

## Current Topics of Pharmaceutical Regulatory Affairs in Japan

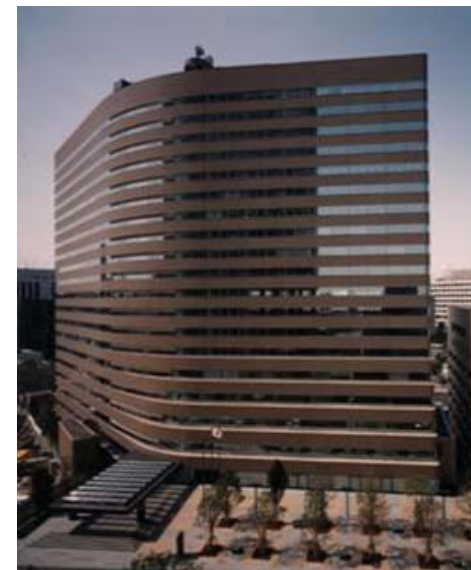


### Takeyuki SATO

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Centre for Product Evaluation

Pharmaceuticals and Medical Devices Agency  
(PMDA)

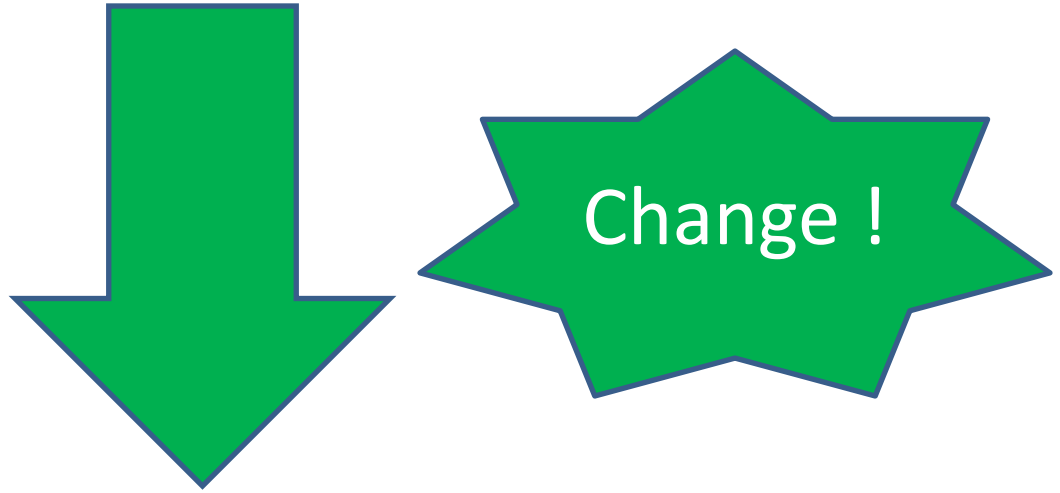
The 3rd China-Japan Symposium on Drug Development  
March 22, 2012, Beijing, China



negative

Resolve the drug or device Lag as an urgent issue

positive



Promote innovative pharmaceuticals and medical technologies from Japan to the world

*Japan's Governmental Policies  
on Life Innovation*

# Policies

- the New Growth Strategy (Cabinet decision in June 2010)

## (2) Health power strategy through “Life Innovation”

*Promoting research and development of innovative pharmaceuticals and medical and nursing care technologies from Japan*

**We will promote research and development of highly safe, superior, and innovative pharmaceuticals and medical and nursing care technologies from Japan.** We will advance unified approaches among industry, government, and academia, foster drug development ventures, and promote research, development, and application in a number of fields. These include new drugs, regenerative medicine and other state-of-the-art medical technologies, remote medical treatment systems making full use of information and communications technologies, the use of manufacturing technologies to improve personal mobility for the elderly, and medical and nursing care robots. As prerequisites, **we will work to resolve the drug and device lag as an urgent issue, improve the clinical testing environment, and expedite drug approval decisions.**

新成長戦略

# Policies

- Strategy for Rebirth of Japan (Cabinet decision dated December 24, 2011)  
Overcoming crises and embarking on new frontiers

## Short-term major high-priority projects in Life Science area

- Developing world-class pharmaceutical and medical technology infrastructures

The government will push ahead with creating world class infrastructures to develop innovative pharmaceuticals and medical technologies. Regarding the commercialisation of new drugs in particular, relevant ministries will examine and reach conclusions on as early as possible an appropriate form for the nationwide system of a “drug discovery support agency”.

