Regulatory and legal frameworks for offering stem cell therapies in Japan

Special Advisor to the Cabinet

Health and Global Policy Institute

(Former Deputy Director of Ministry of Health, Labour and Welfare)

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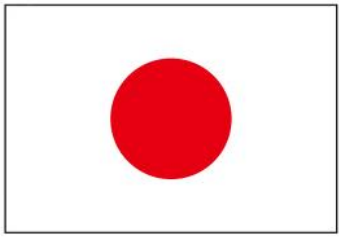


HGPI
Health and Global Policy Institute

Disclosure Information

- I have no financial relationships to disclose.

Japanese Government

- **Cabinet Office (Prime Minister)**
  - National Public Safety Commission(National Police Agency)
- Ministry of Public Management, home Affairs, Posts and Telecommunications*
- Ministry of Justice
- Ministry of Foreign Affairs
- Ministry of Finance
- Ministry of Defense
- Ministry of Education, Culture, Sports, Science and Technology(MEXT)*
- **Ministry of Health, Labor and Welfare (MHLW)***
- Ministry of Agriculture, Forestry and Fisheries*
- Ministry of Economy, Trade and Industry(METI)*
- Ministry of Land, Infrastructure and Transport*
- Ministry of Environment

* merged some ministries and agencies in 2001

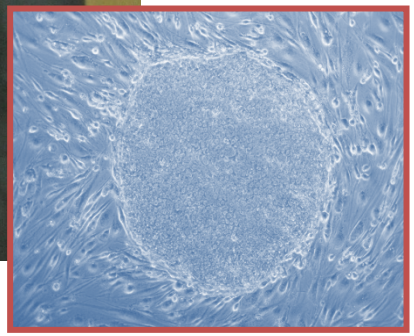
Japan Revitalization Strategy
-JAPAN is BACK-
June 14, 2013

To push forward the development of Japanese outstanding innovation (for example, iPS cell), establish control tower functions (Japanese version of NIH) which will ensure integrated research management.

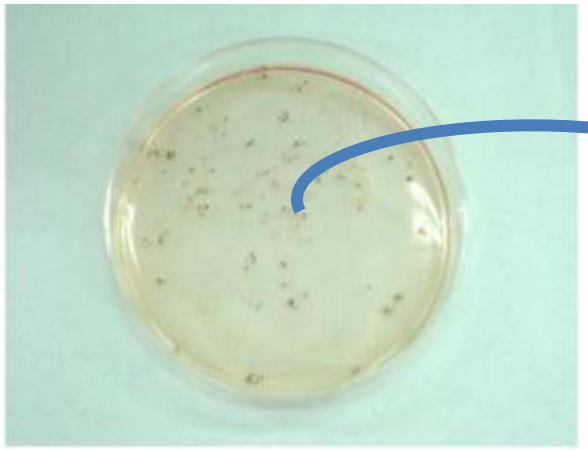
(Submit bill to establish new independent administrative agency to Diet during next ordinary session)

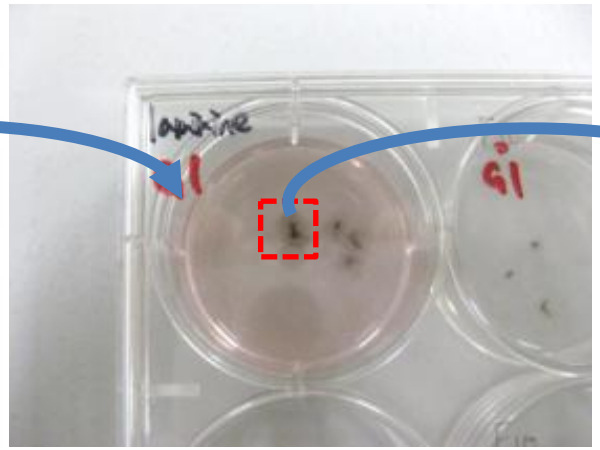
Nobel Prize 2012
Sir John Gurdon & Prof. Shinya Yamanaka

