Future Plan of PMDA for the Next Five Years

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Pharmaceuticals and Medical Devices Agency

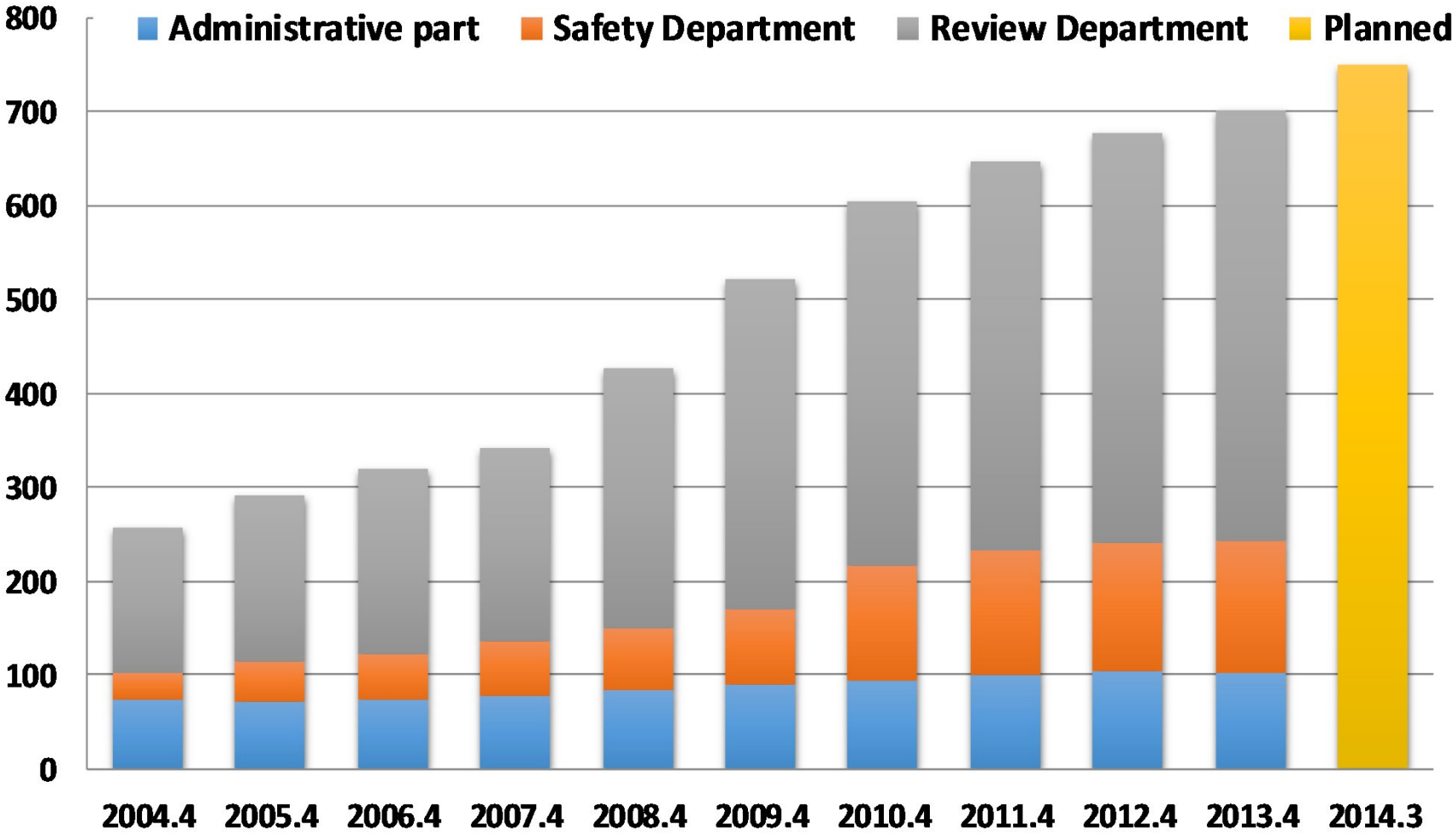
Date of Establishment : April 2004

Kansai Branch

Major Activities

- **Scientific Review for Drugs & Medical Devices**
- **GCP, GMP Inspection**
- **Consultation on Clinical Trials**
- **Safety Measures**
- **Relief Services**

Staff Size


Administrative part
Safety Department
Review Department
Planned
800
700
600
500
400
300
200
100
0
2004.4
2005.4
2006.4
2007.4
2008.4
2009.4
2010.4
2011.4
2012.4
2013.4
2014.3

PMDA Forum as the 10th Anniversary

2014. 2. 8. Tokyo

Guest speakers: Prof. Guido Rasi (EMA); Mr. Jüng H. Schnetzer (Swissmedic);
A/Prof. John C W Lim (HSA); Dr. Chung Seung (MFDS);
Dr. M. Hayatie Amal (NADFC); Mr. Kees de Joncheere (WHO);
Dr. Margaret A. Hamburg (FDA, video presentation)

