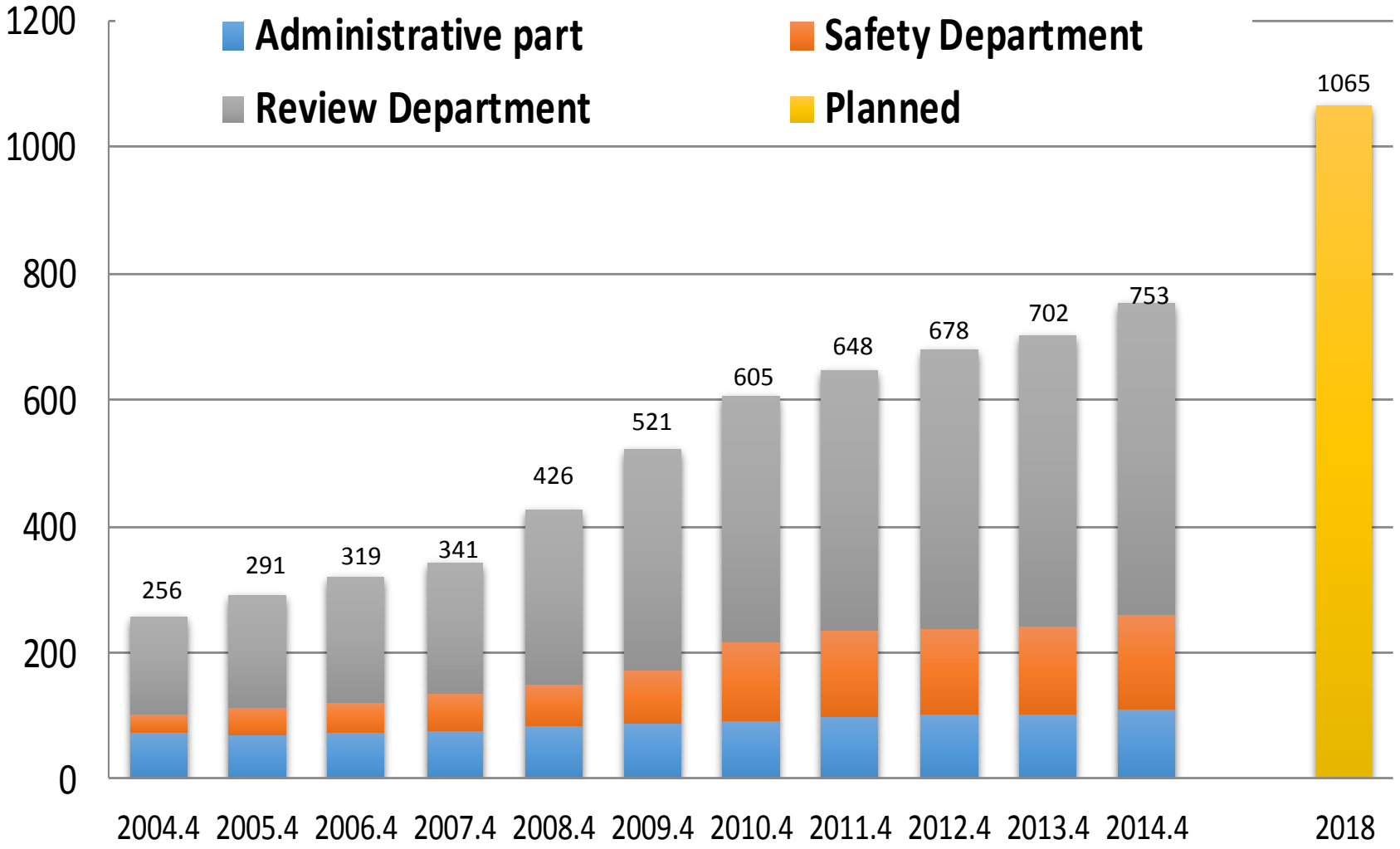
Improvement of Review System

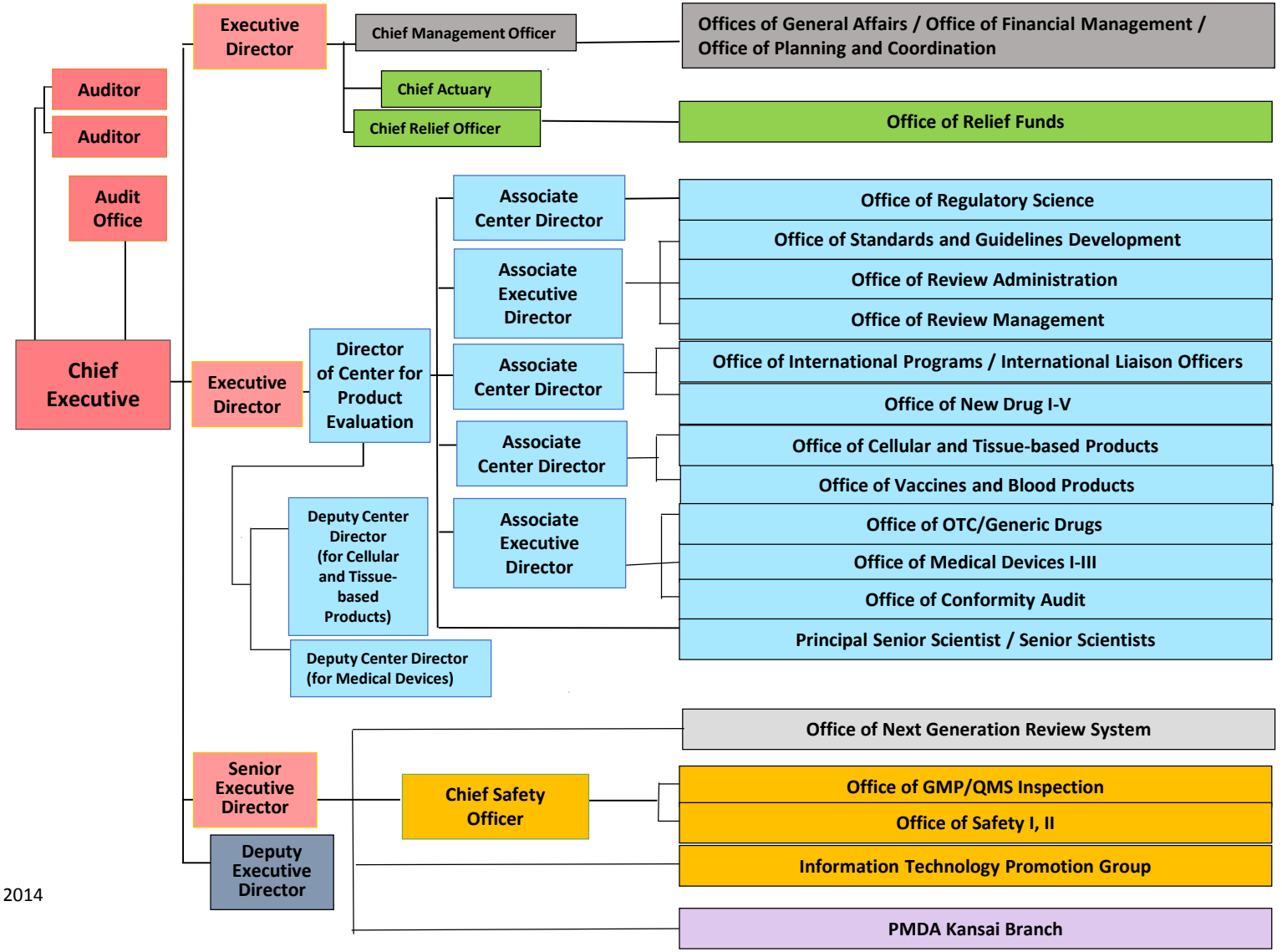


- Improvement of PMDA infrastructure
- Pharmaceutical Affairs Consultation on 1. Clinical trial 2. R&D Strategy
- Science Board
- Personnel Exchanges
- Harmonization or Convergence
- Improvement of Safety Measures

Improvement of Infrastructure (Staff Size)



