JKS READING ROOM

The 2006 Symposium of APEC Network on Pharmaceutical Regulatory Science (key PMDA presentations)

Key presentations from PMDA

October 12, 2006

- Role of Japan and Asian Countries in the Global Pharmaceutical Development

October 13, 2006

- Summary Report APEC 2006 (excerpts)

Role of Japan and Asian Countries in the Global Pharmaceutical Development

Pharmaceuticals and Medical Devices Agency (PMDA)
Akira Miyajima

Oct.12,2006

WHAT ‘S

3 major Operations

Review and Audit for Drugs/ Medical Devices Efficacy and Safety

- Clinical Trial Consultation
- Review of Efficacy and Safety
- Conformity Audit for Application Materials of GLP,GCP and GMP

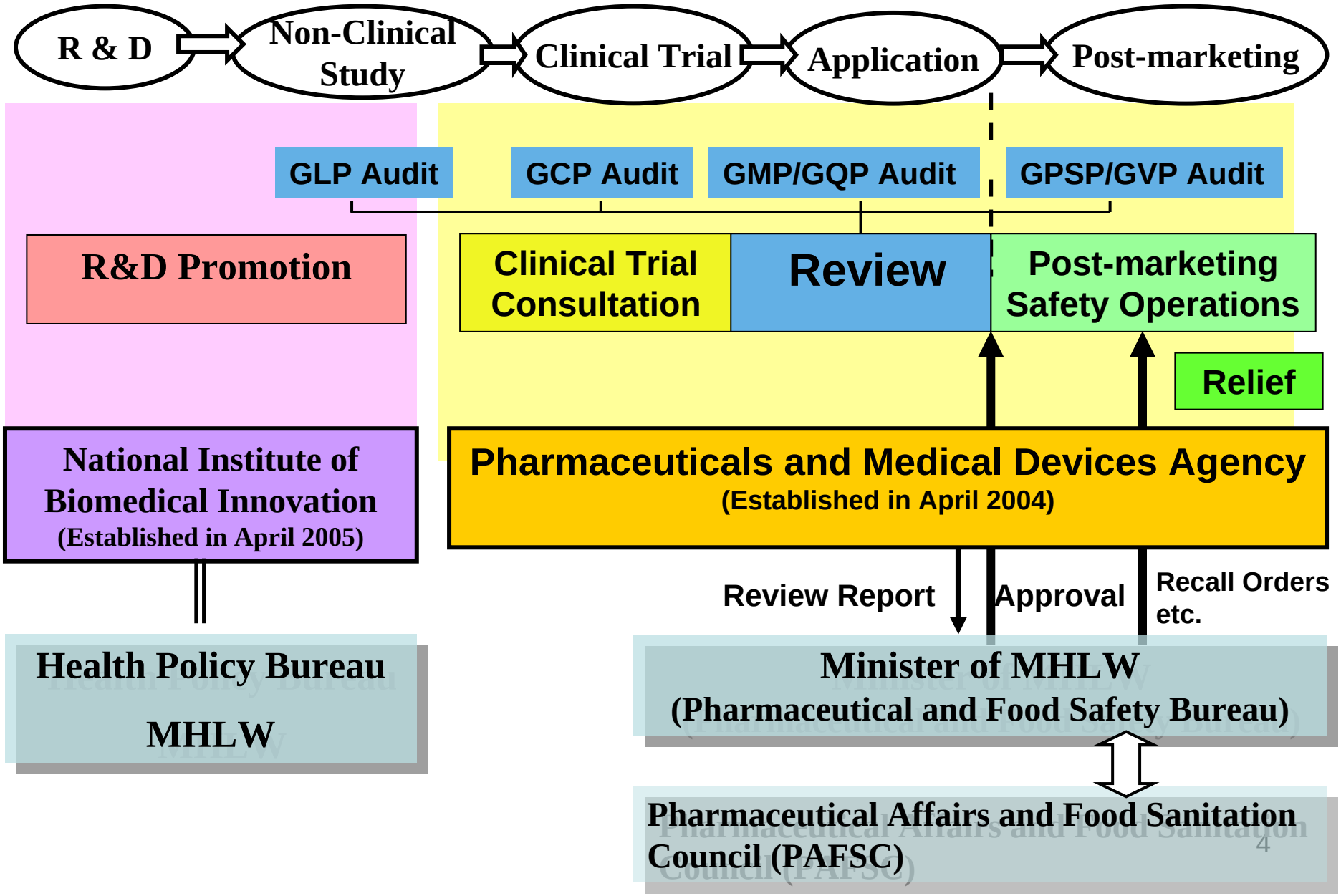
Post-marketing Safety Operations for Drugs/ Medical Devices

- Reinforced Safety Information (Database)
- Scientific Review and Research for Safety Information
- Information Provision (via the Internet), Pharmaceutical Consultation for Consumers

Relief Service for ADR and Other Infectious Disease

- Provision of Medical Expenses, Disability Pensions etc.
- Relief Service for SMON, HIV-positive and AIDS patients