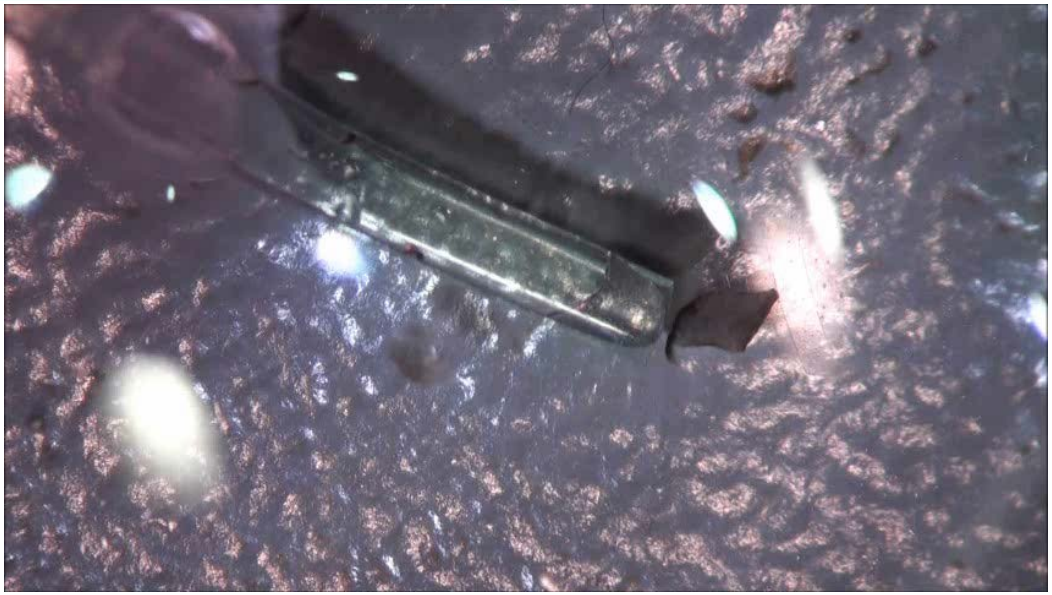
iPS cells

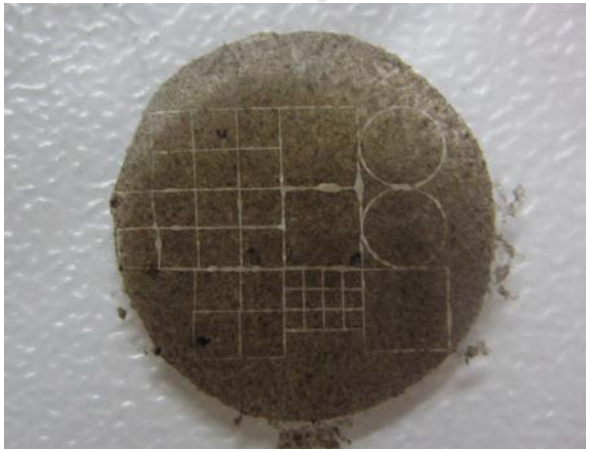


Purification of iPS-derived RPE cells

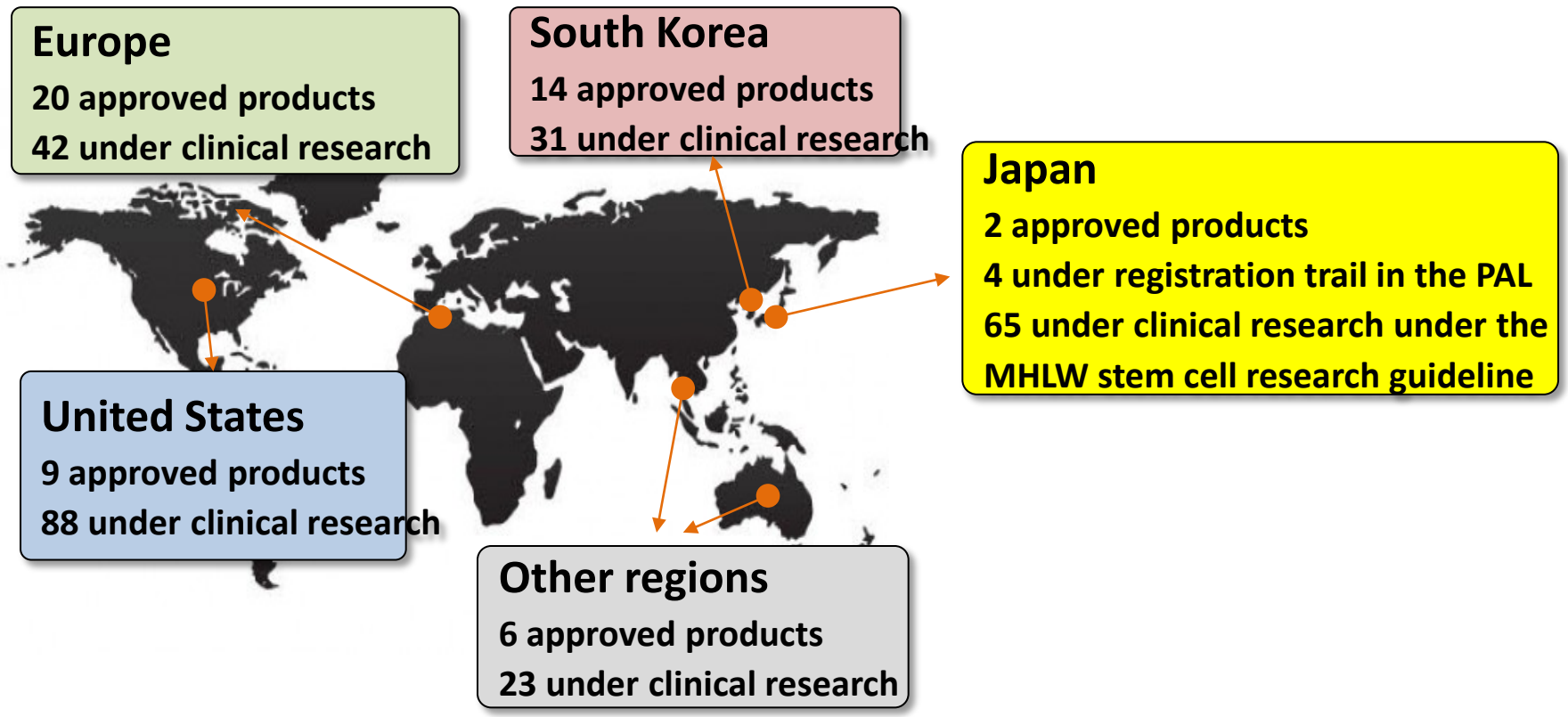