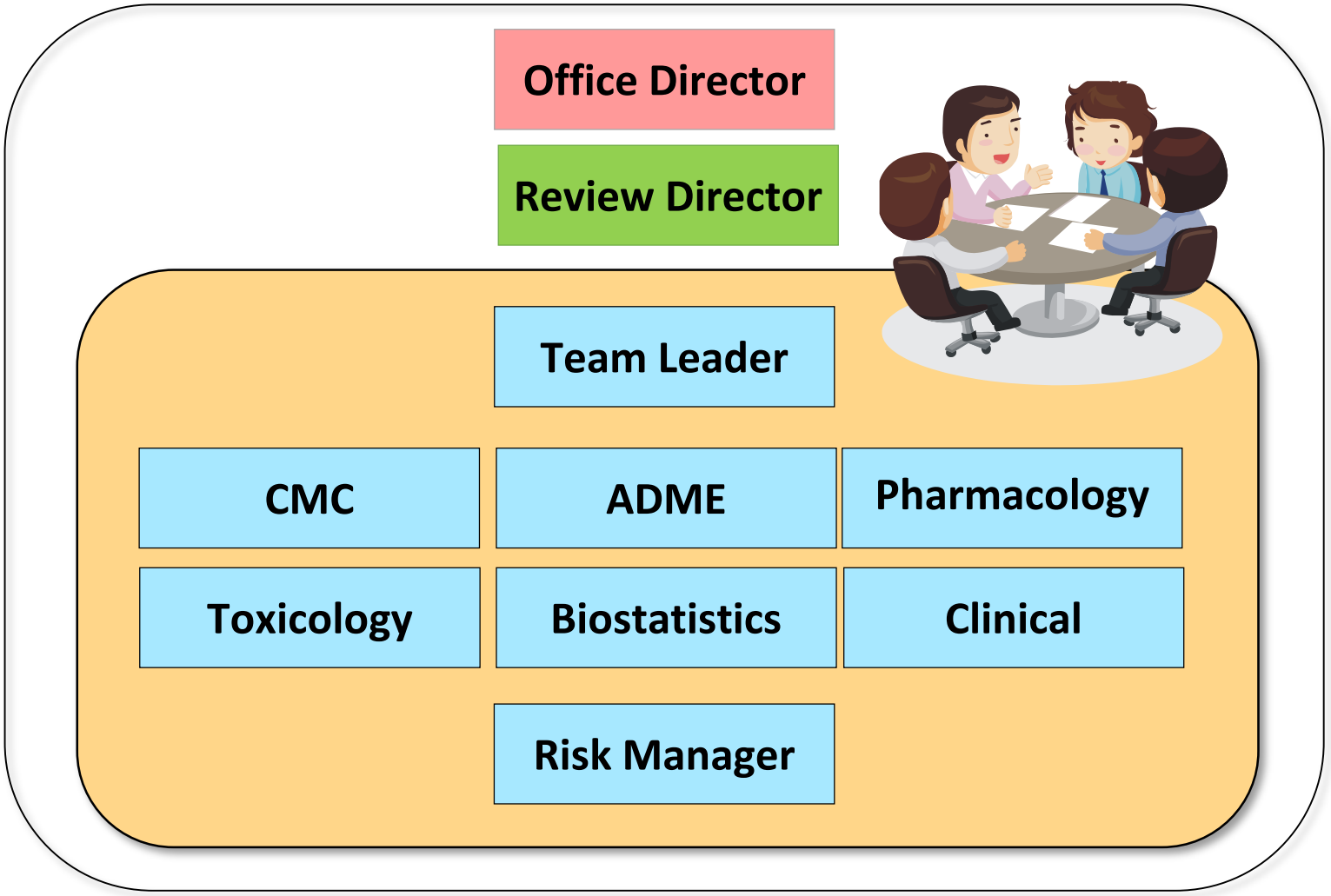
Infrastructure



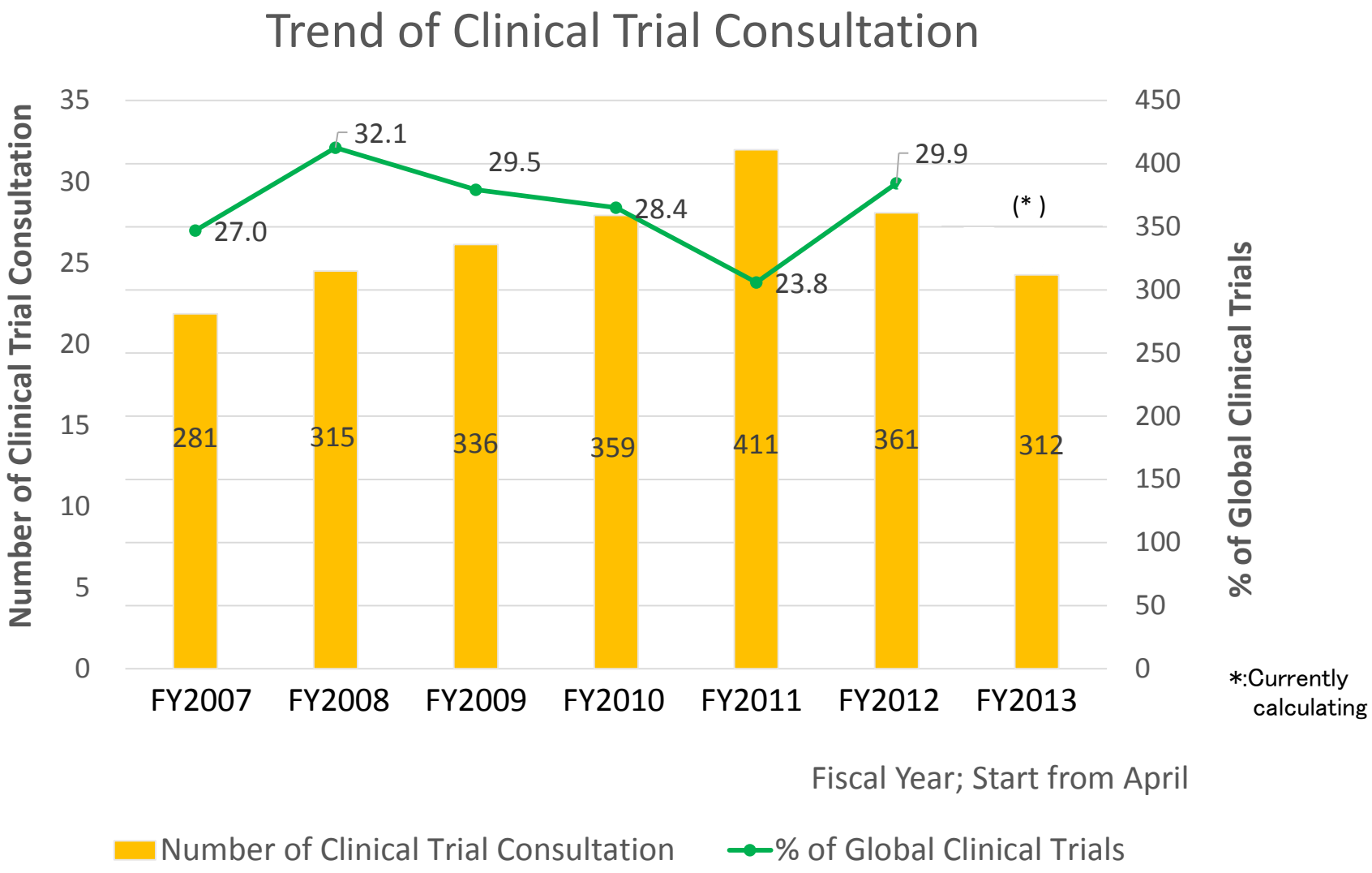
As of April 1, 2014

Team Reviewing at the PMDA

Reviewers are required to have a high level of expertise



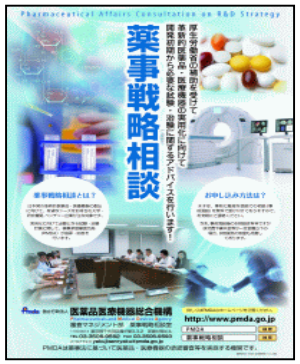
Consultation on Clinical Trial



Pharmaceutical Affairs Consultation on R&D Strategy