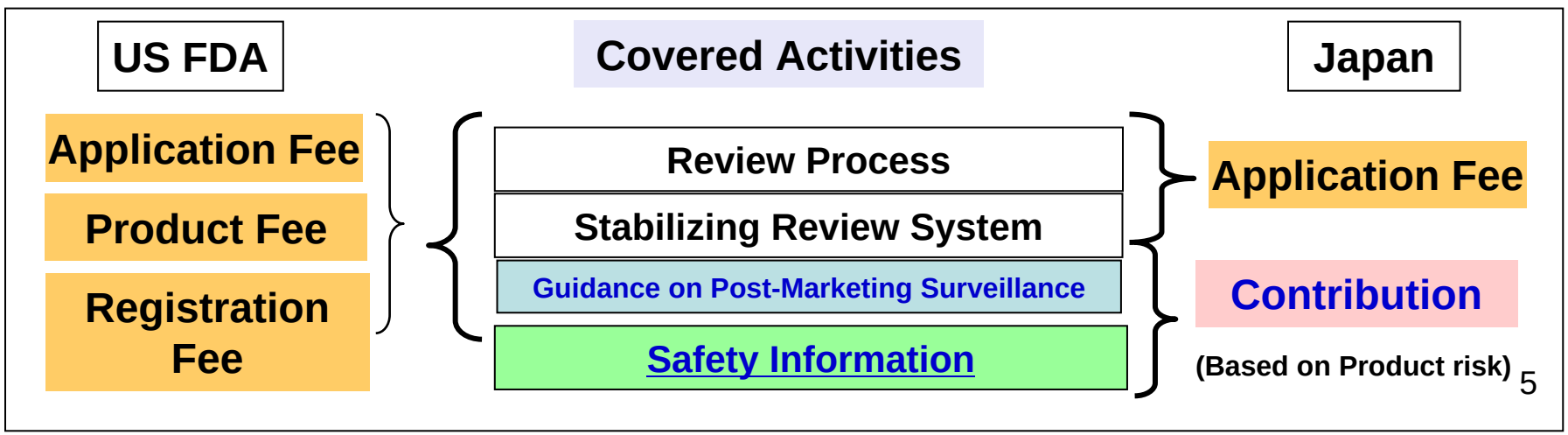
Operational Flow of Drug/Device Development



Comparison of Number of Reviewer, Fees, etc.

	Japan 2003	Japan 2008 (prospect)	US	UK (Drugs only)	France	EMEA
Number of reviewer	183	292 IAA inspection Safety operation	2,600	436	950	248
Application fee, etc	3.4 billion-yen	7.3** billion-yen	32 billion-yen	6.6 billion-yen	6.7 billion-yen	10.2 billion-yen
Public Charger/ Total Expenses	36% *	21%*	46%	0%	34%	36%
Fees /Gross Proceeds	0.05%	0.1%	0.2%	0.5%	0.4%	0.12%