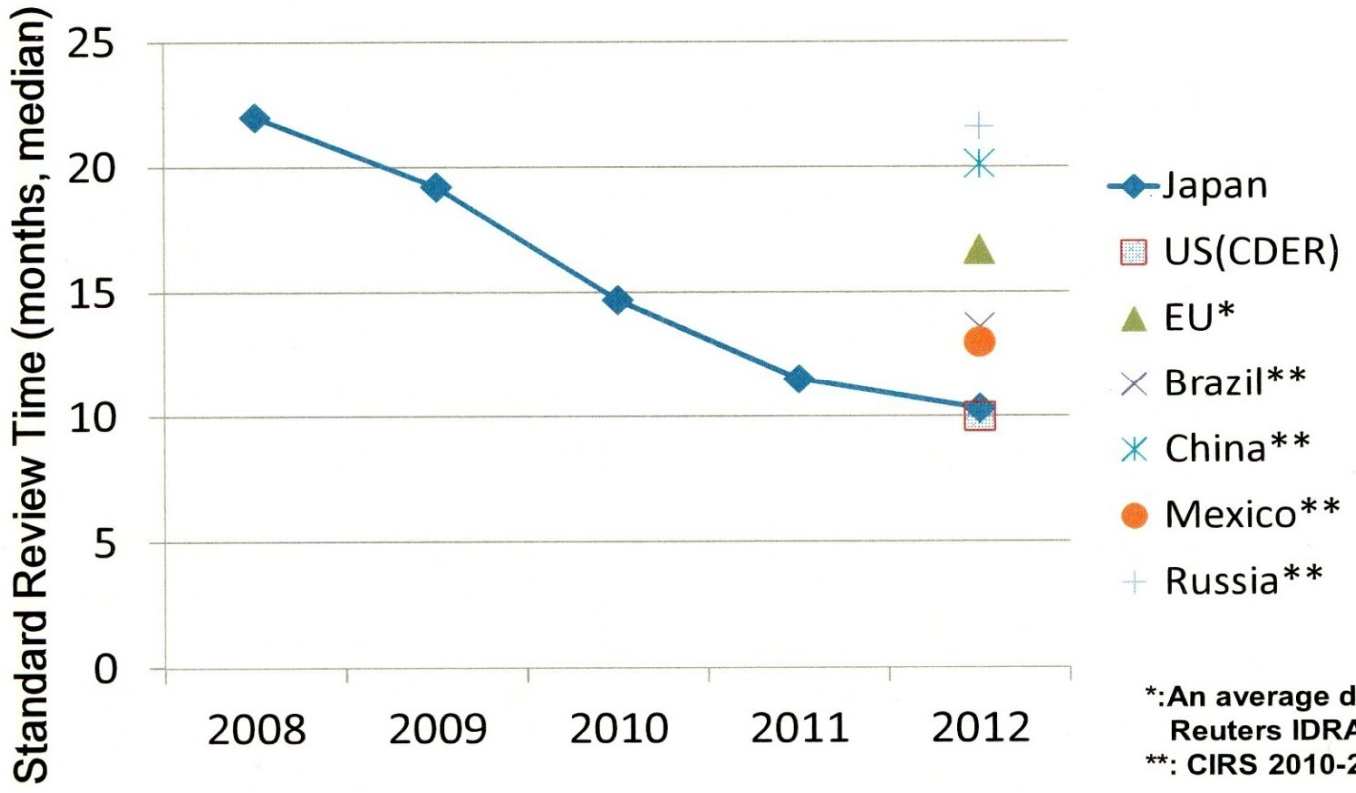
Strategies and Measures for PMDA Innovation

Issues with PMDA (past 5 years)	Basic policies to address the issues	Efforts made so far
◆ Shorten review time ・Reduce drug lag ・Reduce device lag ◆ Strengthen and enhance safety measures	◆ Philosophy (**Mission Statement**) ◆ Regulatory science ◆ Global partnership **(Win-Win Relationship)**	● 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.）

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

Japan's Performance on NDA Review

Japan authority have achieved the target on review, 12 months for standard review and 9 months for priority review as median, in the mid-term plan of PMDA for 2009-2013. Now it has the world's highest performance.



*:An average derived from Thompson Reuters IDRAC database
**: CIRS 2010-2011 benchmark

Japan Revitalization Strategy - JAPAN is BACK -

（Cabinet Decision on June 14, 2013）

Extended national “Healthy life expectancy”

<Future vision of the society>
The society where people can receive necessary healthcare services at the most advanced level in the world

Foster the industry specialized in extended healthy life, by developing innovative pharmaceuticals, medical devices and regenerative medicines first in the world, and by introducing these products to the market through speedy review process.

Measures

- Strengthen PMDA organization both in size and in quality
While maintaining a keen attention to post marketing product quality and safety, further reduction of review time (achieve “0” review lag) and improved quality will be pursued.

- **Establish control tower function (Japanese version of NIH)**
  Build systems where integrated research management, bridge between research and clinical practice, and world-class, high-quality clinical research/trial will be securely carried out.

  *Reform of regulation and system to accelerate generative medicine research and environmental improvement for practical use of regenerative medicine products are required.

Health and Medical Strategy

(Agreed by Chief Cabinet Secretary, Minister of Health, Labour and Welfare and other related Ministers on June 14, 2013)

Basic philosophy (Three philosophies)

- Realize extended healthy life society
- Contribute to economical growth
- Contribute to the world

Measures

- **Establish organization to promote research and development**
  ~ Prepare "All Japan" support system ~
- Establish Japanese version of NIH
- Streamline and enhance the consultation program, in close cooperation with drug discovery support network
- **Strengthen PMDA**
- Expand and enhance the pharmaceutical affairs consultation on R&D strategy program **~ Provide better perspective for development, promoting speedy implementation ~**
- Promote PMDA's own analysis and study of clinical data, etc.

※Development of the security evaluation system using iPS cells is required for better new drug development

Amendment of Pharmaceutical Affairs Act

◆ **Strengthen Safety Measures regarding Drugs, Medical Devices**

- Specify relevant party's obligation to ensure quality, safety, and efficacy of drugs and medical devices.
- MAH's obligation to notify revised Package insert reflecting the latest findings