- Enhancing the review framework of the PMDA

The Government will enhance the PMDA so that innovative pharmaceutical products, medical devices, and regenerative medicine products will be made available as early as possible based on review process using the most advanced knowledge.

- Drawing up new strategy to make Japan the world leader in drug discovery and medical devices development

Regarding Life Innovation, the government will develop a medium-term strategy for Japan to lead the world in the fields of drug discovery, medical device development, regenerative medicine, and personalised medicine by spring 2012. Stakeholders will cooperate and do their utmost on this.

# Measures by PMDA for eliminating drug lag

**Targets :To reduce the “drug lag” by a total of 2.5 years**

Development time

Approval review time

Measures

## *Expansion of the Consulting Service*

- **Increase the number of staff** about 236 approximately in 3 years
- Give adequate training

## *Improve the quality and quantity of consultations*

- Advise on overall development strategy to improve development time
- Reduce the application preparation time through stepping up the pre-application consultations

## *Clarify the review criteria*

- **Further promote Global Clinical Trials**
- Draft a guideline on cutting-edge technologies

## *Expansion of the Review System*

- Increase the number of staff
- Give adequate training

## *Enhancement and improvement of the Review System*

- **Introduce a prior assessment**, and reduce applicant workload.
- Improve productivity of reviews through measures such as the standardization and Streamlining of the review process

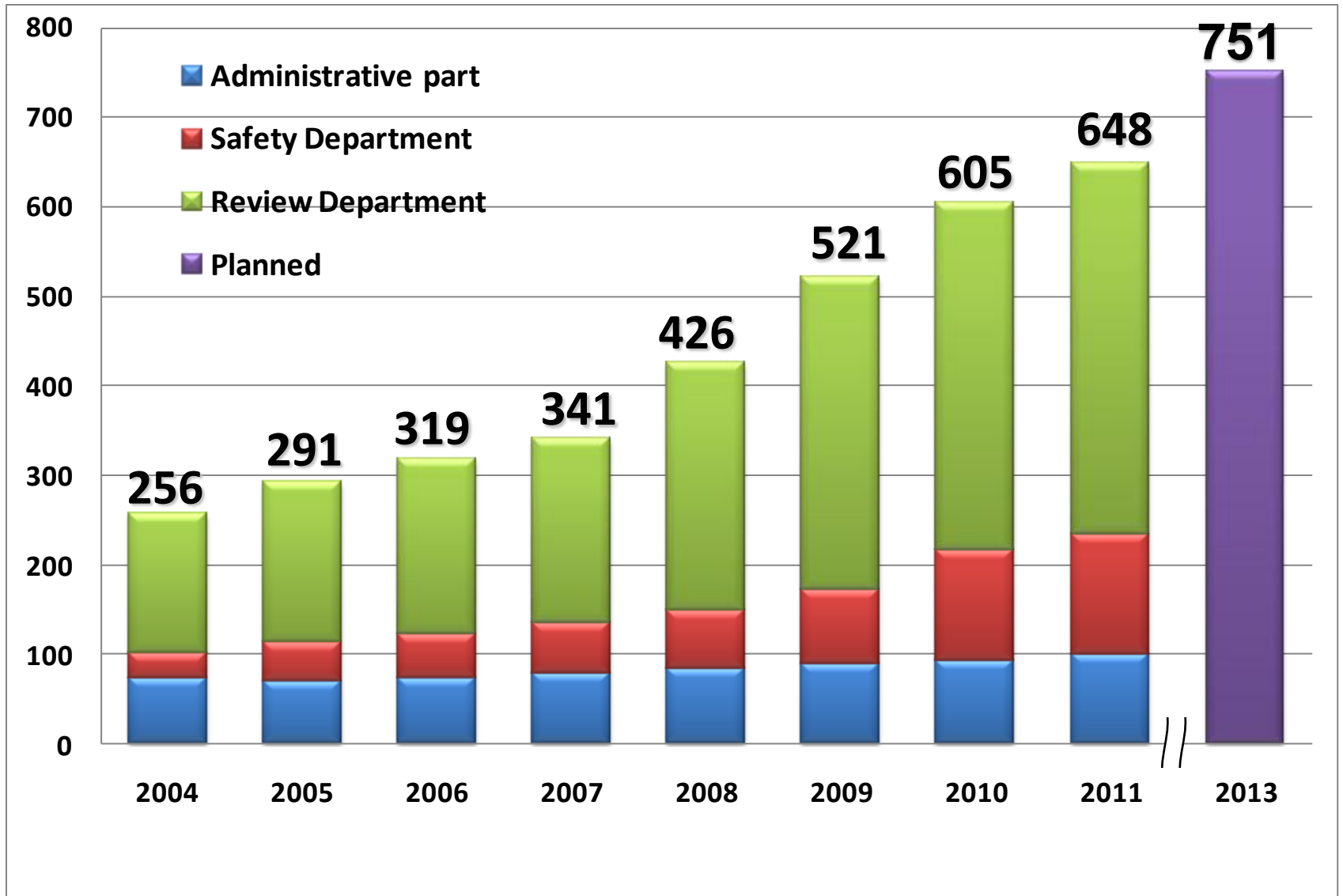
## *Liaise more closely with the FDA and other overseas regulatory authorities*