＊ Total of MHLW HQ, PMDA, ＊＊Total of Application fee and contribution

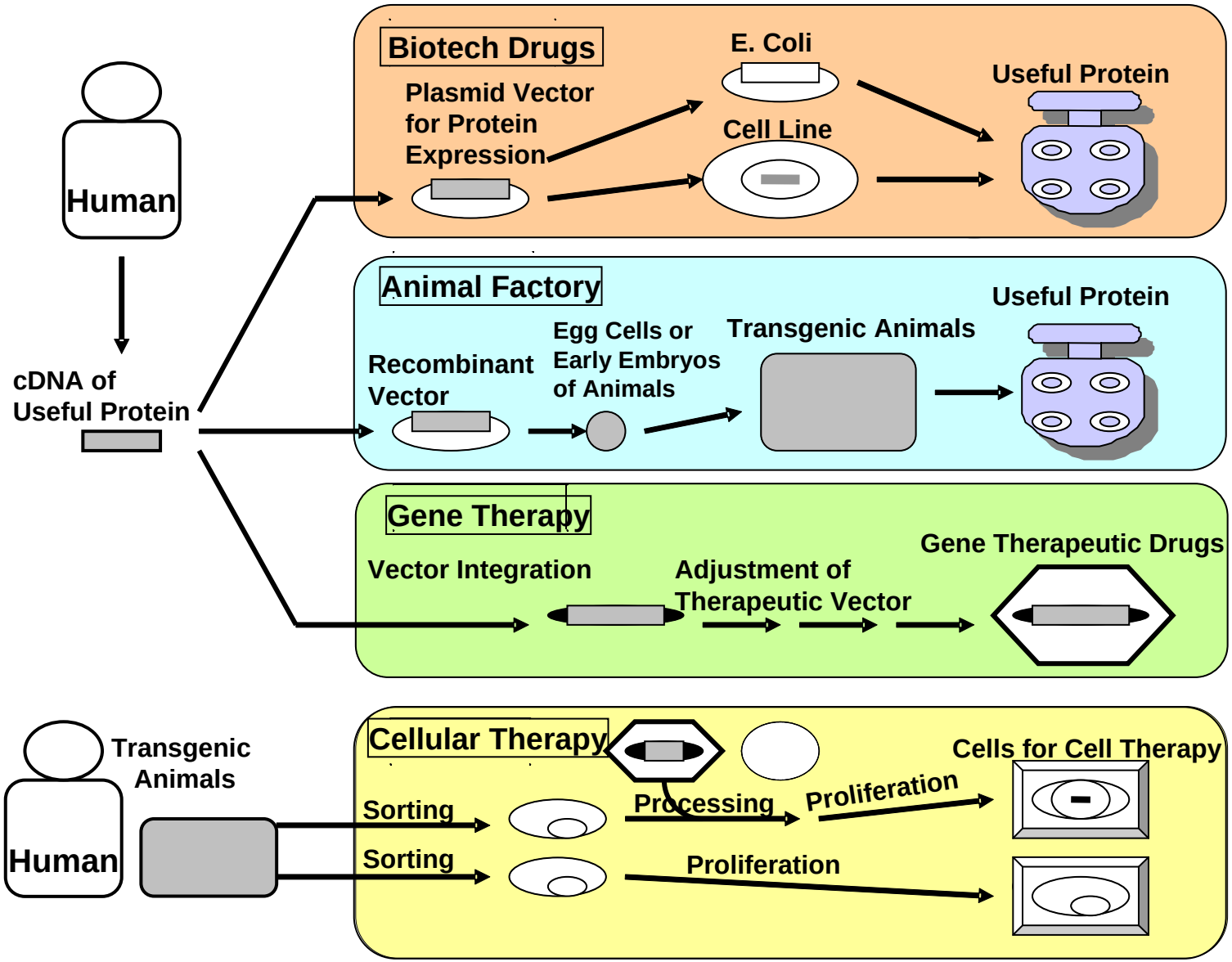


Our Mission

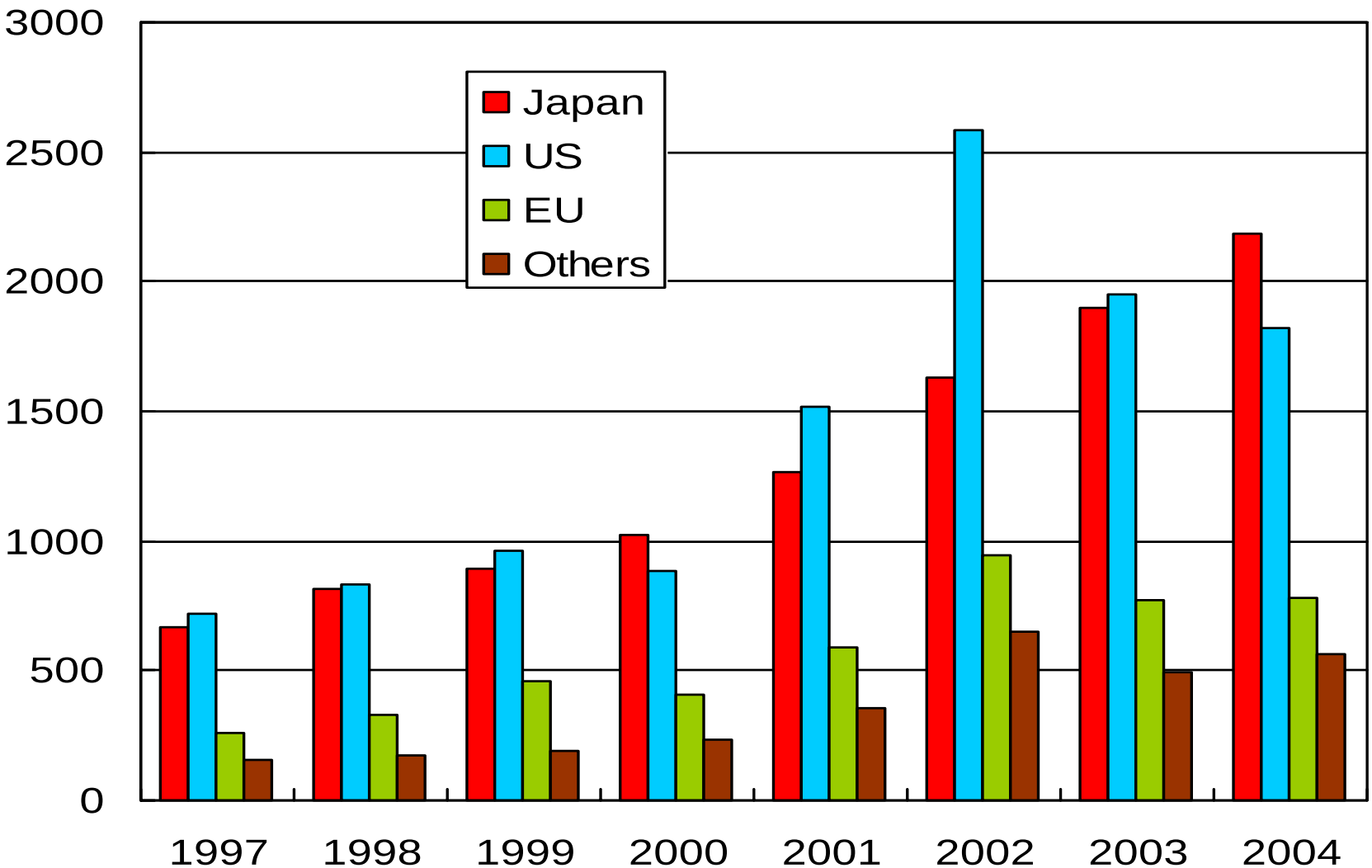
To Ensure **Faster** Accessibility to **More Effective** and **Safer** Drugs/ Devices for the Public