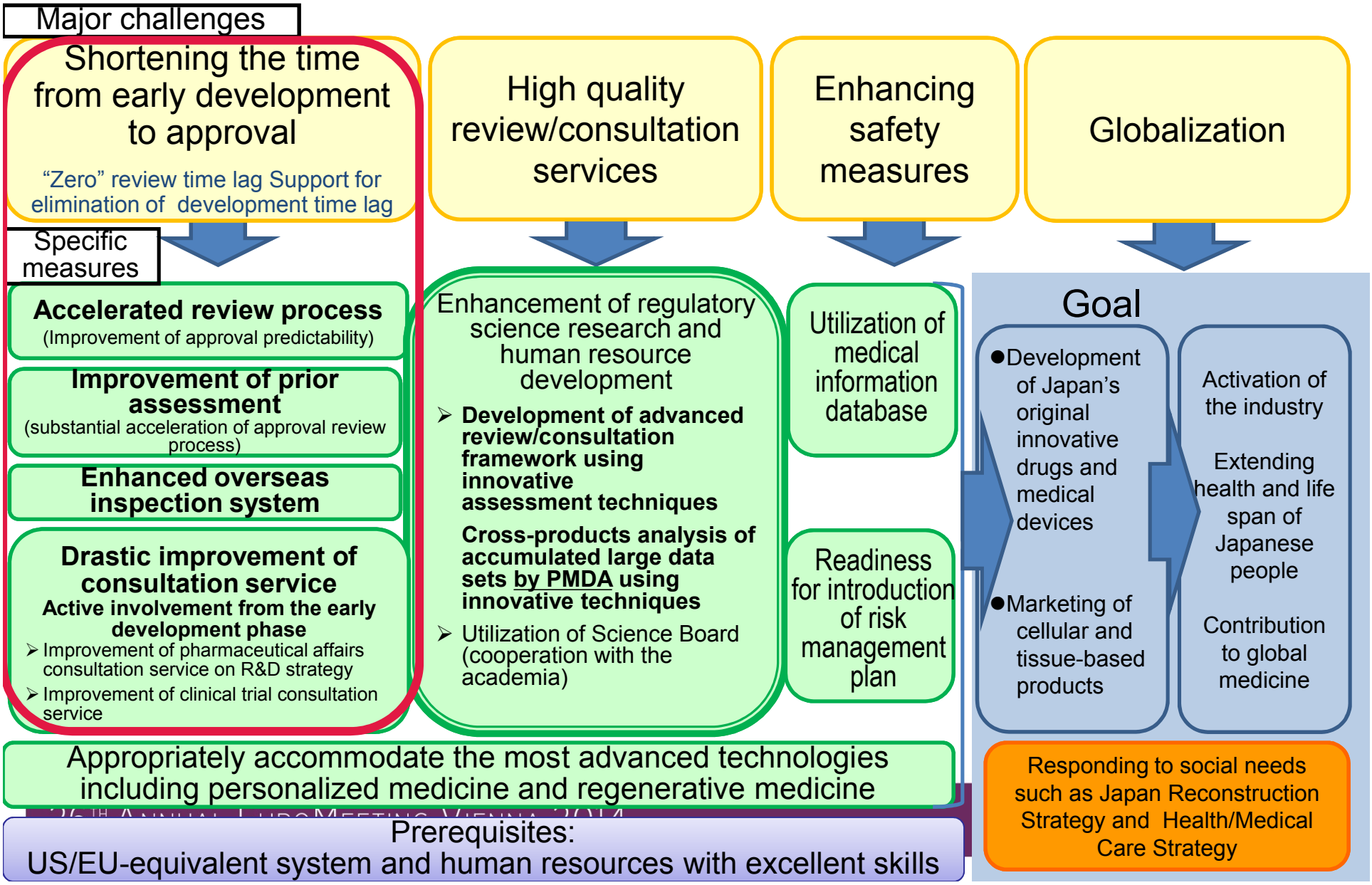
◆ **Regulation considering Medical Devices Character**

- Independent Chapter for "Medical Devices"
- Third party certification system
- Quality Management System (QMS)
- Other revisions related to medical devices
- Regenerative and Cellular Therapy Products, and Gene Therapy Products

◆ **Regulation considering Regenerative Medicines Character**

- Creation for Regenerative Medicines regulations
- Introduction of approval system with condition/period

3rd 5-year mid-term plan of PMDA (FY2014-2018)



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

600 Consultations

If needed

Pre-Consultation

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

669 Consultations

Face-to-Face Consultation

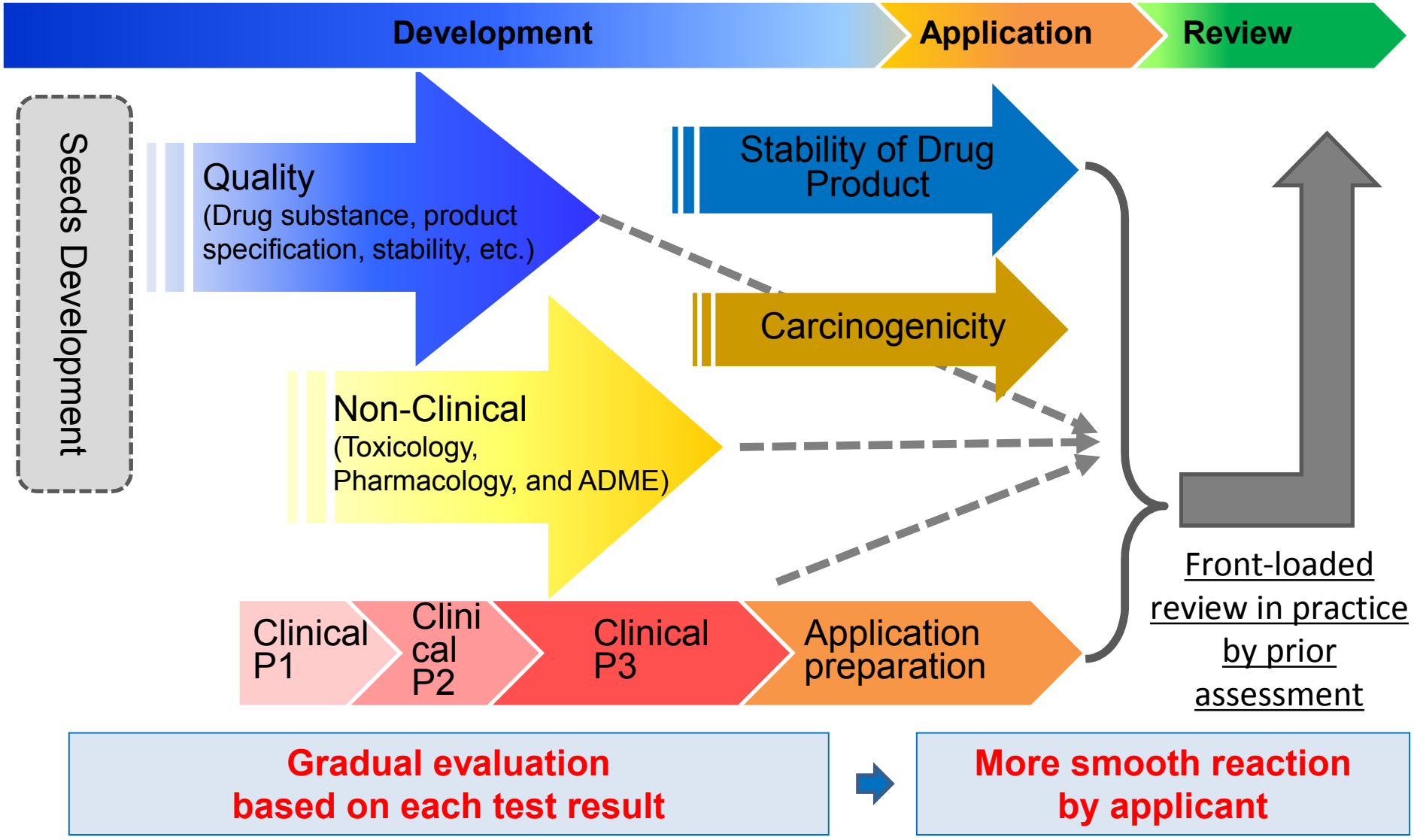
- Scientific discussion
- 2 hours, Charged, Binding, Minutes