Targets (by 2011)

**1.5 year reduction of development time**

**1.0 year reduction of approval review time**

# PMDA Staff Size



# Estimate of Drug Lag Time

Lag	FY2006	FY2007	FY2008	FY2009	FY2010
Pre-Application	1. 2y	2. 4y	1. 5y	1. 5y	1. 0y
In-Review	1. 2y	1. 0y	0. 7y	0. 5y	0. 1y
Drug Lag	2. 4y	3. 4y	2. 2y	2. 0y	1. 1y

Note: Pre-Application Lag: Median years of difference b/w USA/Japan application for each product

IN-Review Lag: Median years of difference b/w Review time (USA/Japan) for each product approved in Japan

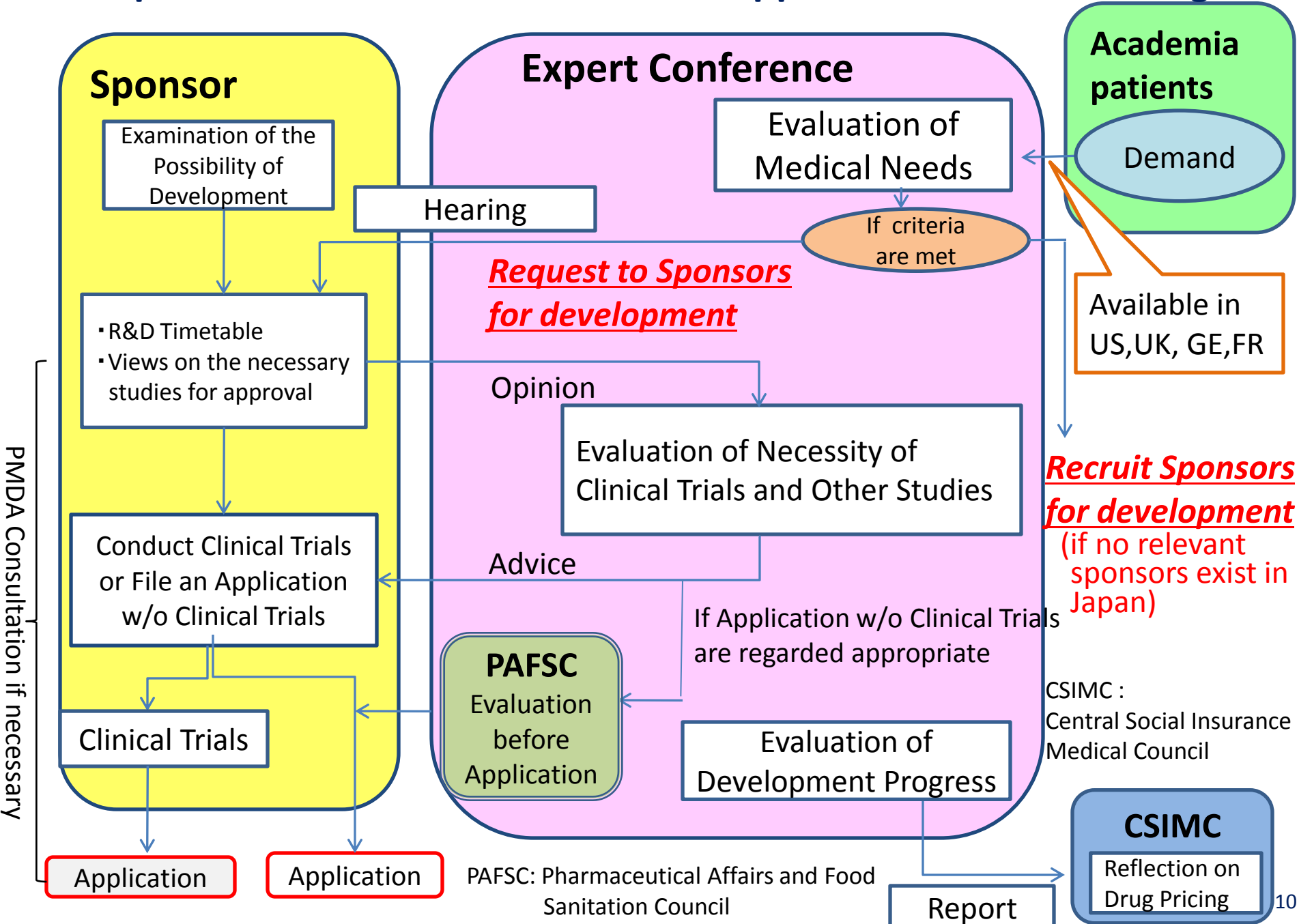
Drug Lag: Pre-application Lag + In-Review Lag