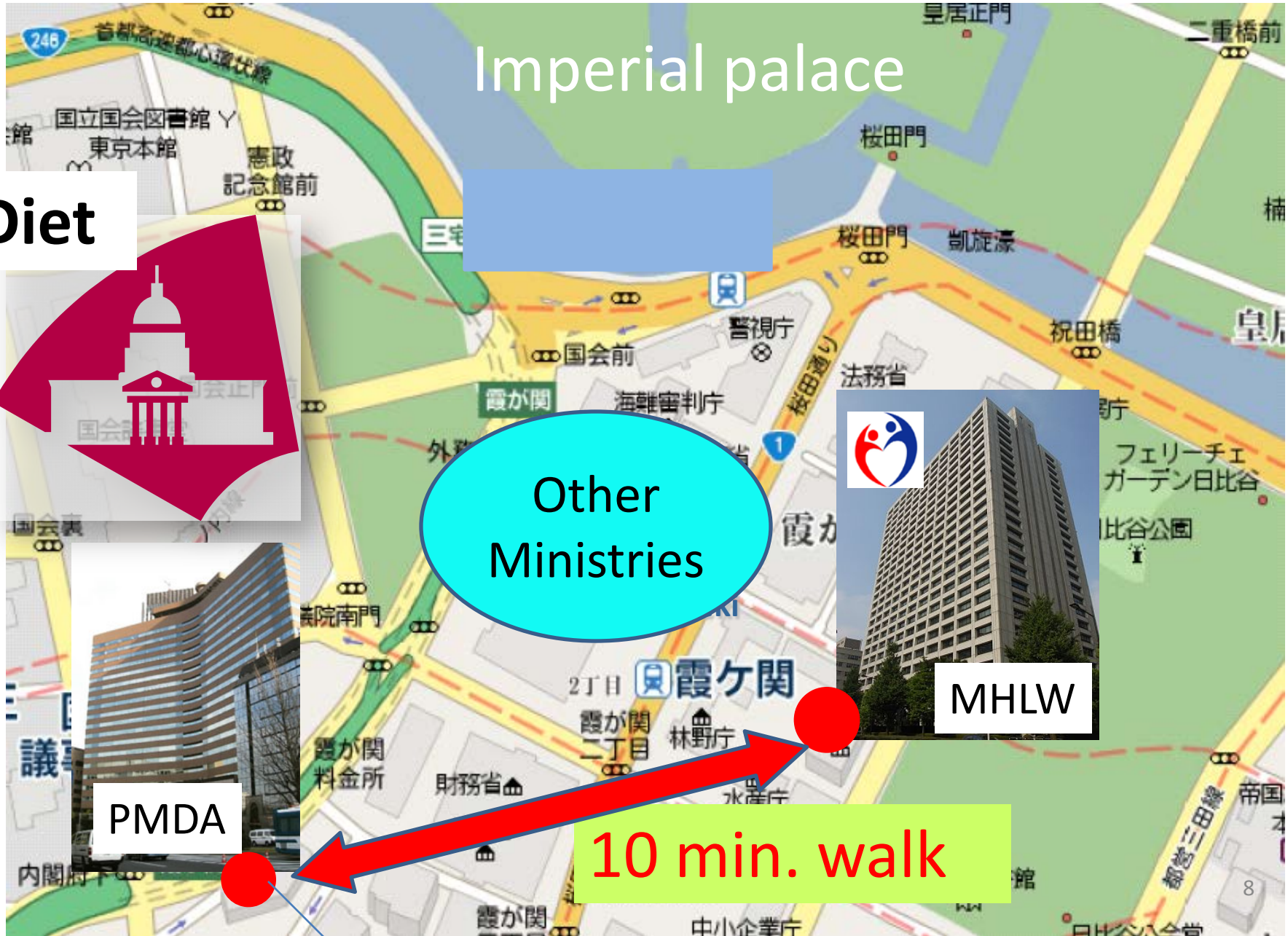


Regenerative medicine products already approved or in clinical research phase in the various regions（as of Dec 2012）