158 Consultations

(7/1/2011 – 12/31/2013)

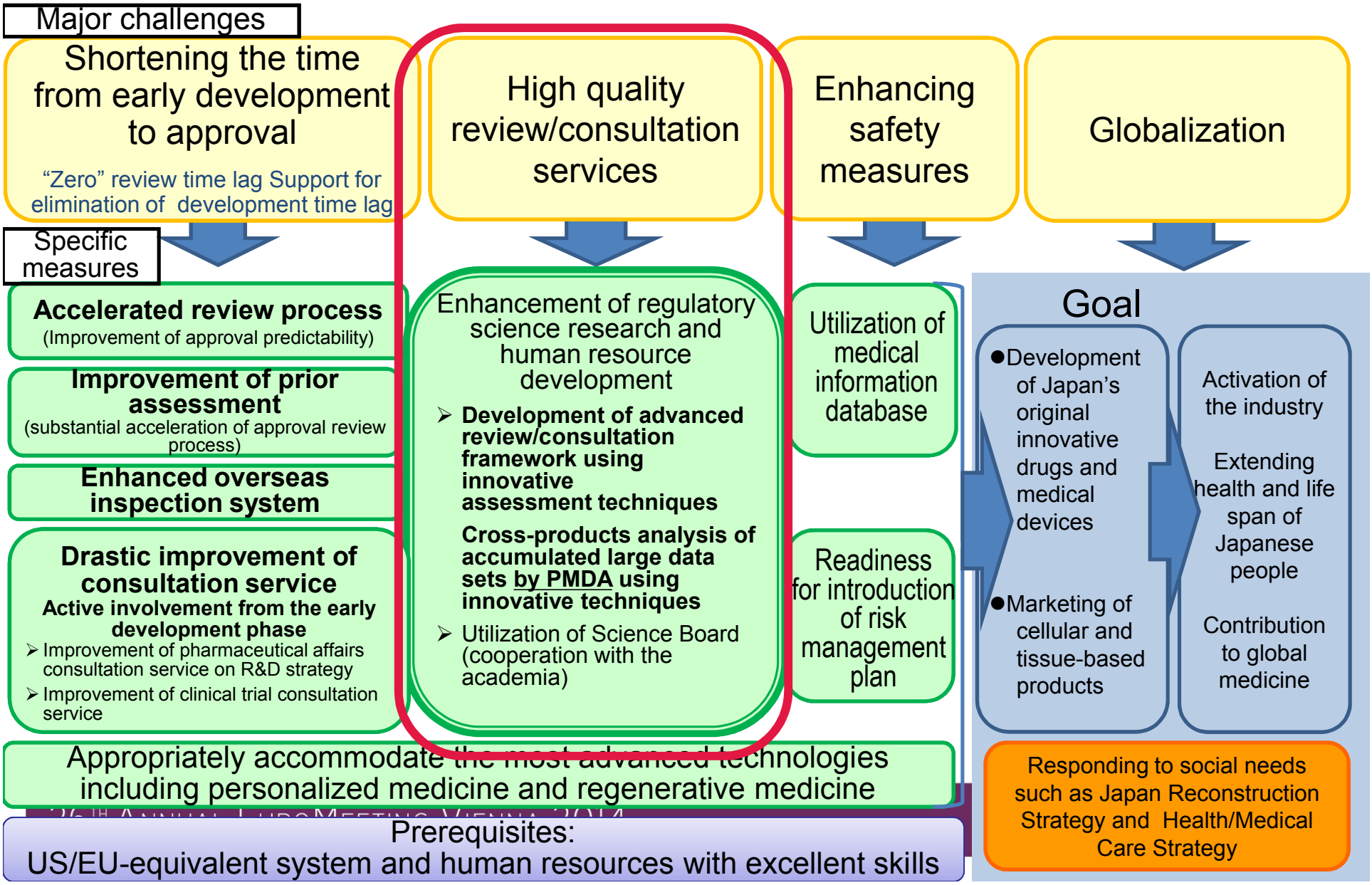
* Further studies are handled by the Regular Consultation

Reinforcement of Prior Assessment Consultations



Gradual evaluation based on each test result → **More smooth reaction by applicant**

3rd 5-year mid-term plan of PMDA (FY2014-2018)



Outcomes of the Science Board

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 (Aug. 20, 2013)

- Tumorigenicity of Cellular and Tissue-based Products
- Assessment on the Undifferentiated Cells/Tumorigenic Cell Contaminants and Tumorigenicity in Cellular and Tissue-based Products Derived from iPS cells, etc.
- Assessment and Management of Tumorigenicity of Human (Allogeneic) iPS Cells Used for Manufacturing iPS Cell-derived Products

Summary of Discussion on Non-clinical Pharmacology Studies on Anticancer Drugs (Nov. 15, 2013)

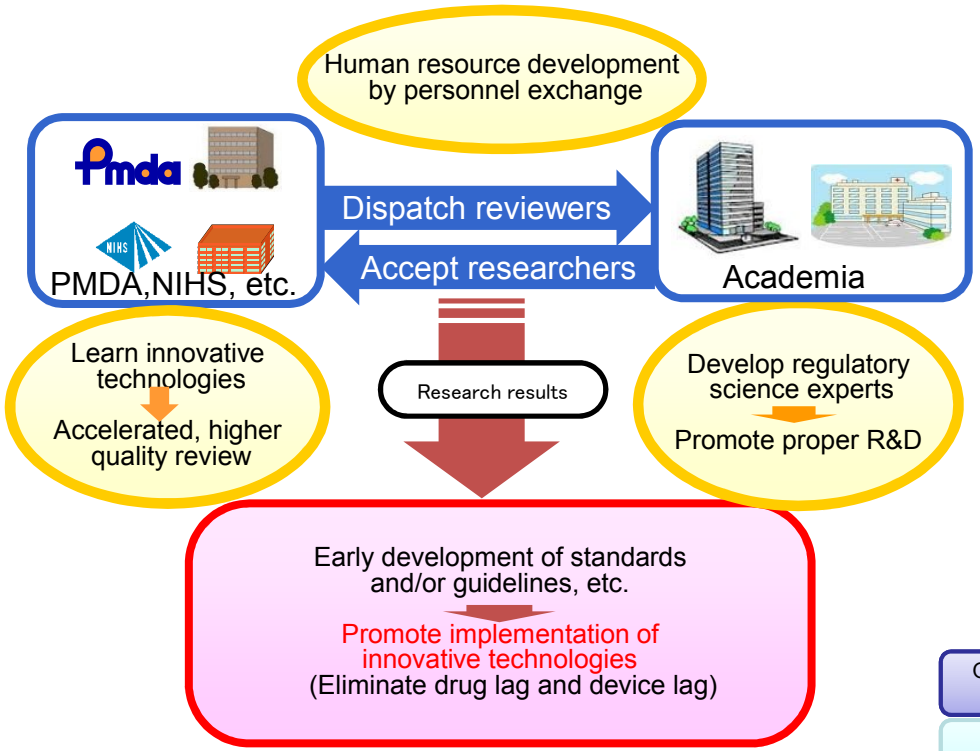
- Current status of non-clinical pharmacology studies on anticancer drugs and the concept of evaluation in regulatory review
- Role and expectations for non-clinical pharmacology studies in future development of anticancer drugs (role of non-clinical pharmacology studies and their contribution to the development of anticancer drugs, taking into account of the recent advancement of personalized medicine)