# Development Promotion Scheme for Unapproved & Off-label Drugs in High Medical Need

- In summer of 2009, MHLW widely solicited the demand for approval of unapproved & off-label drugs\* in high medical need from public.  
\*unapproved & off-label drugs : drugs and/or Indications that are already authorized in US or EU, but are not yet approved in Japan
- Expert conference (EC) has assessed the 374 demands (unapproved: 89, off-label: 285) in terms of medical need and necessary studies (clinical trials etc.) in Japan for approval.
- As for the demands that EC regarded as in high medical need,
  - (i) MHLW requested relevant sponsors (e.g., Japanese affiliates of multinationals for unapproved drugs or marketing authorization holders for off-label drugs ) to develop the drugs / indications. or
  - (ii) MHLW recruited sponsors to develop the drugs when there is no relevant sponsors to develop them in Japan.
- Although the scope of this scheme is not limited to orphan drugs, it could lead to the fast development of orphan drugs authorized overseas.

# Development Promotion Scheme for Unapproved & Off-label Drugs



# Result of EC's Evaluation and Development Status

as of 18 January 2012

## < Results of Evaluation on Medical Need >

①	②	③	④	⑤	⑥	Total
Approved before EC's deliberation	Requested for development	Sponsors recruited for development	Under deliberation	Not evaluated as in high medical need	Not approved in the US etc.	
4	167(19)	19 (1)	0	80	104	374
	186					