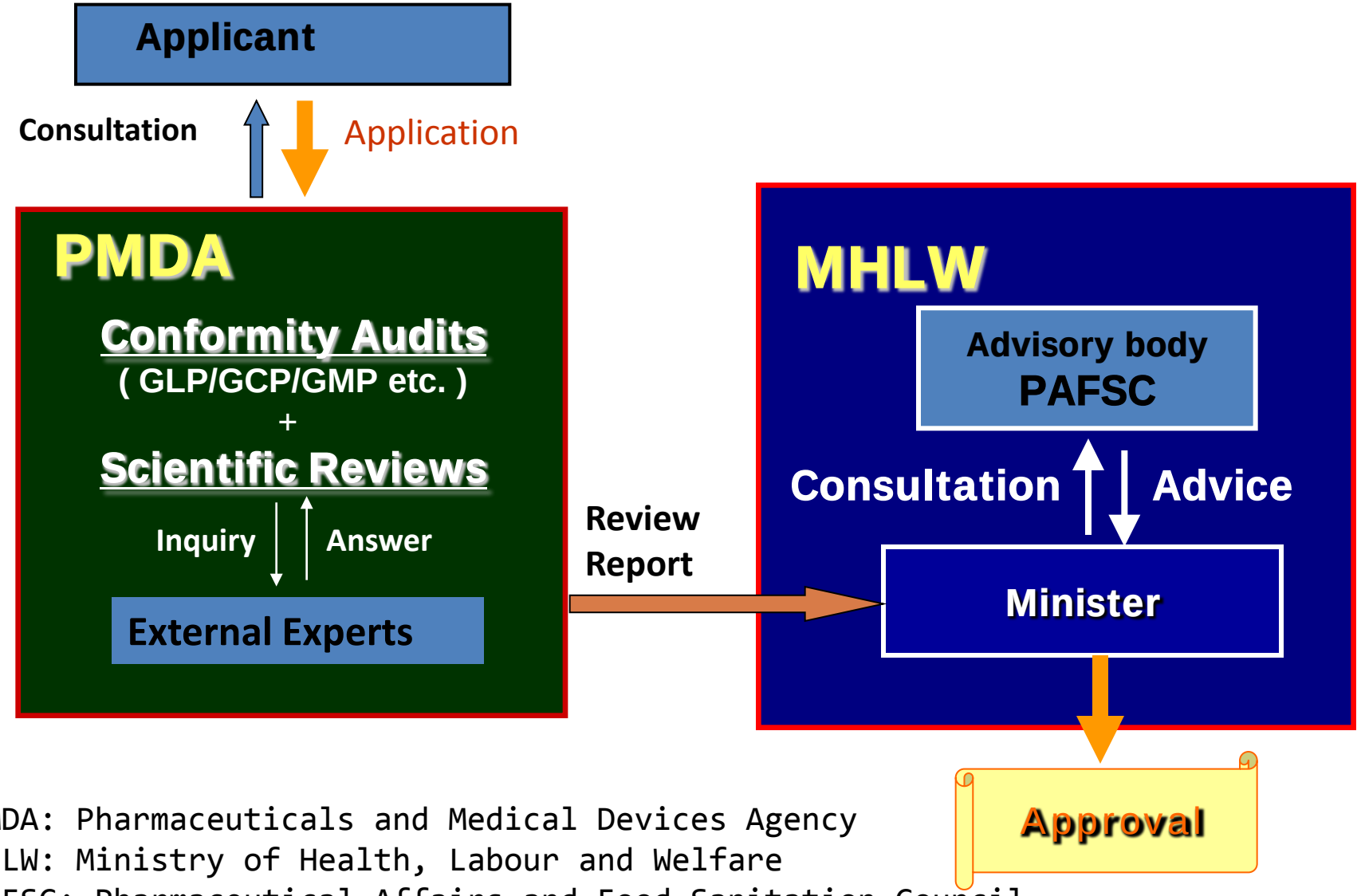


Reference：Survey by Seed Planning (modified)

Ministry of Health Labor & Welfare (MHLW) & Pharmaceuticals & Medical Devices Agency (PMDA)



Outline of Approval Review Process under the Pharmaceutical Affairs Law



PMDA: Pharmaceuticals and Medical Devices Agency
MHLW: Ministry of Health, Labour and Welfare
PAFSC: Pharmaceutical Affairs and Food Sanitation Council

Shared Responsibilities

[MHLW]

Ultimate Responsibilities in policies & administrative measures

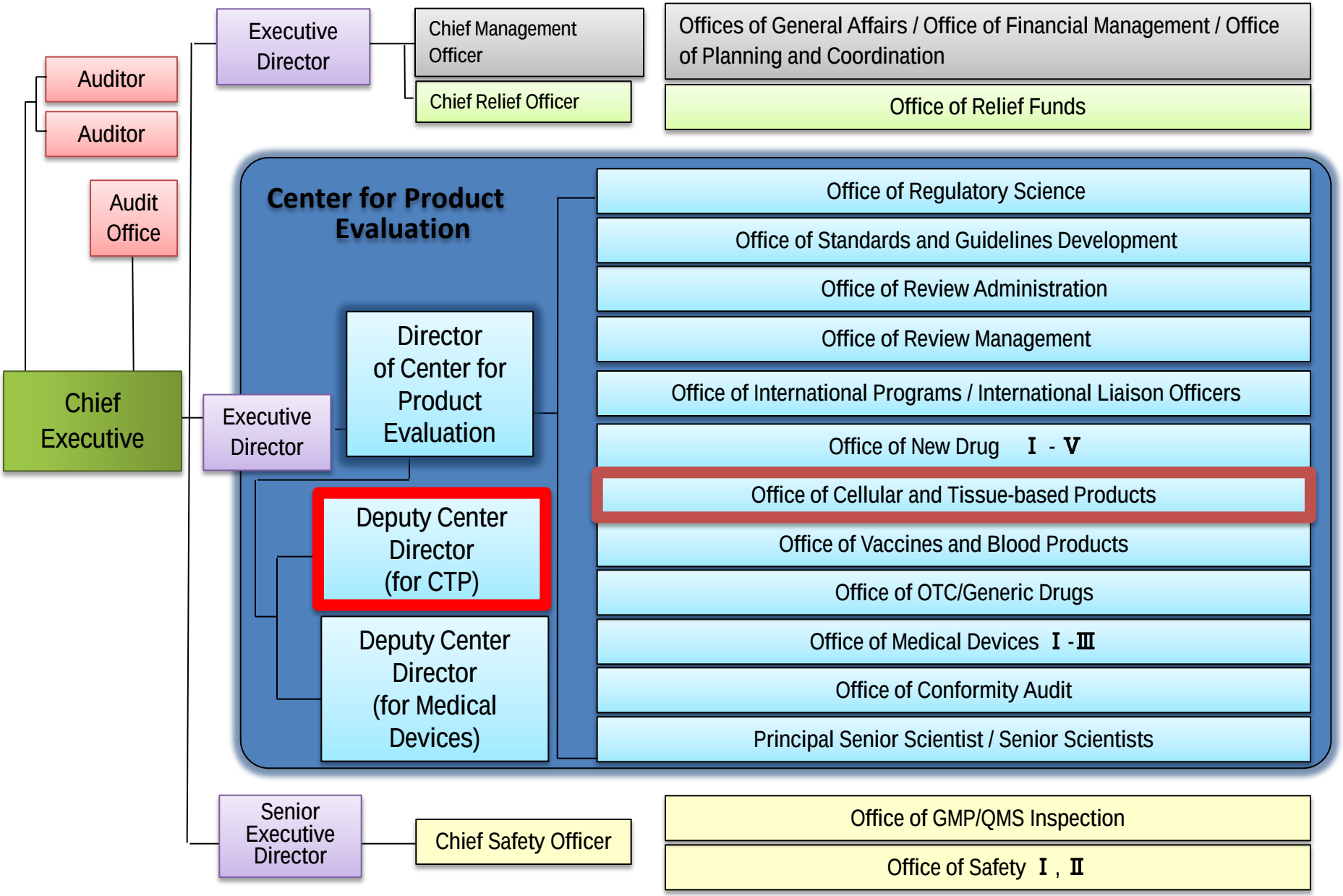
ex.
- **Final judgment on approval**
- **Product withdrawal from market**