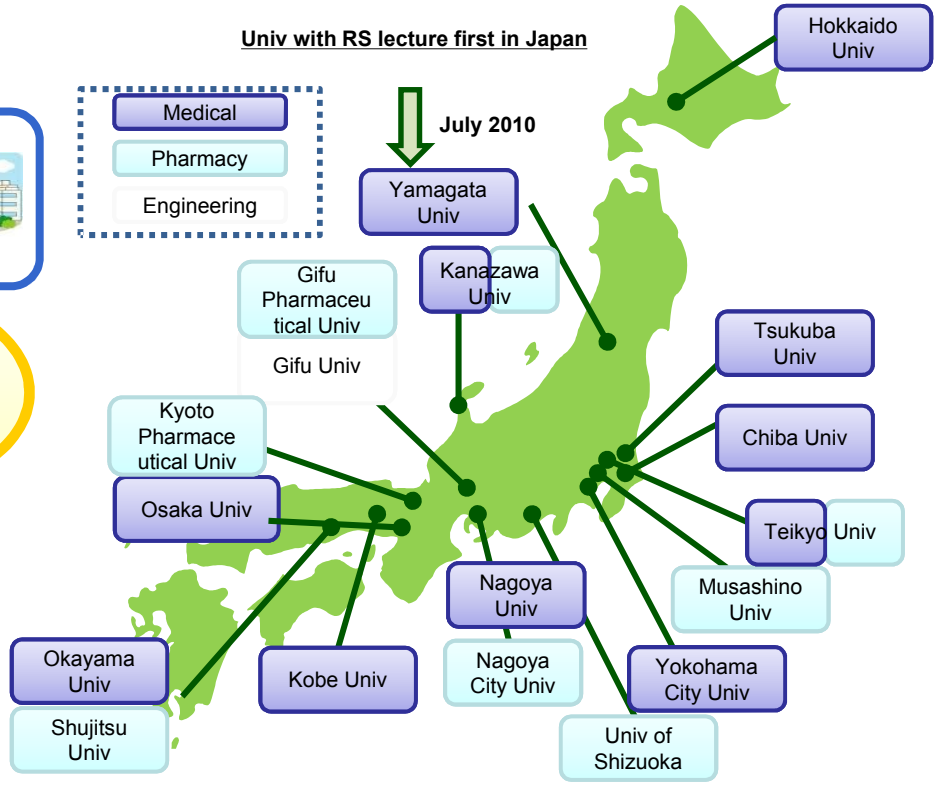
Summary of the discussions on assessment of the current status of personalized medicine relating to drug development and review

- *(English material is in the make and will be up when ready)*

Initiative to facilitate development of innovative drugs, medical devices, and cellular and tissue-based products

- support establishment of evaluation system for safety and efficacy with R&S as the basis at research facilities researching latest technology
- exchange human resources between universities, NIHS, PMDA, and train resources adept in RS