Valley of Death

-Shortage of funds, Knowledge on Regulation and development strategy



Basic Research

Pharmaceutical and Medical Devices candidates

Strategic Consultation

Quality Study

Non-Clinical Study

Clinical Trial

Up to the level of POC studies*

Practical Use

Innovative Products originated from Japan

Introductory Consultation

- Explain procedure
- No Charge

657 Consultations

If needed

Pre-Consultation

- Sort out issues
- 30 min, No Charge, Not binding

753 Consultations

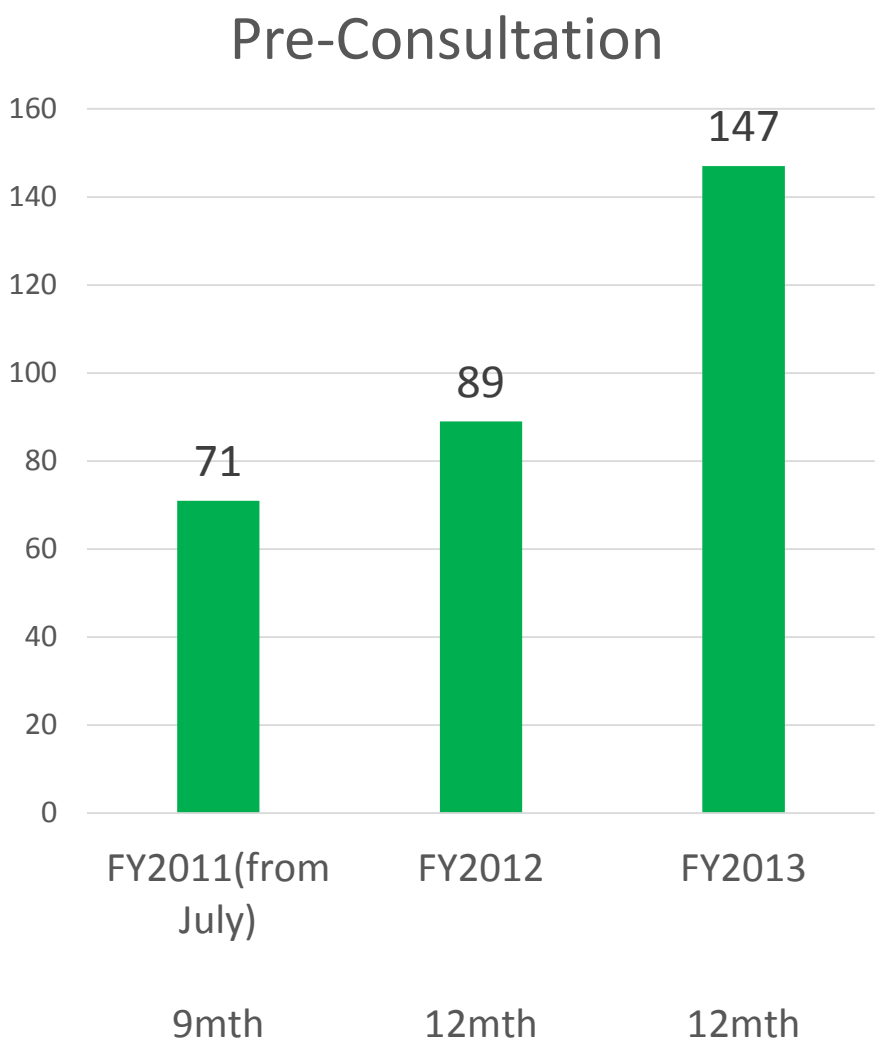
Face-to-Face Consultation

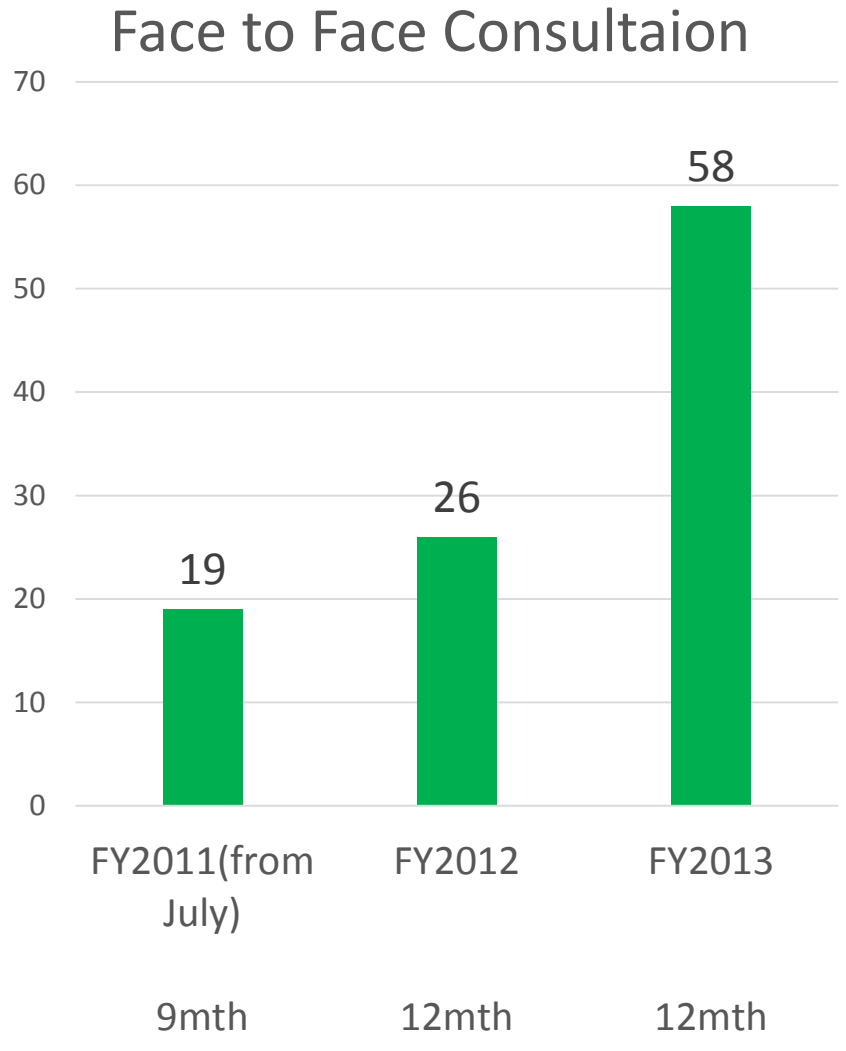
- Scientific discussion
- 2 hours, Charged, Binding, Minutes