Improving Public Health

“ More Effective” Drugs/Devices

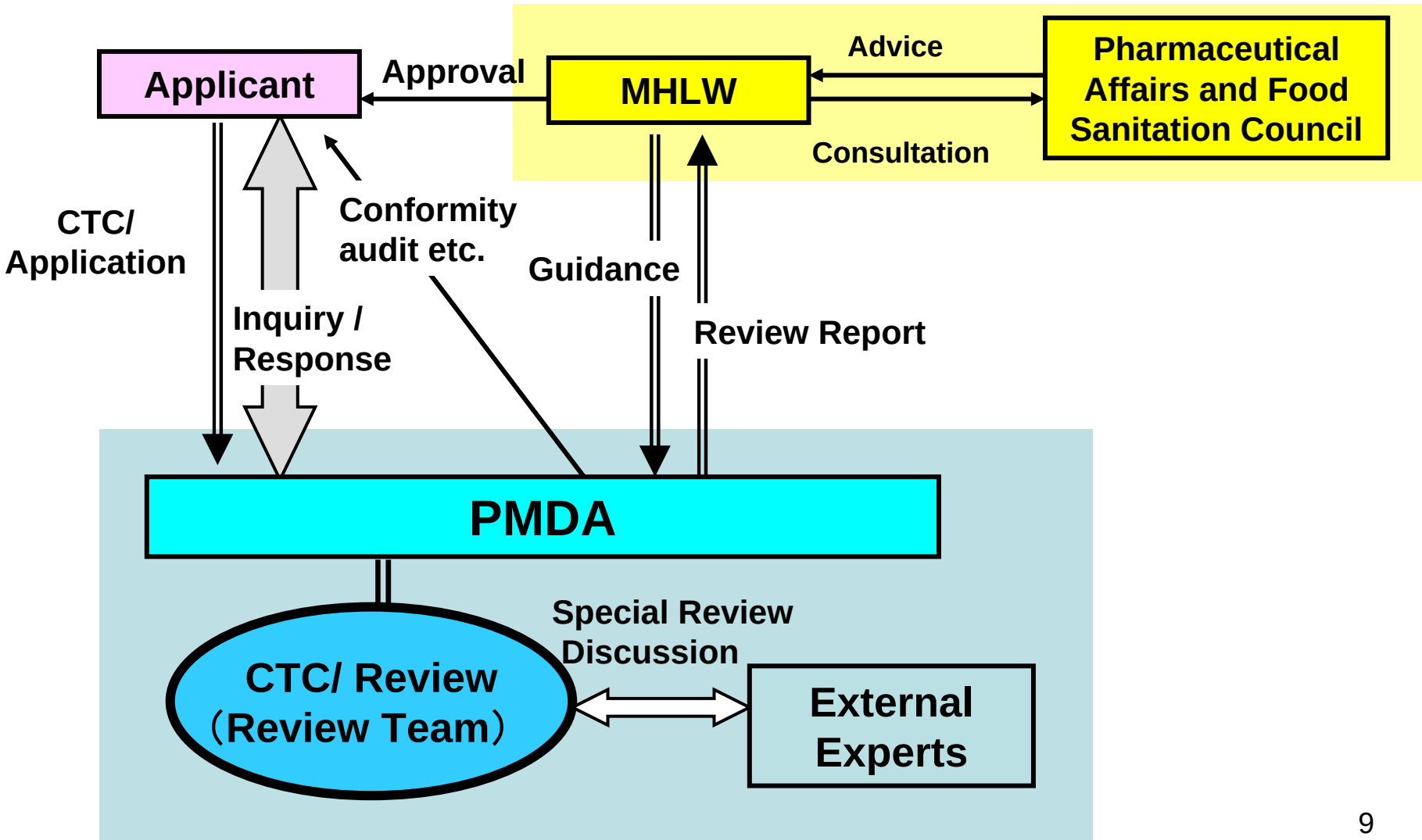


Biotech-related Patents



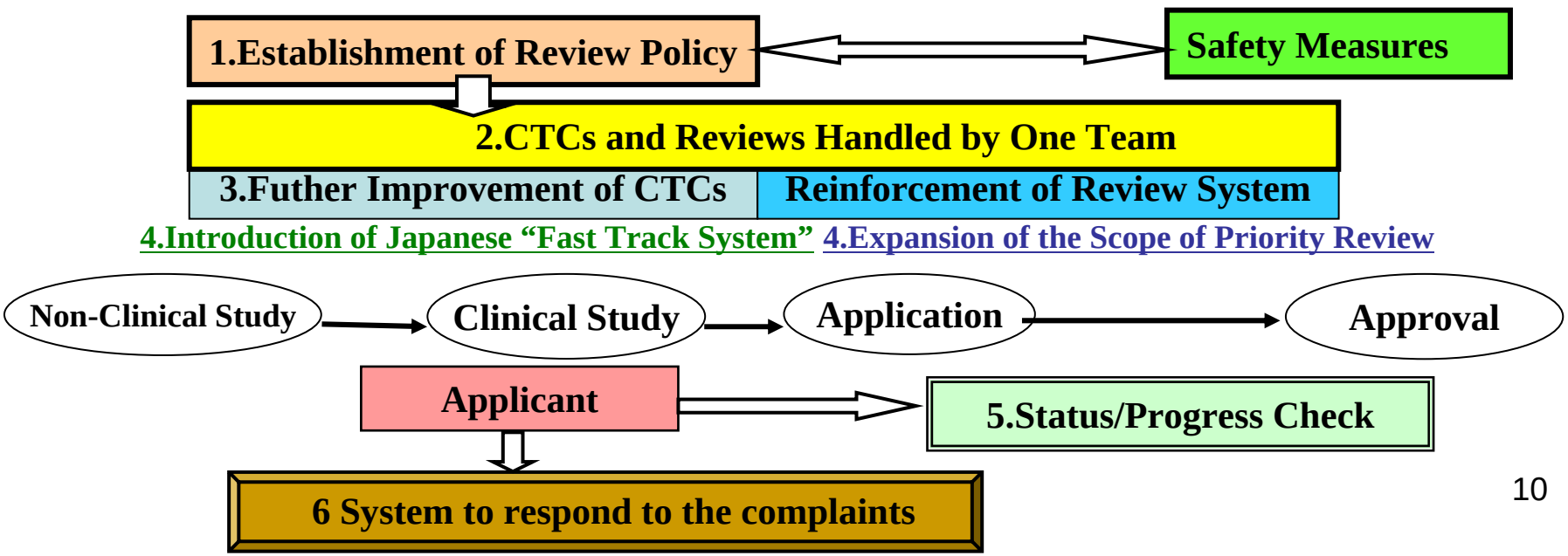
Source (’97 - ’99) : Japan Patent Information Organization (JAPIO)
Source (’00 -) : PATOLIS