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

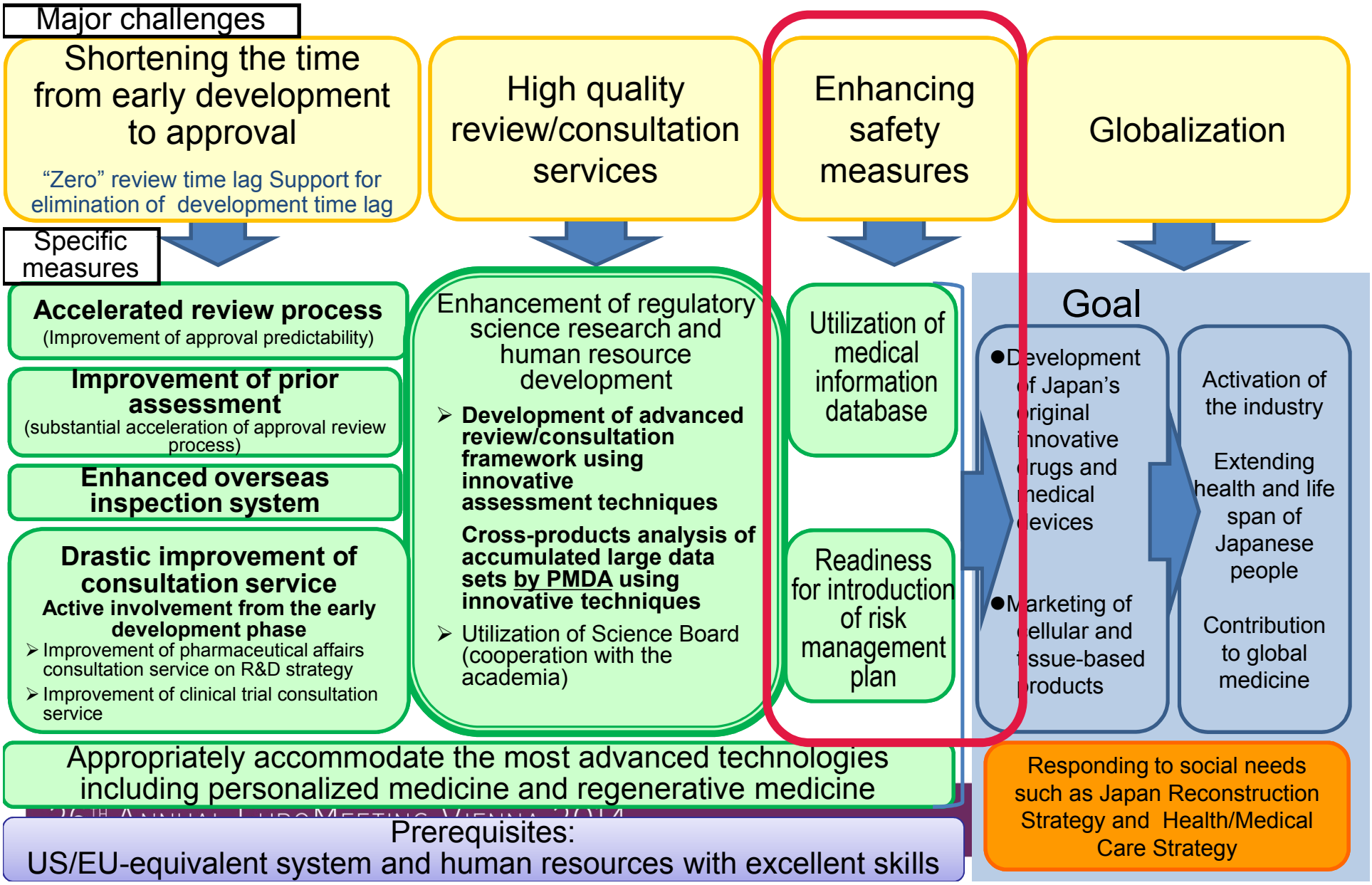
Effective and High Quality Review

- 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

3rd 5-year mid-term plan of PMDA (FY2014-2018)



Initiative to Develop Infrastructure for Medical Information Database

Catch line: Provide safe and secure medical care by collecting 10 million patients scale medical information

- Build database hubs at 10 cooperating medical institutions nationwide such as university hospitals.
- Target is to make more than 10 million patients data ready for use in 2015.

＜Expectations＞
Faster and more appropriate safety measures by utilizing the database for safety study.
(Ex. Understanding of adverse reaction ratio, risk assessment, evaluation of safety measure effects, etc.)

Cooperating medical institutions (10 University and group hospital sites)

Associated medical institutions of hub medical group

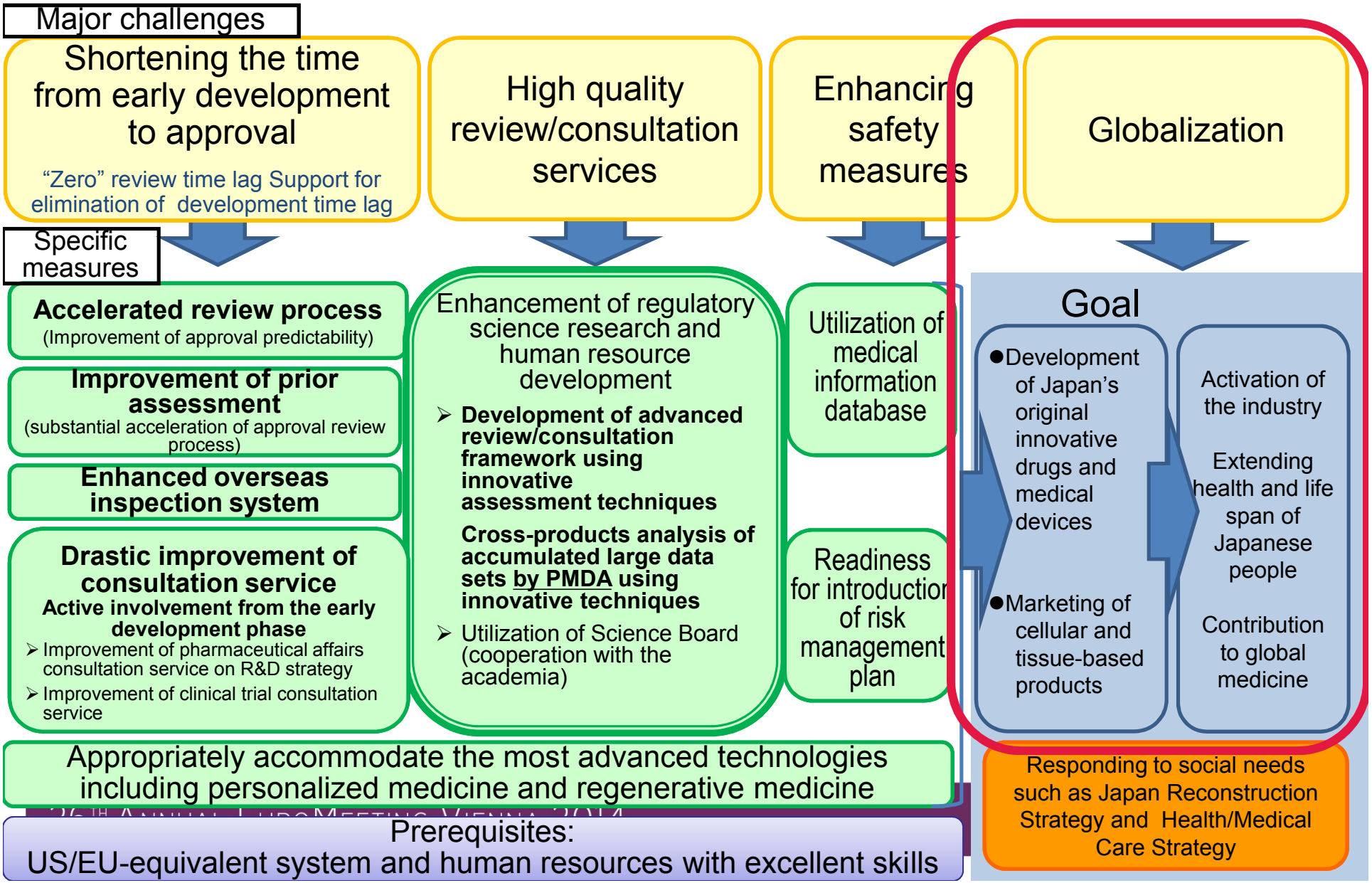
Utilization by PMDA and researchers

Data collected at 10 hub medical institutions will be retrieved and studied for analysis and evaluation of adverse reactions

Priority Issues to be Consolidated for Post-Marketing Safety Measures

1. Strengthening of information gathering on adverse drug reactions and malfunctions
2. Organization of information on adverse drug reactions and systemization of evaluation and analysis
3. Establishment of the medical information databases
4. Establishment of a post-marketing safety system through information feedback
5. Fulfilling information distributed to general public related to Pharmaceuticals and Medical Devices Safety
6. Appropriate safety measures based on the Risk Management Plan
7. Reinforcement of safety measures adapted to new review system as well as consistently monitoring the safety of drugs from the clinical trial stage to post-marketing stage
8. Strengthening and improvement of follow-up on implemented safety measures
9. Organizing, evaluating, and analyzing information gathered from Vaccine Adverse Reaction Reporting System

3rd 5-year mid-term plan of PMDA (FY2014-2018)



Roadmap for the PMDA International Vision

Five Important Areas Where RMs are needed

1) Response to advanced science and technology

・Proactively provide information about the policies for review and scientific consultation of cutting-edge products and recommendation for relevant guideline developments.
・Introduce progressive analyzing and predictive methods.