193 Consultations

* Further studies are handled by the Regular Consultation

Number of R&D strategic consultation for Drugs
（except for cellular & tissue-based products）





Fiscal Year; Start from April

For PMDA To Be More Science-Based

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

Office of Review Innovation

Establishment of the Science Board

The Science Board was established in May 2012 to discuss how PMDA can better cope with products with advanced science & technology, in each developmental stage such as basic research, development support, product review, and post market safety measures.

Board members

Academia

Working policy of discussion on Subcommittee

(1st Stage)

Pharmaceuticals

Bio-based Products

Aiming at summary of " Recommendation for the review policy of the pharmaceuticals regarding personalized medicine" and discuss needed items in order of priority.

Cellular & Tissue-based Products

Discussing how to ensure the safety of cellular and tissue-based products and aiming at revealing the predictable risks in the products as possible.

Medical Devices

Starting from discussion about the common issues as many kind of medical devices as possible because of big differences among product attributes of the medical devices.

Outcome of the Science Board

Cellular & Tissue-based Products

- Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from iPSCs and iPSCs as Their Starting Materials (Aug. 21, 2013)

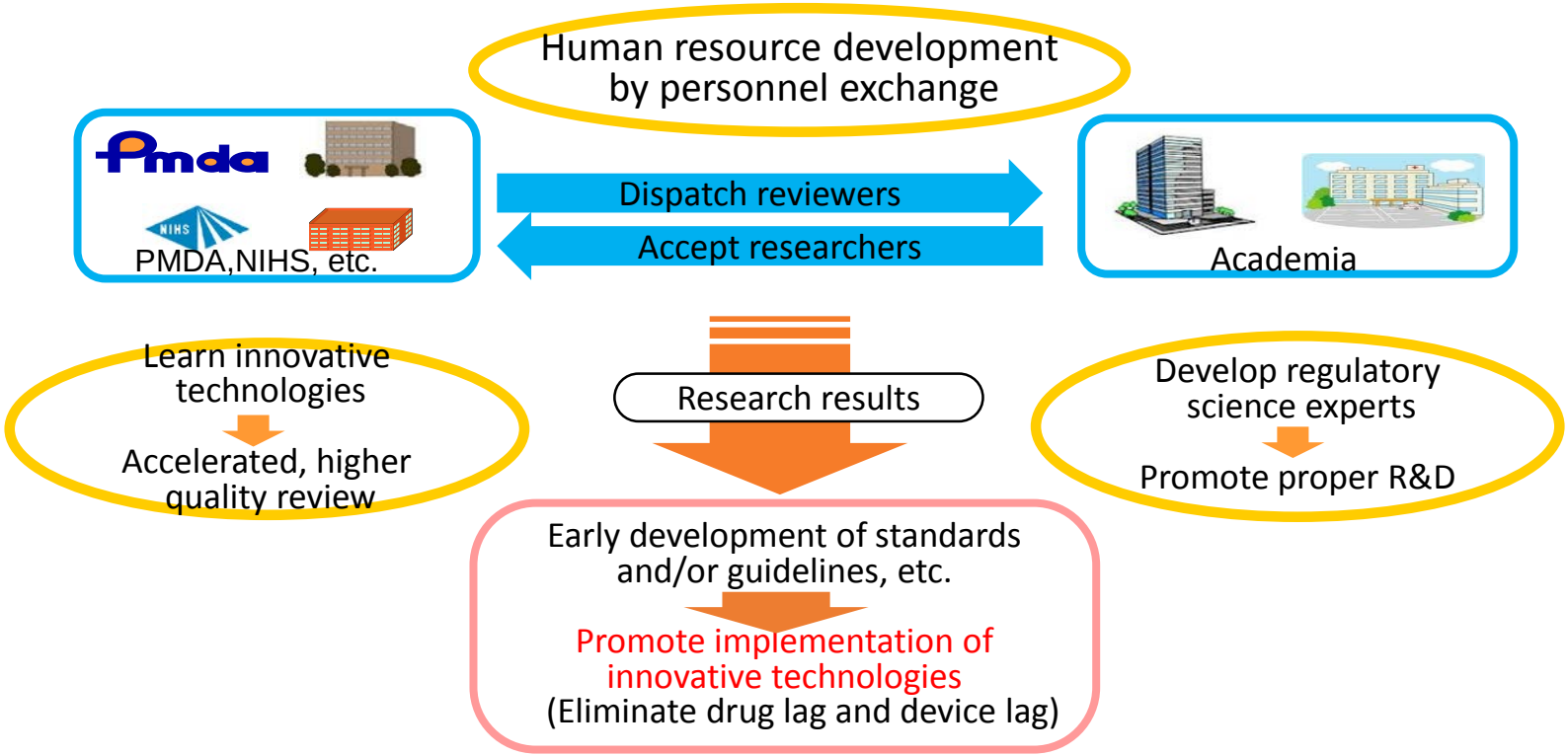
Pharmaceuticals, Bio-based Products

- Summary of Discussion on Non-clinical Pharmacology Studies of Anticancer Drugs (Dec. 10, 2013)