( ):Number of Orphan Drugs

## < Details of Evaluation >

Sponsor candidates were found for all drugs

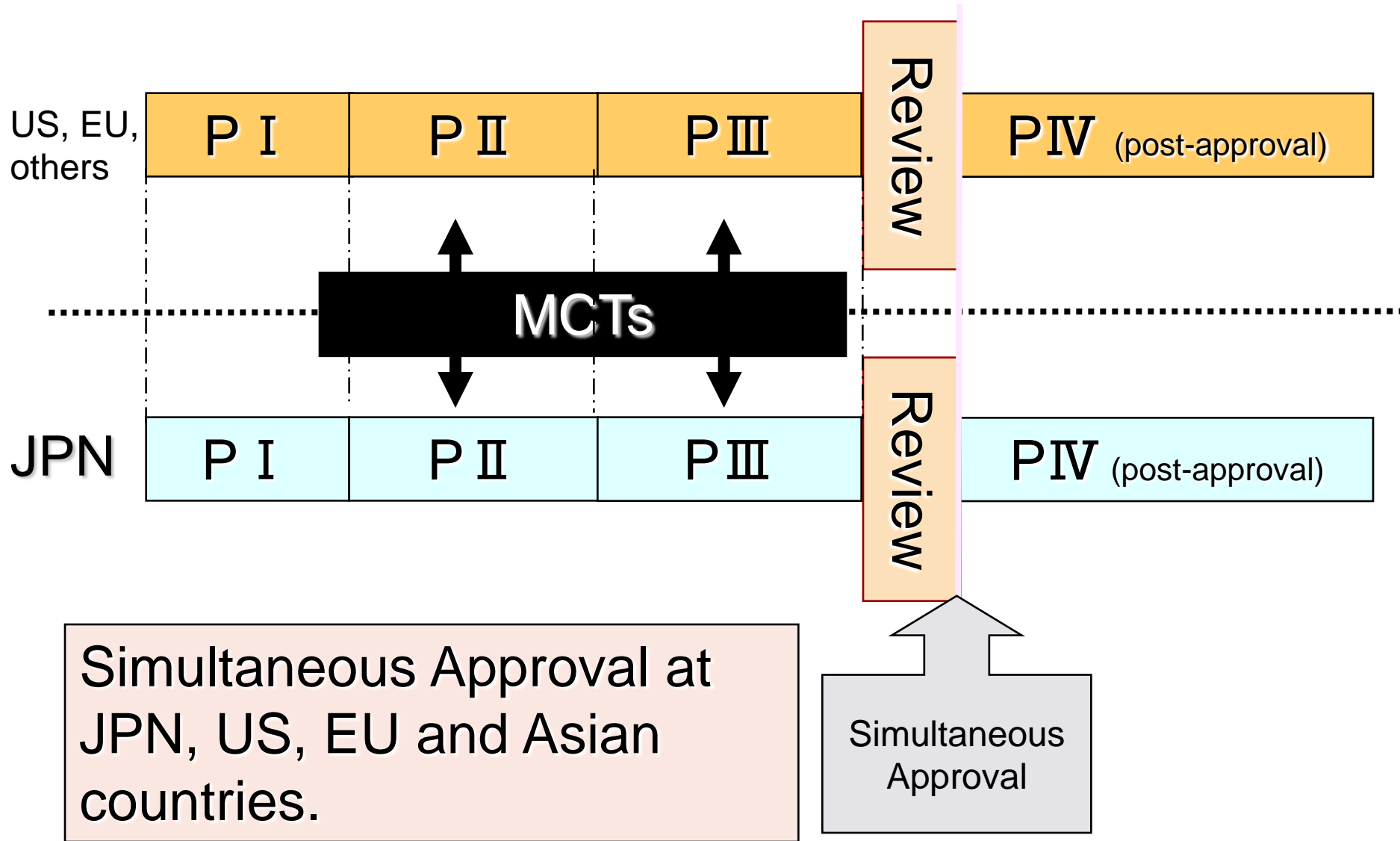
①	②	③	④	Total
Application w/o clinical trials appropriate	Already started development	additional clinical trials necessary	Under deliberation on the necessity of clinical trials	
54	54	52	7	167

## < Development Status >

- 55 drugs including **5 orphan drugs** were already approved.
- Applications for 48 drugs including **6 orphan drugs** were filed.

*For Speed-up, For Innovation*

# Global Simultaneous drug development



# Guidance document for global studies

## Japanese version

薬食審査発第0928010号  
平成19年9月28日

各都道府県衛生主管部（局）長 殿

厚生労働省医薬食品局審査管理課長

### 国際共同治験に関する基本的考え方について

従来、我が国においては、ICH-E5ガイドラインに基づく「外国臨床データを受け入れる際に考慮すべき民族的要因について（平成10年8月11日医薬審第762号 厚生省医薬安全局審査管理課長通知）」により、いわゆる「ブリッジング」による海外臨床試験成績を承認申請資料として活用することを認めており、また、欧米諸国における市販後調査等の結果についても必要に応じ承認審査に際して活用しているところである。

<http://www.pmda.go.jp/operations/notice/2007/file/0928010.pdf>

## English version

September 28, 2007  
Notification No.0928010

Attention to:  
Commissioner of Prefectural Health Supervising Department

From Director of Evaluation and Licensing Division,  
Pharmaceutical and Food Safety Bureau  
Ministry of Health, Labour and Welfare

### Basic principles on Global Clinical Trials\*

Up to the present according to “Ethnic Factors in the Acceptability of Foreign Clinical Data” based on ICH-E5 guideline (Notification No. 762, Director of Evaluation and Licensing Division, Pharmaceutical and Food Safety Bureau, Ministry of Health and Welfare, dated August 11, 1998), utilizing foreign clinical trial data in a new drug application what is called “Bridging” has been accepted in Japan, and post-marketing data in USA and EU have been taken into consideration in a review for regulatory approval where necessary.

<http://www.pmda.go.jp/operations/notice/2007/file/0928010-e.pdf>

# Life Innovation Project for Prolonging Healthy Life Expectancy

FY2011 budget request: about ¥23.3 bn (Joint project among MHLW, MEXT, and METI)

## R&D

Prolong healthy life expectancy by effectively researching practical applications of medical technology related to intractable diseases, cancer, etc.