2) Improvement of international operation basis

・Improve the organizational structure enabling wide range international activities and cultivate new internationally minded personnel* in a prompt manner.

*A personnel who has 1) good command of foreign languages, 2) an international human network, 3) abundant knowledge of his or her related area of expertise , 4) ability to make appropriate decisions under the given circumstances domestically and internationally, and 5) trustworthy international relations.

3) Dissemination of English information on regulatory review of medicinal products, especially publication of review reports in English

・Increase the number of English version of review reports (aiming to cover all the necessary review reports in English in the future).

4) Dissemination of information and international cooperation on safety measures

・Enhance exchanging information and establish a system to share evaluation reports with our overseas counterparts.
・Enrich the contents related to safely information in the English website.

5) Increase of the leverage of Japanese Pharmacopoeia (JP)

・Publish the newest JP version simultaneously in English and Japanese.
・Enhance cooperative relationship with the USP, EP, WHO and each Asian pharmacopeia.

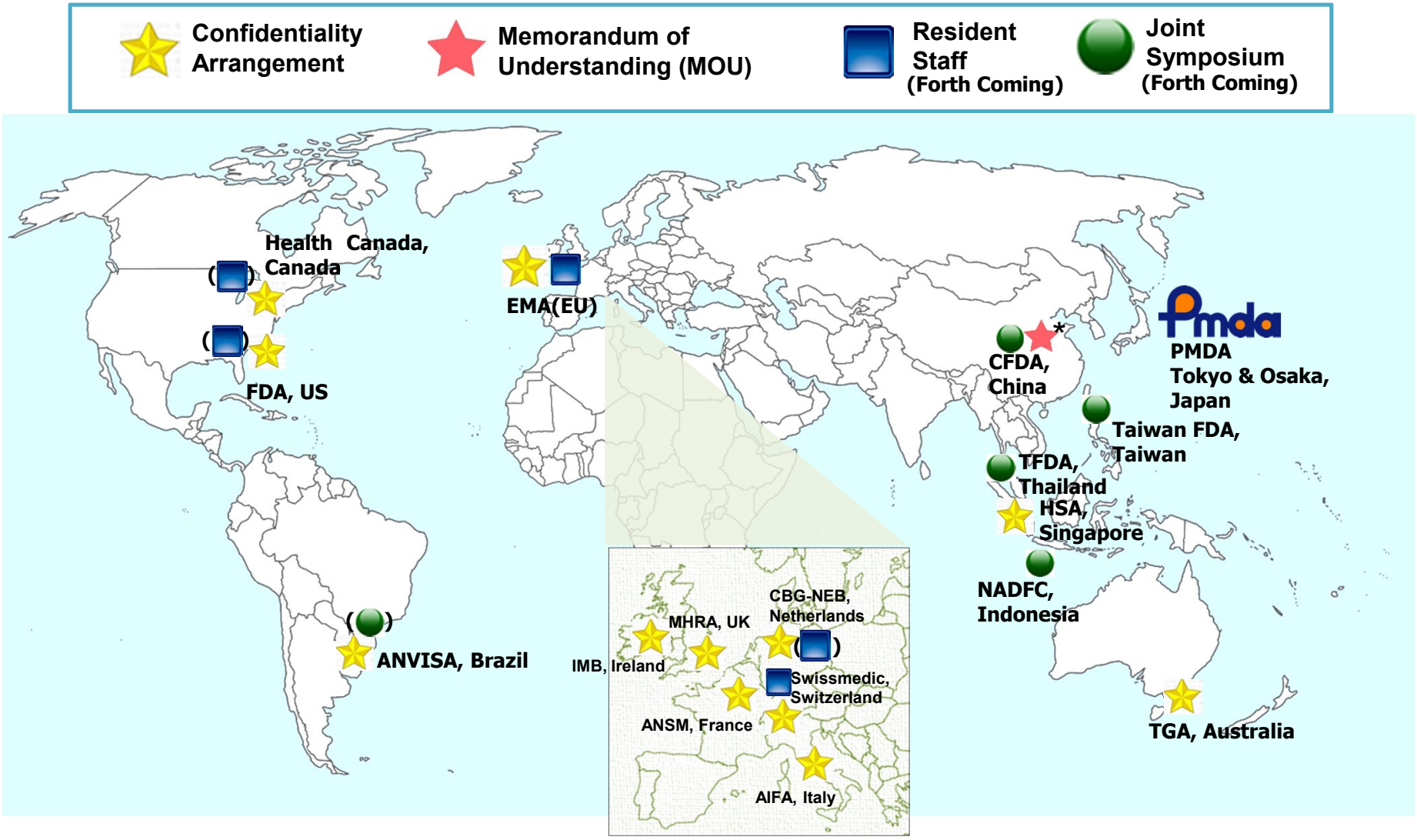
Note) As we have been committed to emphasize the activities with ICH, IMDRF and other foreign regulatory agencies, the effort should continue for the future development.