To Ensure **"Faster"** Access to Drugs/Devices for the public

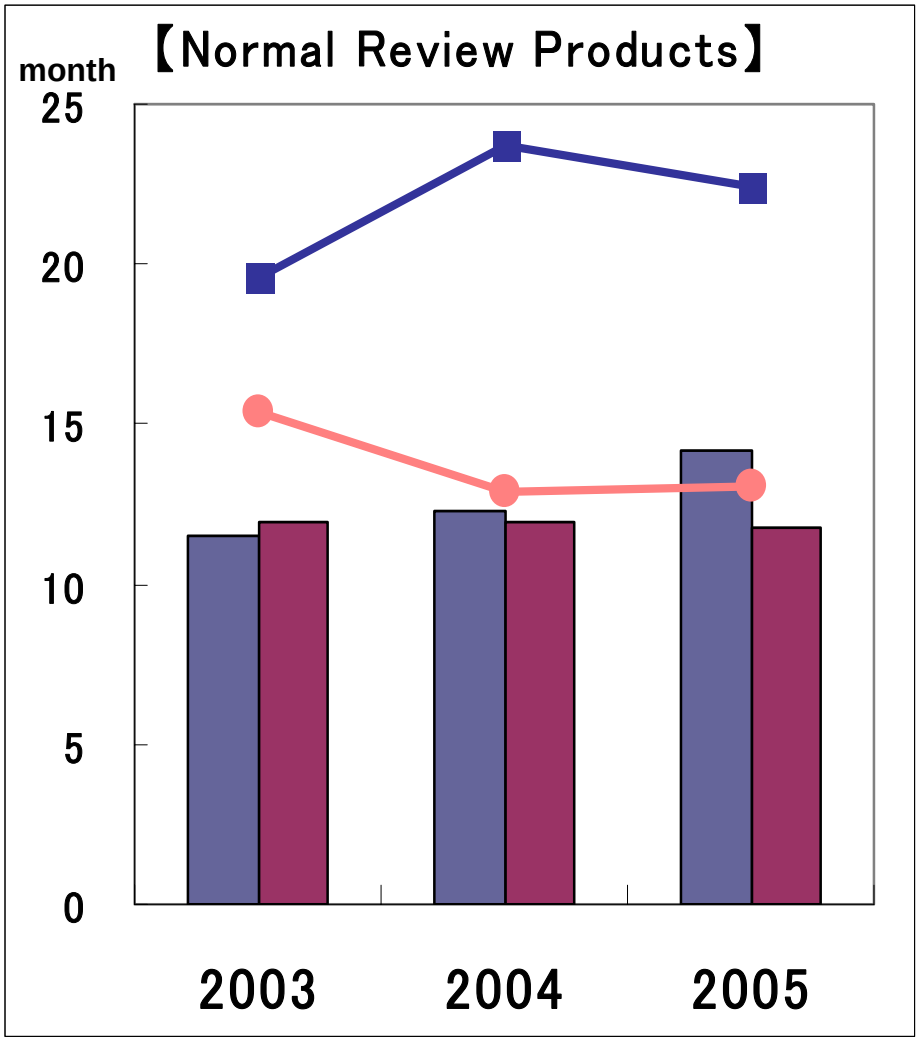


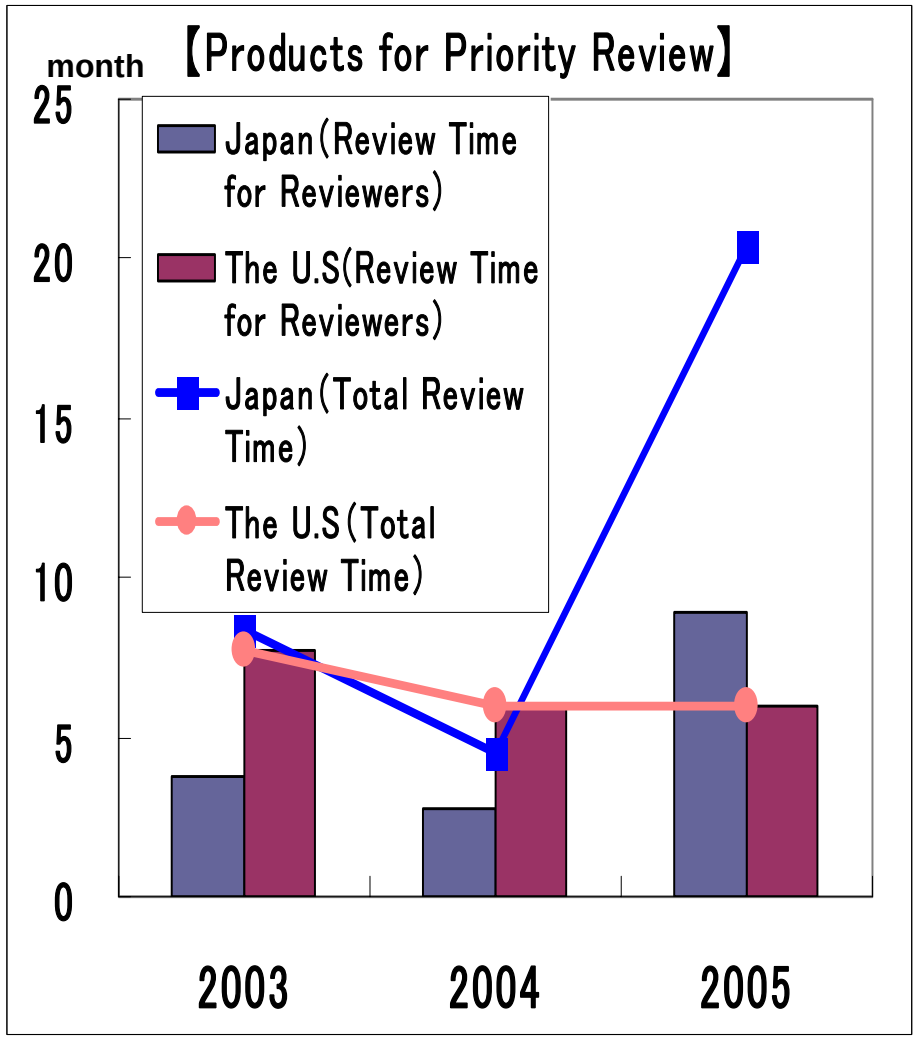
Our New Review System ～ For Faster Approval ～