[PMDA] "TECHNICAL ARM of MHLW"

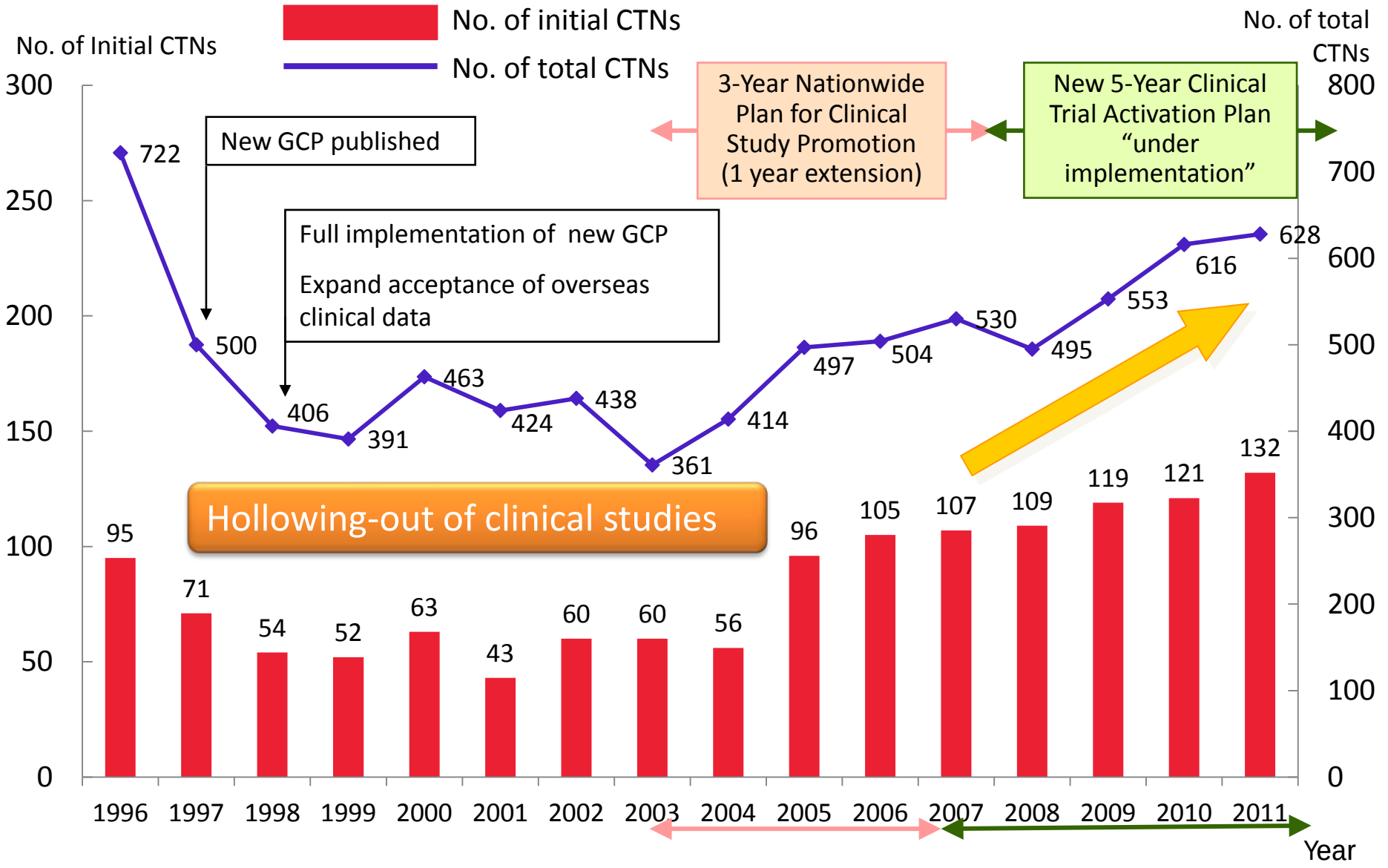
Actual review, examination, data analysis, etc. to assist MHLW'S measures

ex.
- **Approval Review of New Drugs or MDs**
- **GMP/QMS/GLP/GCP inspection**
- **Collection and analysis of Adverse Event Reports**

ORGANIZATION OF PMDA AS OF OCT. 2012



Drug Clinical Trial Notifications (CTN)



・**Poteligeo (mogamurizumab) – Kyowa Hakko Kirin Pharma**

Incication: Relapsed or refractory CCR4-positive adult T-cell leukemia-lymphoma

Companion Diagnostic Assay (CCR4) was approved by MHLW/PMDA simultaneously for the first time in the world.

Drug lag in US/EMA.

→ Multi-regional clinical trial is important.