## Infrastructure Development

Revitalize Japan by creating innovative Japanese drugs and medical devices

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

- Research to realize innovation in medicine, including clinical applications of regenerative medicine and an understanding of pathogenesis, as well as prevention, diagnosis, and treatment of socially significant diseases, including intractable diseases, cancer, hepatitis, and psychiatric disorders.

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

- Focus on large-scale clinical R&D for practical application of Japanese therapeutic cancer vaccines that can improve QOL of cancer patients by enabling cancer therapy without interfering with work and other aspects of daily life.

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

- Support practical application of robots, assistive care devices, etc. by offering clinical evaluation during prototype phase and opportunities for monitoring studies at nursing facilities (goal of 20 devices)

### 3. Create study center infrastructure necessary for clinical trials to create innovative drugs and medical devices ahead of other countries

- Create innovative drugs and medical devices from Japan by providing financial aid for human resources, diagnostic and other equipment, and operational budgets for study centers vital to clinical trials in which new drugs and medical devices are used for the first time in humans.

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

- Leverage the large number of patients and expertise of National Specialized Medical Research Centers to accumulate bio-resources that can form the basis of research into innovative Japanese drugs and medical technology, developing drugs and medical devices while constructing a system for managing intellectual property to achieve rapid practical application of fruits of research.

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

- Promote a unified system among industry, academia, and government to achieve practical application of projects originating in Japan (drug and medical device candidates, etc.), and make strategy consultations for the trials, protocols, etc. required by universities, ventures, and other entities from final stages of candidate selection for drugs and medical devices to clinical studies.

### 6. Construct medical information database infrastructure

- Improve drug safety by collecting data on more than 10 million patients through a medical information database leveraging e-medical charts and other methods at five university and other hospitals nationwide.

Organic cooperation

## Create New Drugs and Medical Devices (Clinical Trial Infrastructure Creation/Research Expenses)

Motto: **“Perform world-leading clinical trials to create innovative Japanese drugs and medical devices”**

Background: Japan suffers from a **lack of infrastructure (HR and facilities) for world-leading, first-in-human trials of new drugs and medical devices**. Therefore, **even though the basic research projects may have been launched in Japan, practical application is achieved first in other countries**, which do have such an infrastructure, with **Japanese launch following**.

Summary: **Provide support to five medical centers with plans to create an infrastructure enabling early-stage and exploratory clinical trials of new drugs and medical devices held by Japanese companies and research institutions** (solicit candidates from key areas of **cancer (biologics, diagnostics, etc.), neurology/psychiatry, and cardio-/cerebrovascular (medical devices)**).

Evaluate candidate programs with potential and perform the following to **create world-leading innovative new drugs from Japan**:

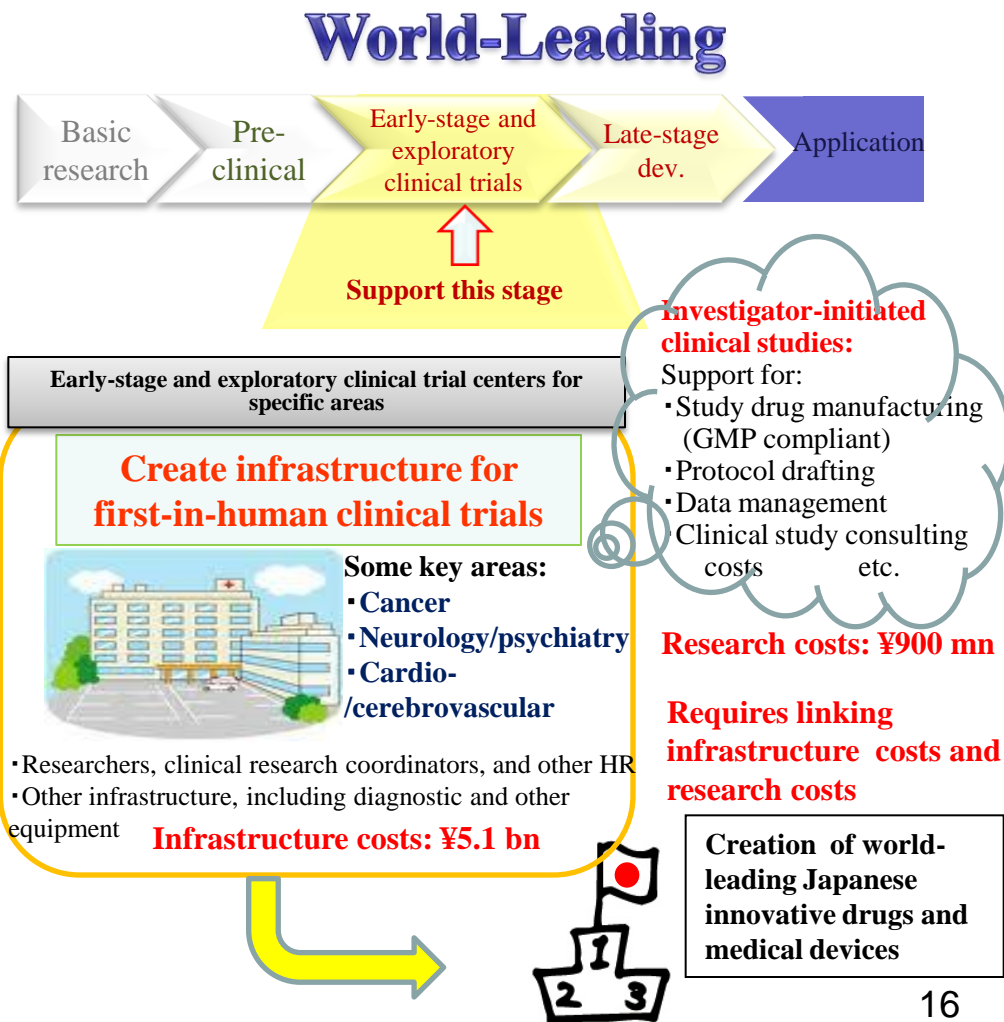
- **Create infrastructure required for exploratory, early-stage clinical trials (for development by specific prospective companies)**
- **Link** medical center infrastructure costs with specific individual research costs to achieve rapid application.

Infrastructure costs: About ¥1 bn/year/center About 5 centers (for 5 years)

Research costs\*: About ¥180 mn/year/project About 5 projects (3-5 years)

\*Assuming doctor-lead development, when there are no companies to take on project

Goal: Realize **world-leading approval or most-advanced development within Japan** for new drugs and devices.

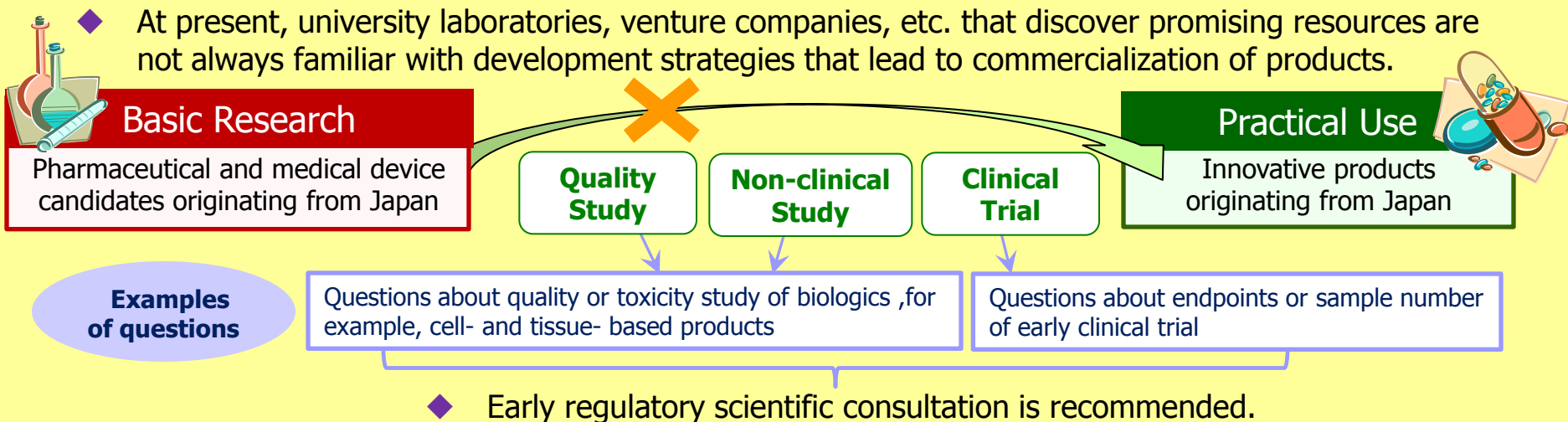




- To create innovative pharmaceuticals and medical devices originating from Japan, PMDA started new scientific consultation service 'Pharmaceutical Affairs Consultation on R&D Strategy' for university laboratories, venture businesses, etc on 1 July, 2011.
- The targets of this new consultation, as a general rule, are products that correspond to the following priority areas.