1. Early clarification of review policy tailored to each product （Cooperation with Post-marketing Vigilance）
2. Integrated organization to perform NDA reviews in consistency with pre- NDA (clinical trial) consultation
3. Early detection and prompt problem solving through the use of pre-NDA consultation
4. Introduction of “Fast Track System” and expansion of the scope for priority reviews
5. More transparency in review process（Improvement in Predictability）
6. Development of appeal system



Comparison of Time for New Drug Approval Between Japan and The U. S. (Median)

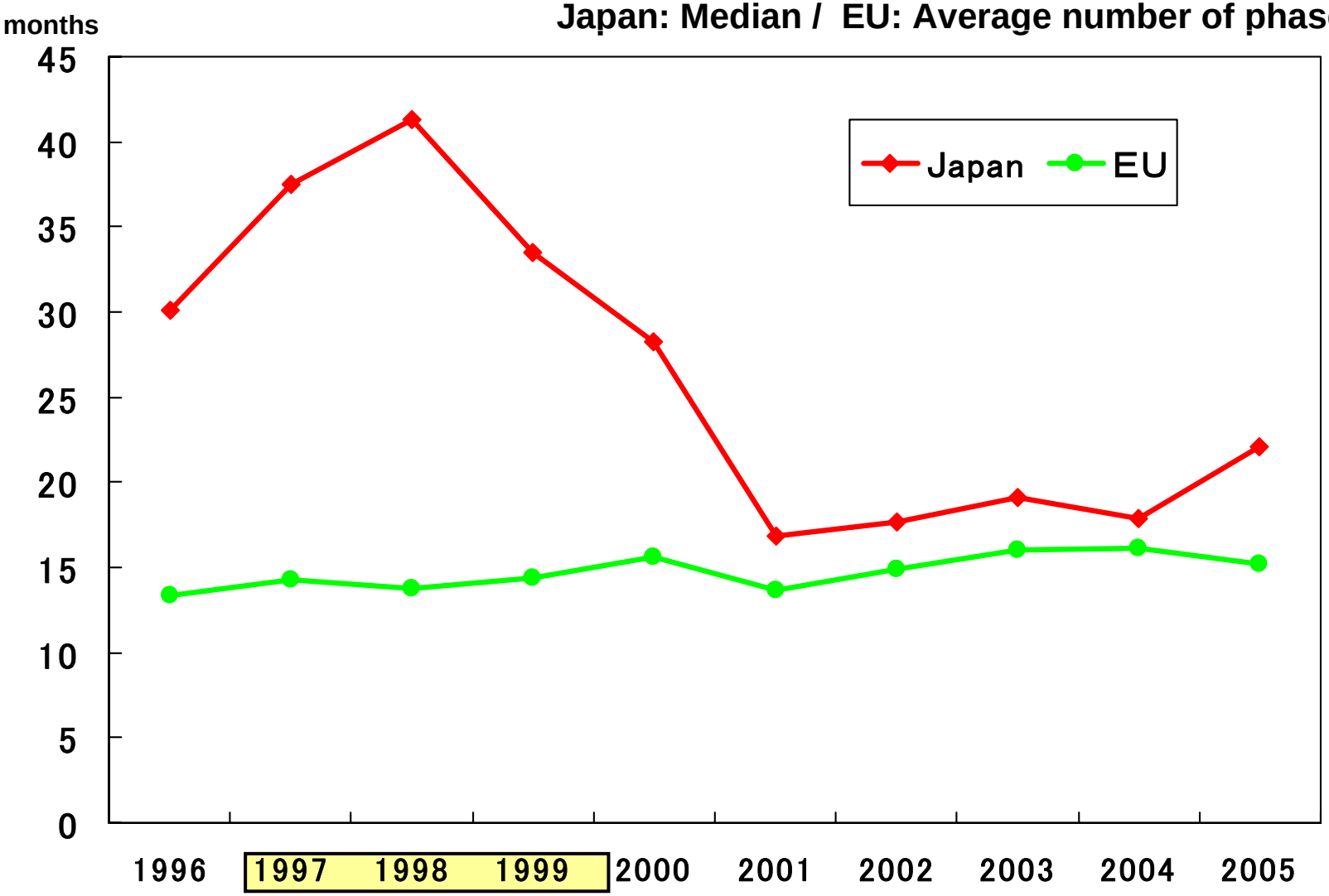




Note1: Review Time for Reviewers means in total review process, actual time for reviewers to review. It does not include time for applicants to submit additional documents on reviews 's request.
Note2:Japan :Number is on a fiscal year basis. The U.S: Number is on a calendar year basis.