- Summary of the discussion on assessment of the current status of personalized medicine relating to drug development and review (Mar. 11, 2014)

Personnel Exchanges

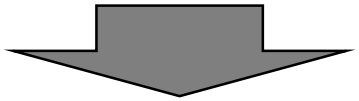
- support establishment of evaluation system for safety and efficacy with R&S as the basis at research facilities researching latest technology



RS activities (Expanding Personnel Ex.) as of March 2014	
Exchanging Program with Universities / Research Institutes, etc.	Drugs: 8 Medical Devices: 7 Cell & Tissues: 6
Collaborative Graduate Schools	18

Outcomes of ICH

◆ICH have harmonized over 80 guidelines regarding technical elements about the evaluation of quality, efficacy and safety, as well as the format of application form and the post-market safety measures.



- Preventing duplication of clinical trials and reducing research resources
- Reducing International barriers
- Facilitating the dissemination and communication of information on harmonized guidelines and their use for non-member countries

IMDRF Current work items

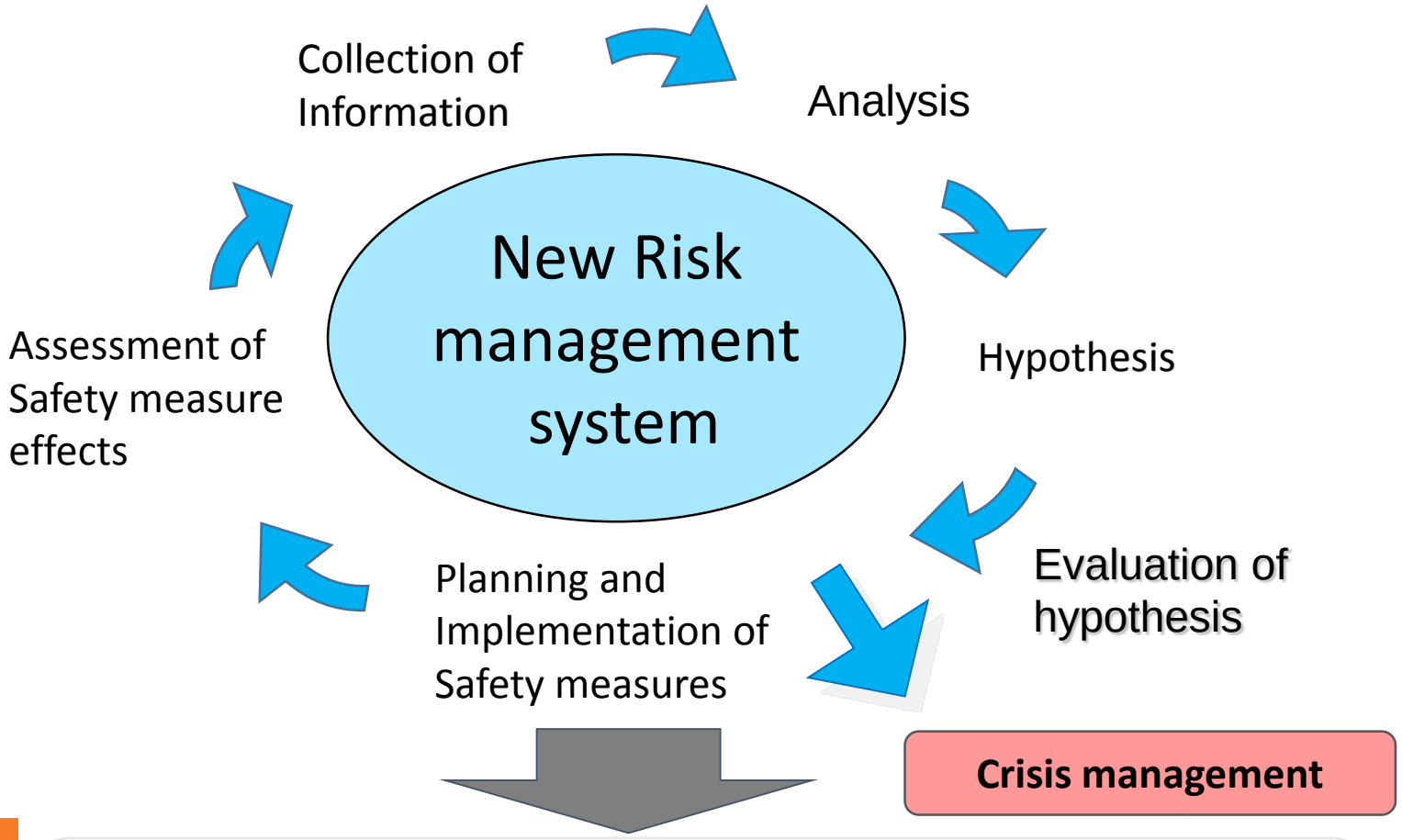
IMDRF International Medical Device Regulators Forum

- A review of the National Competent Authority Report (NCAR) system
- Roadmap for implementation of Unique Device Identification (UDI) system
- Medical Device Single Audit Program (MDSAP)
- IMDRF recognized standards
- Regulated Product Submission
- Standalone Medical Device Software Harmonization (SaMD)

Six guidance documents have been published (as of July 15th, 2014)

Chair: US (2014), Japan (2015)

Improvement of Safety Measures



Goal

- Prevention of serious drug safety-related crisis from Japan
- Effective encouragement of proper drug use.
- Ensuring credibility to post-market safety management system.