Priority areas	
◆ Regenerative medicine (cell- and tissue- based products)	◆ Cancer
◆ Difficult-to-treat disease and <b>rare disease</b>	◆ Pediatrics
◆ Other than the above, products utilizing particularly innovative technologies	
(Note) Regardless of the order among the areas.	

◆ At present, university laboratories, venture companies, etc. that discover promising resources are not always familiar with development strategies that lead to commercialization of products.



## ニュースルーム Newsroom

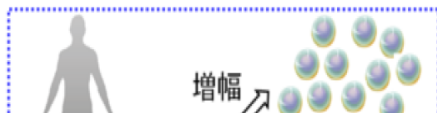
### • ニュース

2011.10.18

#### ■ 再生医療用iPS細胞バンク構築に向けた薬事戦略相談を開始

京都大学iPS細胞研究所(CiRA)は、再生医療用iPS細胞バンクの構築準備を進めていますが、規制科学部門の木村貴文教授、青井貴之教授と藤原沙都姫研究員が中心になり、このほど、医薬品医療機器総合機構(PMDA)<sup>(注1)</sup>との薬事戦略相談<sup>(注2)</sup>における対面助言を開始し、iPS細胞バンク構築に向けた規制的課題を克服するための第1歩を踏み出しました。

CiRAは、細胞移植治療に用いることのできるiPS細胞バンクの構築を目指し、細胞のHLA型<sup>(注3)</sup>のうち、他のHLA型との拒絶反応が低い3座(HLA-A、HLA-B、HLA-DR)ホモ接合型を持つ人からのiPS細胞をバンク化する計画を進めています。このように様々な移植適応型提供者より頂いた皮膚等の組織から作製した「再生医療用iPS細胞バンク」を構築することにより、品質の保証されたiPS細胞及びiPS細胞から作製した移植用細胞をあらかじめ準備しておくことができ、個々の患者さんからiPS細胞を作製する必要がなくなります。これによって、移植細胞を準備する期間の大幅な短縮や、患者さん1人あたりにかかる費用の削減に貢献し、より多くの難治性疾患や急性期の傷病の治療に対する再生医療を実現することが可能となります。



Pharmaceutical Affairs Consultation on R&D Strategy

# 薬事戦略相談

厚生労働省の補助を受けて、革新的医薬品・医療機器の適用化に向けて、開発初期から必要な試験・治験に関するアドバイスをを行います！

お申し込み方法はこちら

薬事戦略相談とは？

お申し込み方法はこちら

**医薬品医療機器総合機構**  
Pharmaceuticals, Medical Devices Agency  
薬事戦略相談部 薬事戦略相談室  
〒100-8535 東京都千代田区千代田1-1-1  
TEL: 03-5481-6161 FAX: 03-5481-6162  
E-mail: yakuji@pmda.go.jp

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

PMDAは国庫に属して医薬品・医療器械の製造販売承認を行う機関です。

# PMDA International Vision

## PMDA EPOCH Toward 2020

○ As one of the world's top three medical products regulatory agencies comparable to its American and European counterparts, PMDA aims to:

1. Secure the highest level of **Excellence in Performance in the following aspects:**
  - A. Quality and speed of product reviews, safety measures, and relief services (PMDA's Safety Triangle)
  - B. Quality and quantity of regulatory science\* research
  - C. Quality, quantity, and speed of information transmission to the world
2. Maintain a close **P**artnership with the **O**rient for the common benefit through:
  - A. Cooperation to improve the level of medical products regulation across Asia
  - B. Communication of information and opinions to the world as a member of the Asian community
3. Actively **Contribute to International Harmonisation of regulations, guidelines, and standards for the benefit of both Japan and the world.**

○ To achieve the above goals, PMDA employees will need to be more internationally minded and have effective communication skills, including a good command of English. Furthermore, PMDA must develop and maintain a sound interactive partnership with foreign counterpart agencies.

\* Regulatory science is the science that serves to regulate the fruits of technology to ensure that they assume the most desirable form in harmony with humankind and society to benefit the public and society.

*Thank you for your attention !*