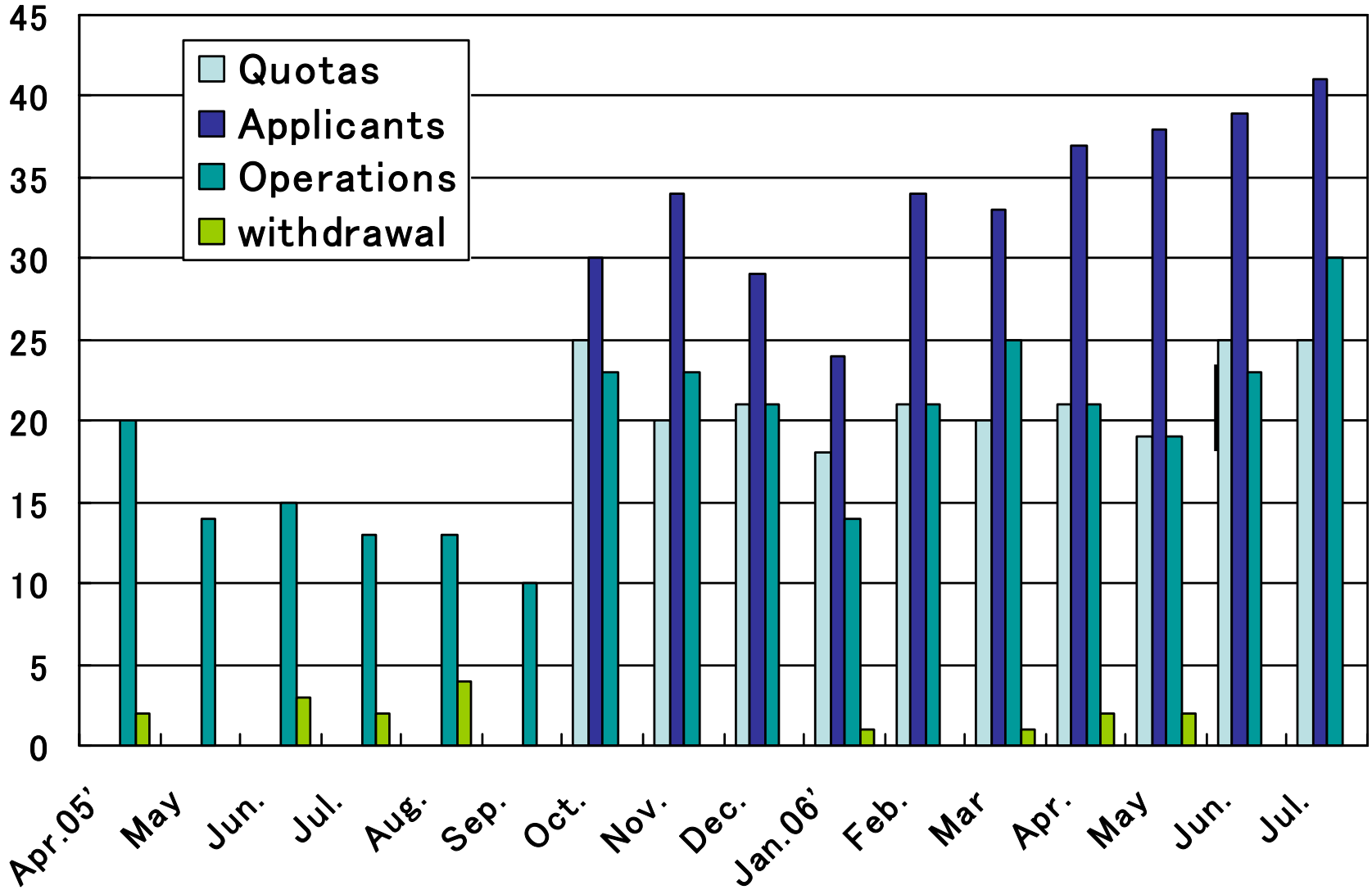
Comparison of Total Review Time for New Drug Approval Between Japan and EU

Japan: Median / EU: Average number of phase



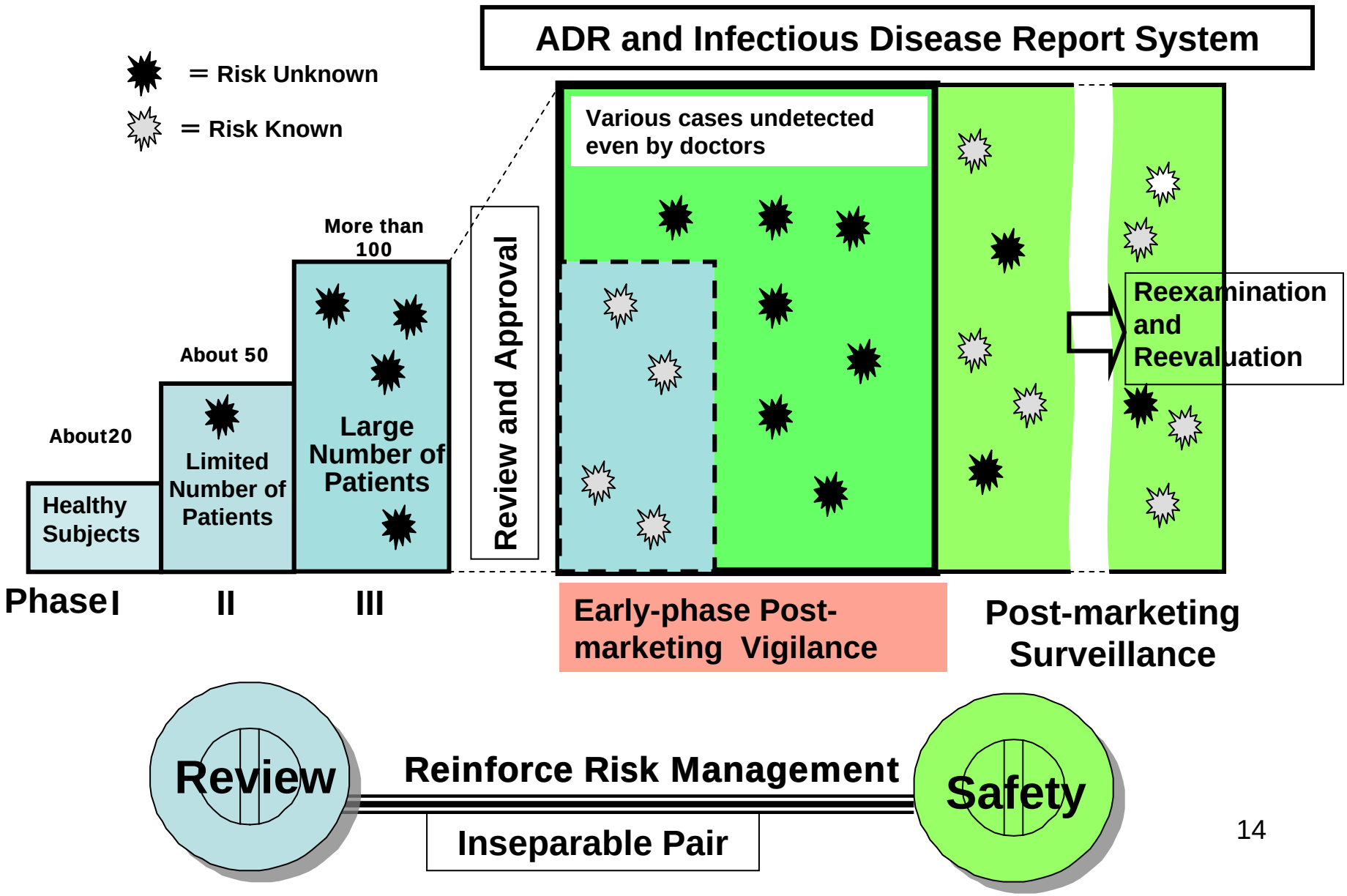
Ref: JPMA-Institute of Pharmaceutical Industry Policy