・metreleptin - Shionogi

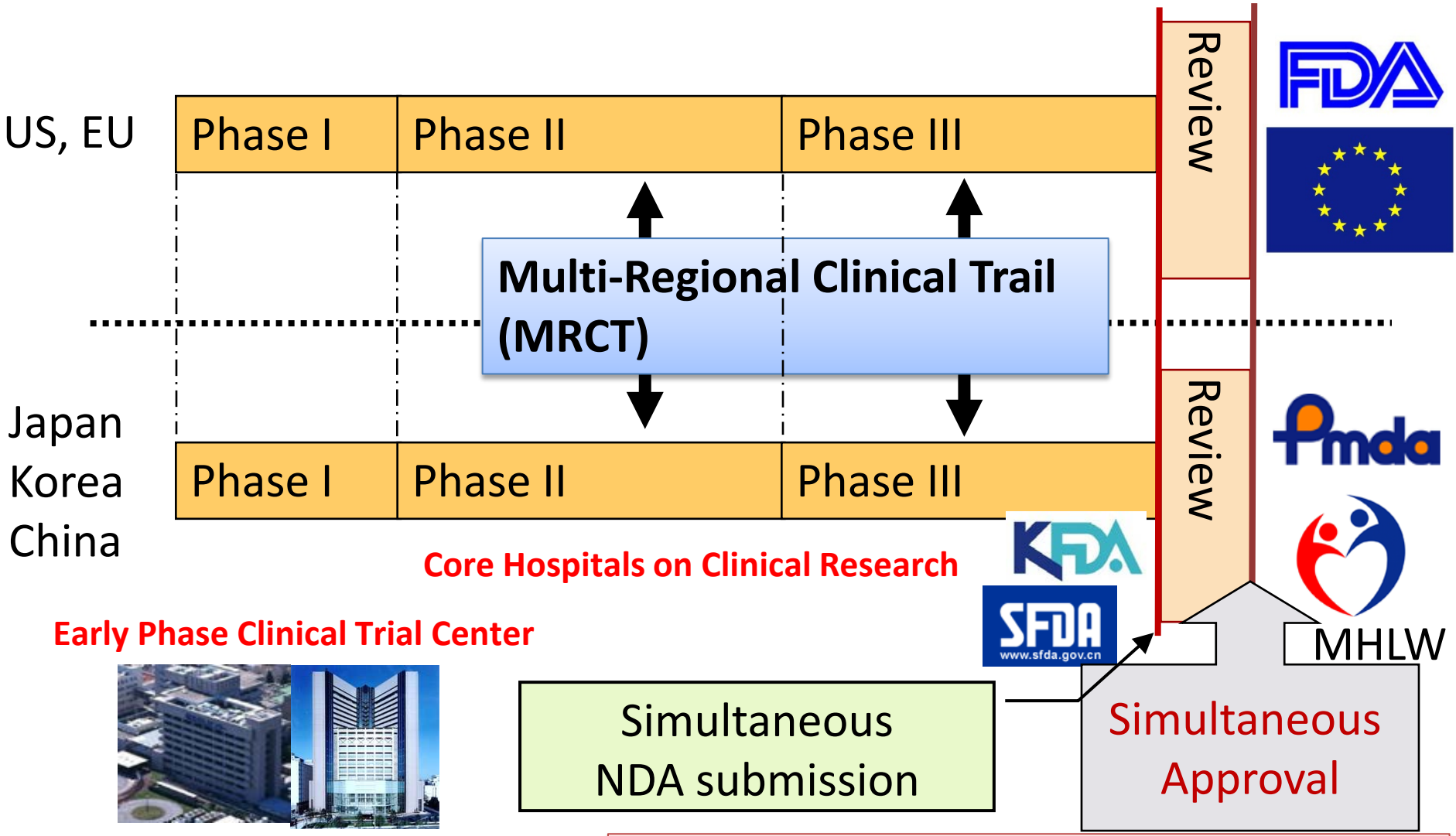
Indication: lipodystrophy (ultra-orphan disease)

First approval in Japan Mar/2013

Research IND trial is conducted by Kyoto University.

The MHLW reformed Japan GCP ordinance to facilitate research IND trials (Dec 2012).

Simultaneous Global Drug Development



Life Innovation Project for Health Care

FY2011 budget request: about ¥13.1 bn (Joint project among MHLW, MEXT, and METI)

R&D

1. Research into practical applications of treatments for cancer, intractable diseases, etc.

2. Development of innovative cancer treatments from Japan using cancer vaccine methodologies

7. Support for practical application of robots, assistive care devices, etc.

Infrastructure Development

5. Strategy consulting for drugs and medical devices to achieve practical application of projects originating in Japan

6. Construct drug information database infrastructure

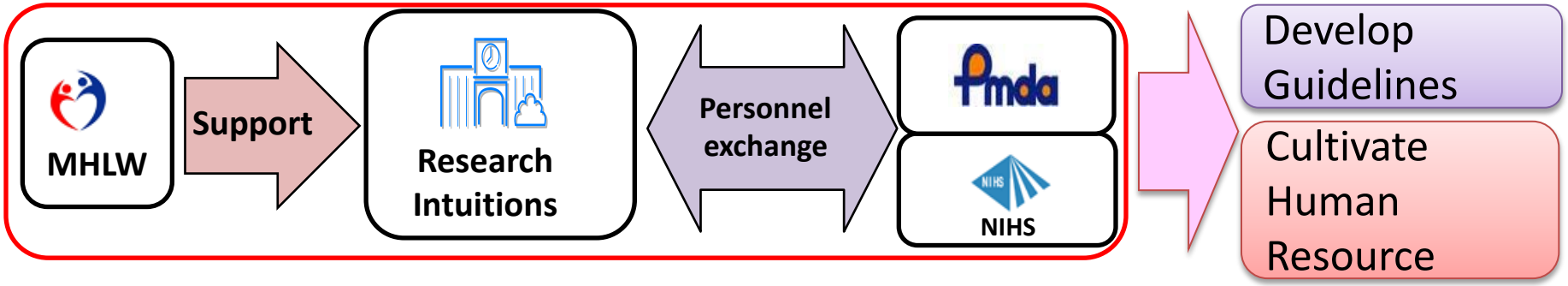
3. Create early phase clinical trial centers for innovative drugs and medical devices