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Potential Topics in Science Board

1. Drugs
   - Placebo-controlled trials
   - Utilization of non-clinical testing

2. Medical Devices
   - Application of numerical analysis for non-clinical testing
   - Evaluation of medical devices for pediatric use (including application of non-clinical testing)

3. Cellular & tissue-based products
   - CPC (Cell Processing Center)

Advanced Review/Consultation System

Analysis by PMDA

Giving additional scientific value to submitted data

Cooperation with Academia

Regulatory Science

A rational & effective evaluation process for regulatory decision

Practical use of Innovative Medical Products

NDA etc.

e-Submission of study data

Data Accumulation

Database

Sophisticated NDA review

- Each reviewer utilizes innovative assessment techniques

Cross-Products Analysis

- Innovative evaluation methods
- Active utilization of Modeling & Simulation
  - Disease model
  - Objective B/R assessment
  - Identifying AE-related factors etc.

Sophisticated Consultation

- More evidence-based consultation

Effective and High Quality Review

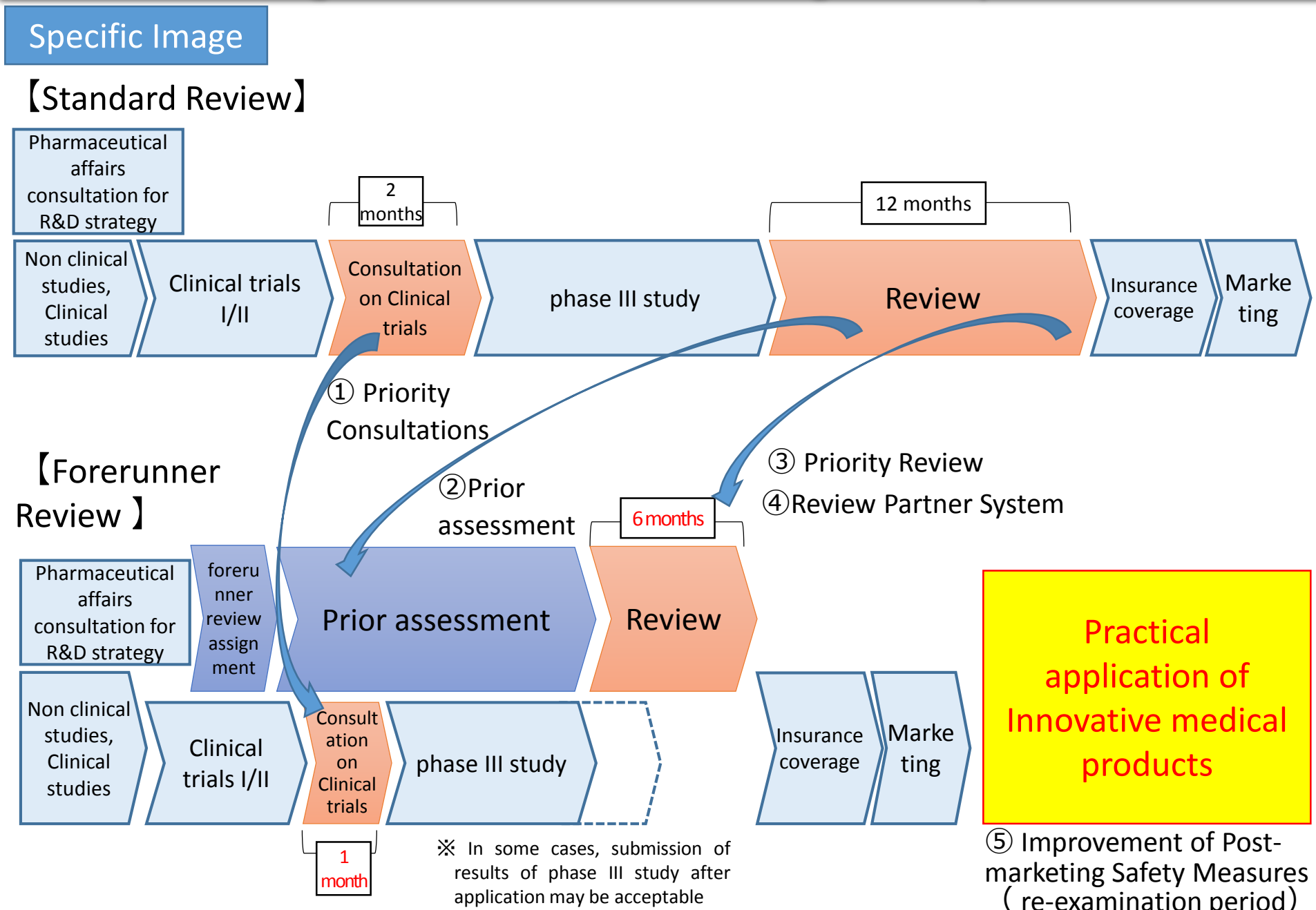
- More predictable efficacy/safety after approval
- Reduction of applicant's work load
- More scientific regulatory decision