Current Global Activities

and more…

ICH	International Conference on Harmonization
IMDRF	International Medical Device Regulators Forum
OECD MAD	OECD Mutual Acceptance of Data
PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
APEC LSIF RHSC	APEC Life Science Innovation Forum Regulatory Harmonization Steering Committee
ICCR	International Cooperation on Cosmetics Regulation
PDG	Pharmacopoeial Discussion Group
IGDRP	International Generic Drug Regulators Pilot

PMDA and the World



** MOU between the Chinese SFDA (present CFDA) and the Japanese MHLW, under which PMDA supports cooperative activities*

Training for Foreign Regulatory Officers

PMDA Training Seminar

Pharmaceuticals:

1st (Nov. 2010) Reviewing of New Drugs
2nd (Dec. 2011) GMP inspection
3rd (Jan. 2013) Post-Marketing Safety & Relief Services
4th (Feb. 2014) Reviewing of Generic Drugs

Medical Devices:

1st (Mar. 2014) Review and Safety

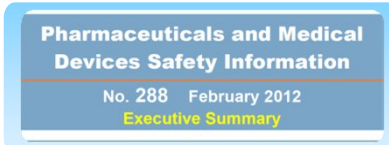
Individual Training (including OJT)

- ✓ NADFC (Indonesia) officials: 5 days, 2013
- ✓ FDA (US) analyst: 6 months, 2014-2014
- ✓ NPBC (Malaysia) officials: 1 month, 2014 (forthcoming)
- ✓ Thai FDA (Thailand) officials: 5 days, 2014 2014 (forthcoming)

etc.

Dissemination of Information

Review Report



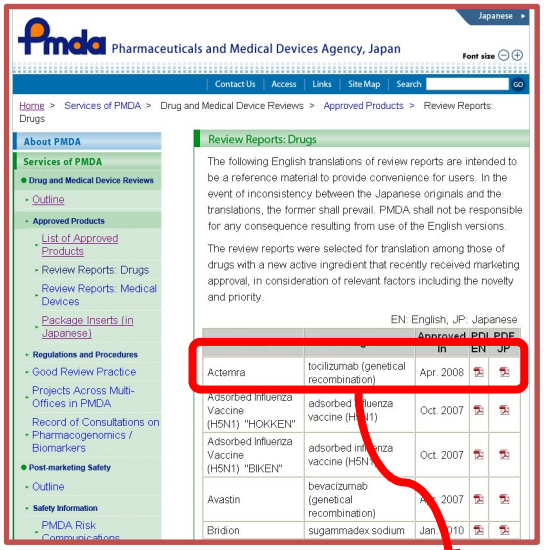
Safety Information

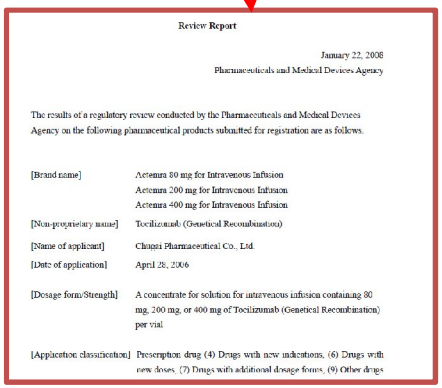
Pharmacopeia

PMDA Updates

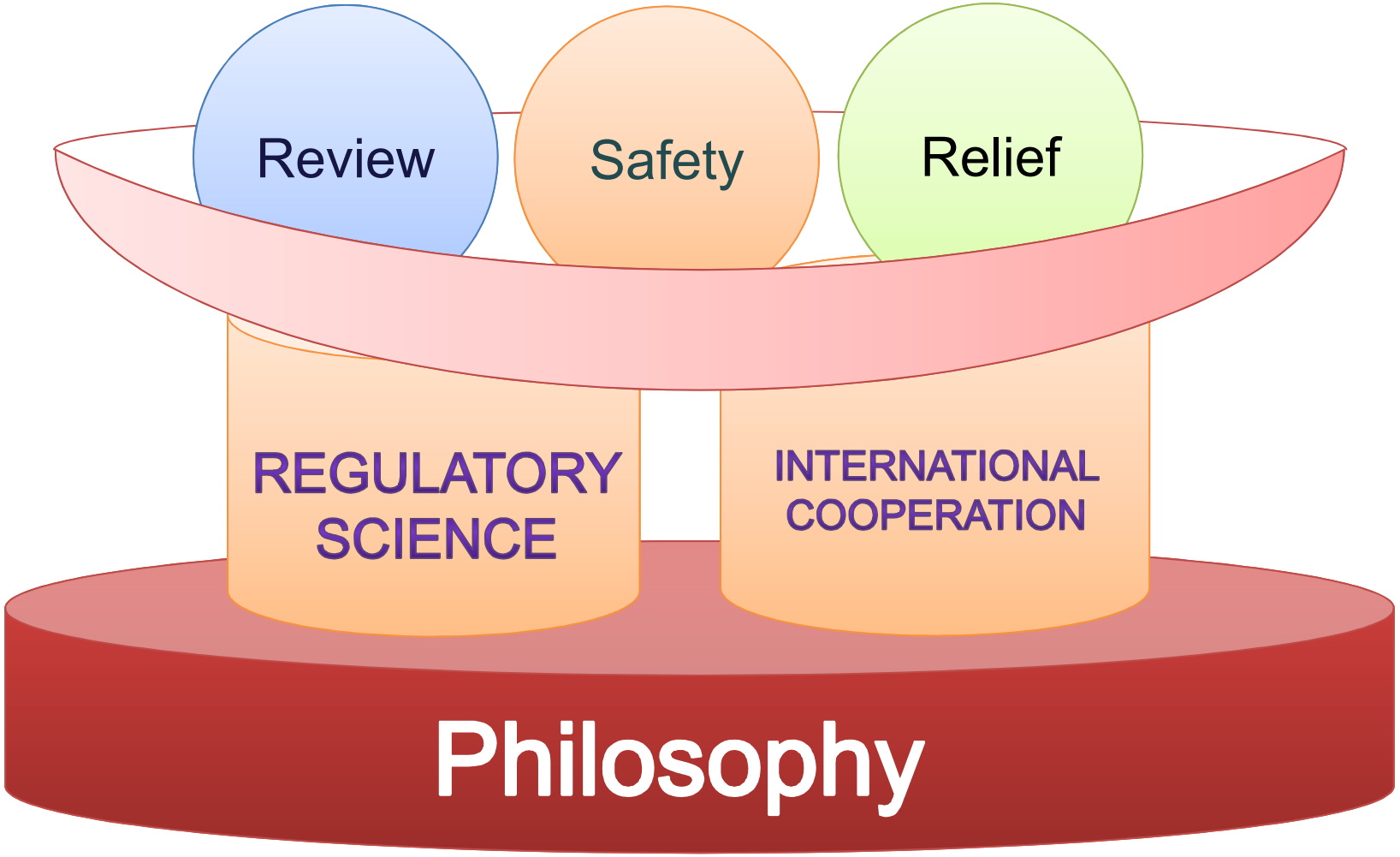
News Release

And more…





To Improve Public Health



Thank you for your attention!