4. Cutting Edge Medical Technology R&D（National Specialized Medical Research Centers）

MHLW FY 2012 Budget for Enhancement on Approval Review/ Safety Measure in Response to the Progress of Technology

1.2 billion yen (about 97 million RMB) for;

- Develop draft guideline/guidance based on Regulatory Science
- Promote human resource exchange between PMDA & research institutions



366 million yen (about 30 million RMB) for;

- Developing guideline/guidance for innovative drug/medical device/biologics to streamline regulatory review based on Regulatory Science

Examples

Alzheimer's Disease

the University of Tokyo, Kyoto University

Personalized Medicine (Cancer)

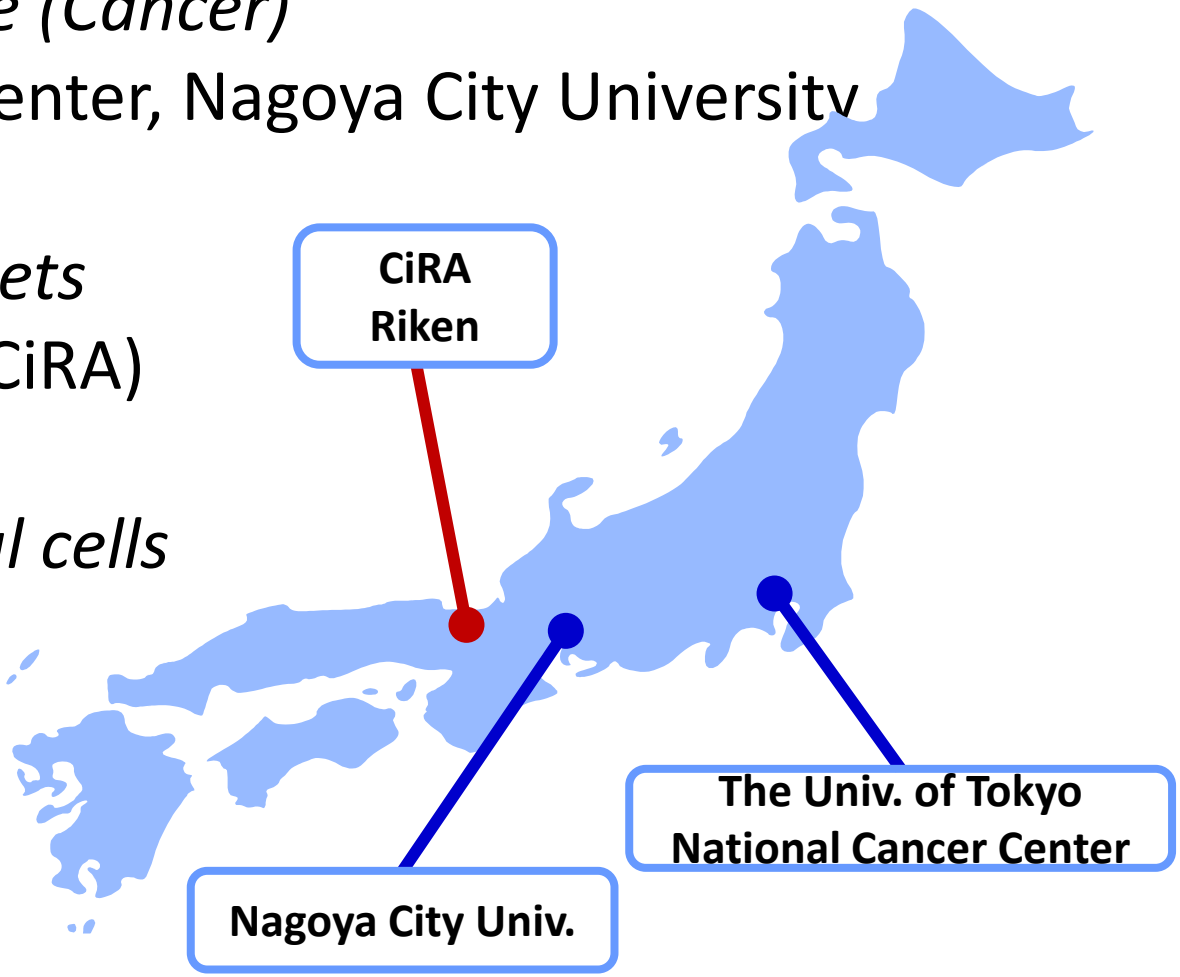
National Cancer Center, Nagoya City University

iPS Cell-derived Platelets

Kyoto University (CiRA)

iPS Cell-derived retinal cells

Riken (Kobe)



Establishment of regulation considering unique characteristics of regenerative medicine products

[Direction of Revision under consideration]