Effective and Successful Development

- Epoch-making proposal leading the world
- Proactive publication of guideline

Image of forerunner review assignment system

Specific Image



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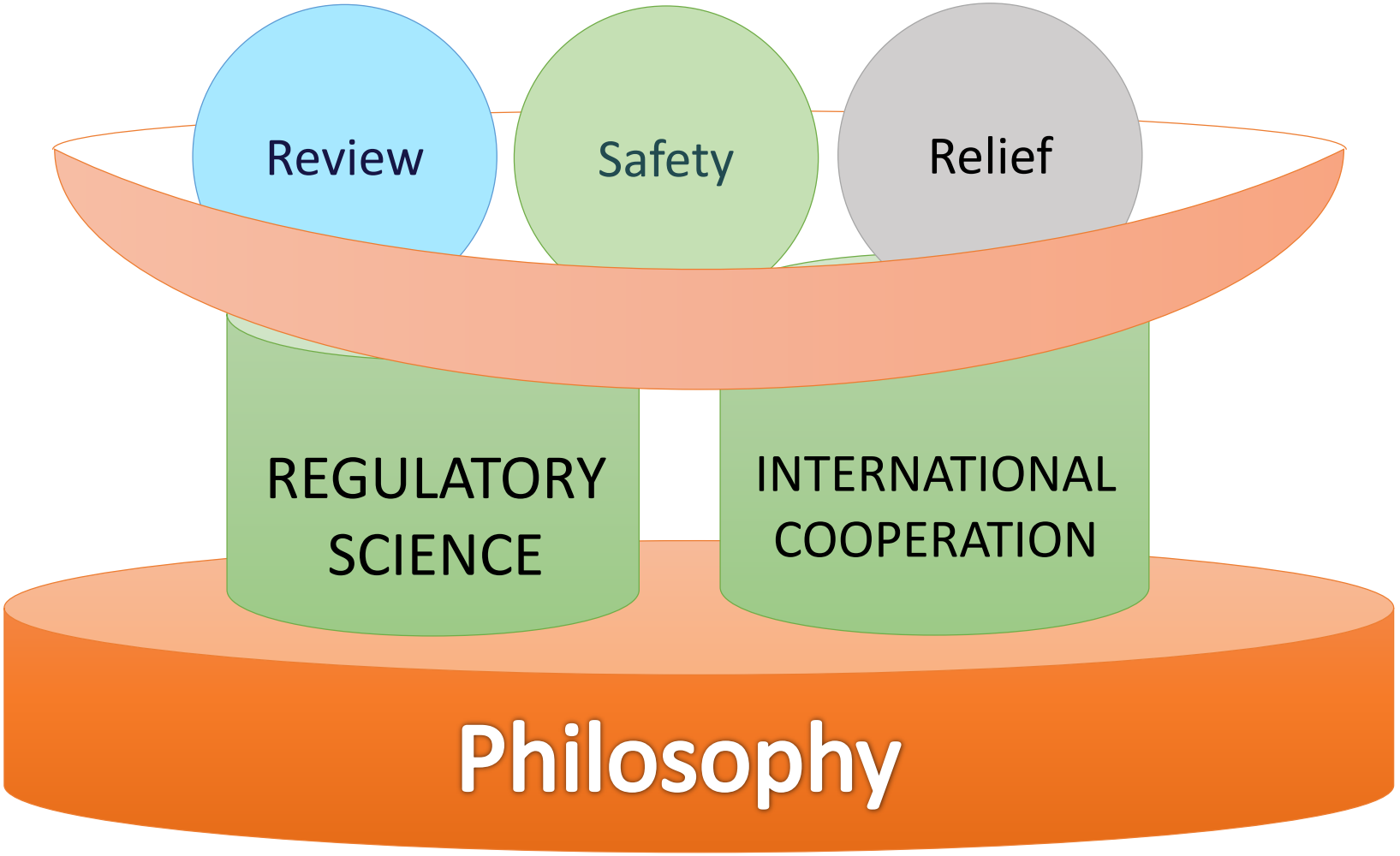
To Improve Public Health



Pharmaceuticals and Medical Devices Agency

Thank you for your attention !
Obrigado!

http://www.pmda.go.jp/

Back Up

Forerunner Package Strategy

～leading the world in promoting practical application of Innovative medical products ～

Promote a strategic package to support the product regulatory process from basic research to clinical research/clinical trial, review/safety measures, health insurance coverage and globalization as a whole in order to lead the world in early practical application of innovative drugs/ medical devices/cellular and tissue-based products for the treatment of life-threatening diseases (serious diseases including orphan cancer and intractable diseases) for which no effective therapies have been available

forerunner review assignment system

Scheme for practical application of unapproved drug

Strategic policy Ⅰ

Strategic policy Ⅱ

Basic・Practical Research, Non clinical studies → **Clinical studies・trials** → **review・approval** → **Insurance coverage** → **Organizing Industrial activity** → **Globalization**

Drug development accelerated by supporting each stage

- collaboration of Pharmaceutical affairs consultation for R&D strategy and innovation support network
- Supporting Off-label use/drug repositioning
- establishment of global standards and safety assessment methods using human iPS cells
- Collaboration of Gov't/non-Gov't organizations
- conduct high quality clinical research by NC/hospital specialized in clinical research collaboration with researchers of intractable diseases
- packaging of drug development support system for orphan drugs etc.
- Support drug innovation by promotion of ICT in medical area
- Modeling & Simulation by PMDA
- Prior Assessment Consultation
- Enforcement of post-marketing safety measures
  - ・promotion of registration system
  - ・biomarker research
- Prediction of rug pricing system
  - ・licensing innovative products
  - ・evaluation on releasing off-label use
- Increase competitiveness between industries
- Supporting smaller enterprises and ventures industries
- utilization of clinical data of intractable disease/cancer research for post-marketing surveillance system
- promote product export and mutual understanding of regulatory processes with partner countries

Strengthening PMDA（enhancement of consultation・review・safety measure systems）

Promotion of Regulatory Science（Establishment of assessment techniques and guidelines for latest science technology）