1. Establishment of specific definition of regenerative medicine products

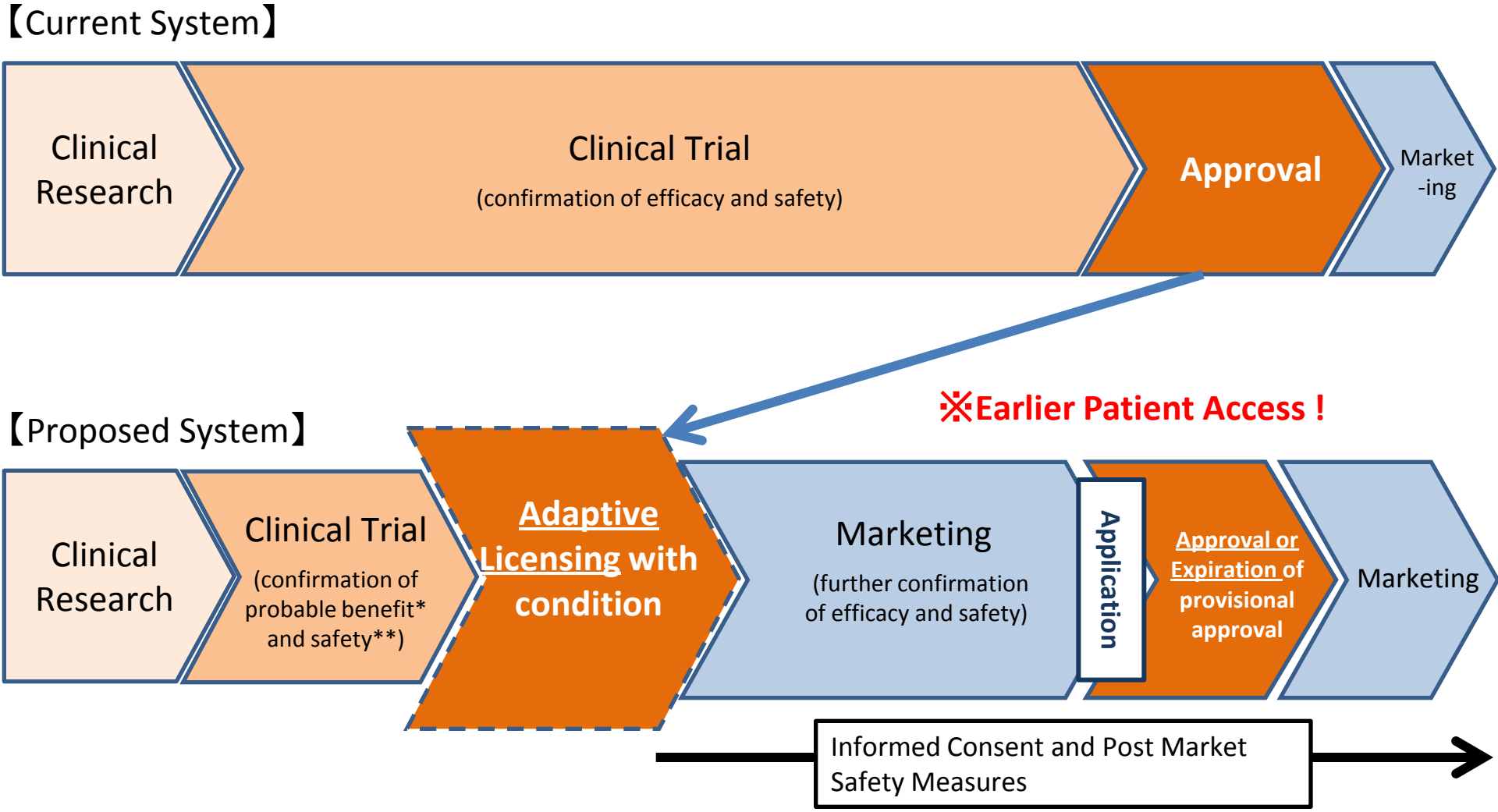
- Introduction of new definition of regenerative and cellular therapeutic products apart from pharmaceuticals and medical devices in the PAL

2. Approval system for earlier commercialization of regenerative medicine products

- Introduction of Tentative Approval with condition and effective period
- Efficacy and safety will be further confirmed after tentative approval

NEW APPROVAL SYSTEM FOR COMMERCIALIZATION OF CELLULAR THERAPY PRODUCTS

Draft Under Consideration



* Probable benefit: Confirmation of efficacy with small patient population.
** Safety: Earlier detection and evaluation of adverse events.

3. Safety an ethics in the post market phase

- Informed consent
- Post market safety measures (infectious disease periodic reports, record retention etc.)

The reform of the pharmaceutical affairs law will be approved by the national diet soon!

Korean patient, travelled to Japan, received stem cell therapy in Nov/2010.

He died of pulmonary embolism as soon as he came back to Korea.

the Bill for Ensuring Regenerative Medicine Safety

[Direction of Revision under consideration]

1. Procedures for providing a regenerative medicine

- The bill prescribes procedures for providing regenerative medicine such as prior notification to the authority in order to ensure safety of regenerative medicine.

2. Permitting/Notification system for a cell processing facility even if this facility exists in hospital or clinic

3. Measures for appropriate provision of regenerative medicine.

- informed consent
- protection of the personal information
- report the adverse events to the authority.

1. Simultaneous Global Development

1. Phase I Trials in Japan, the US, the EU, and other countries Simultaneously

2. Promotion global clinical trials

2. Accelerating Regulatory Science Initiative

1. Early Communication between MHLW/PMDA, FDA, EMA, and other regulatory bodies

2. Harmonization of Guidelines and Regulations

"Guideline on ensuring the quality and safety of human autologous induced Pluripotent Stem (-like) cells-derived medical devices or pharmaceuticals" issued by the MHLW on Sep, 2012.

3. Simultaneous Approval in Various Countries