Number of Application and Actual Operation of Clinical Trial Consultations

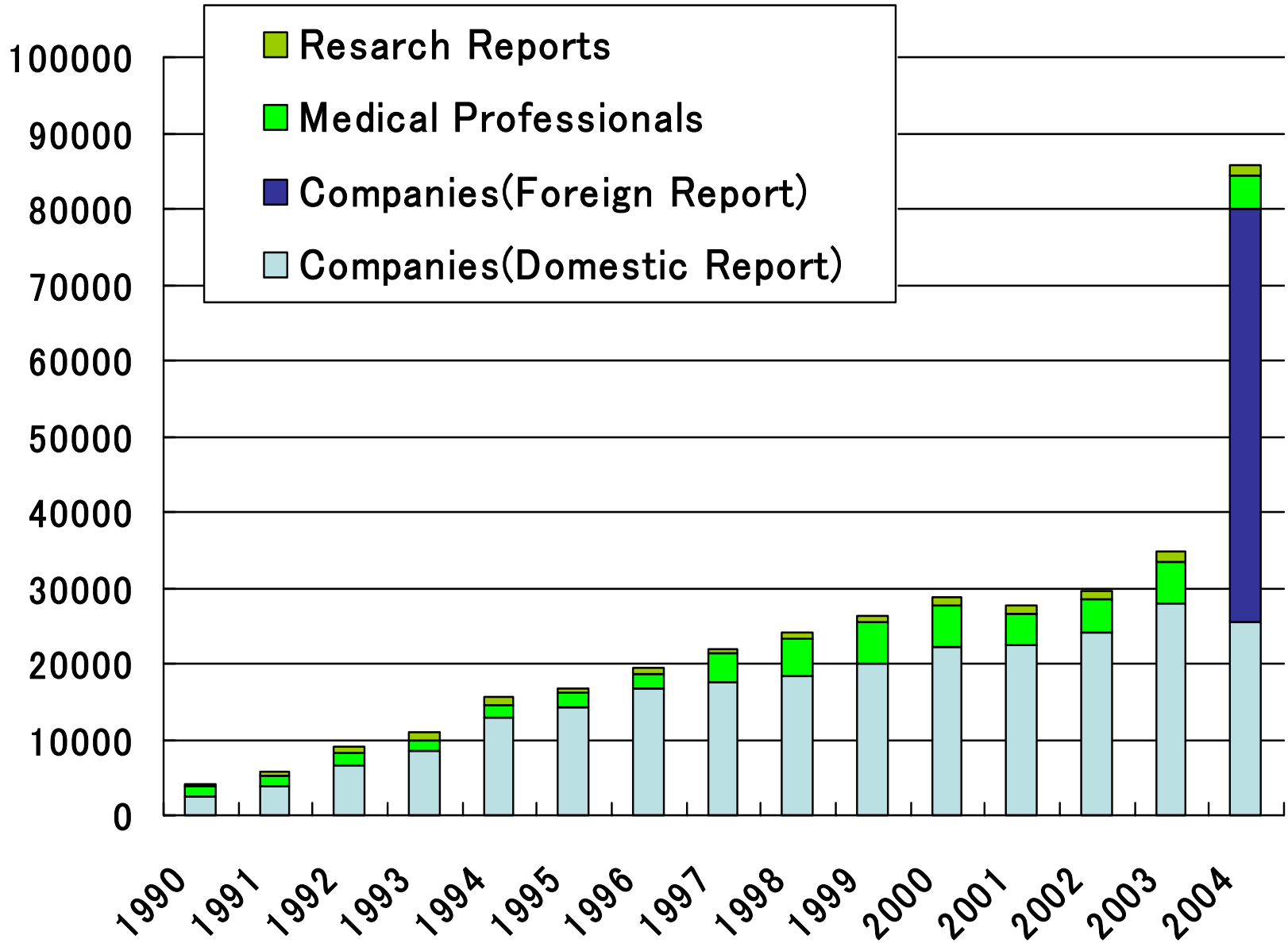


Note: 20–30% of applicants are those who applied before

For "**Safer**" Drugs/Devices

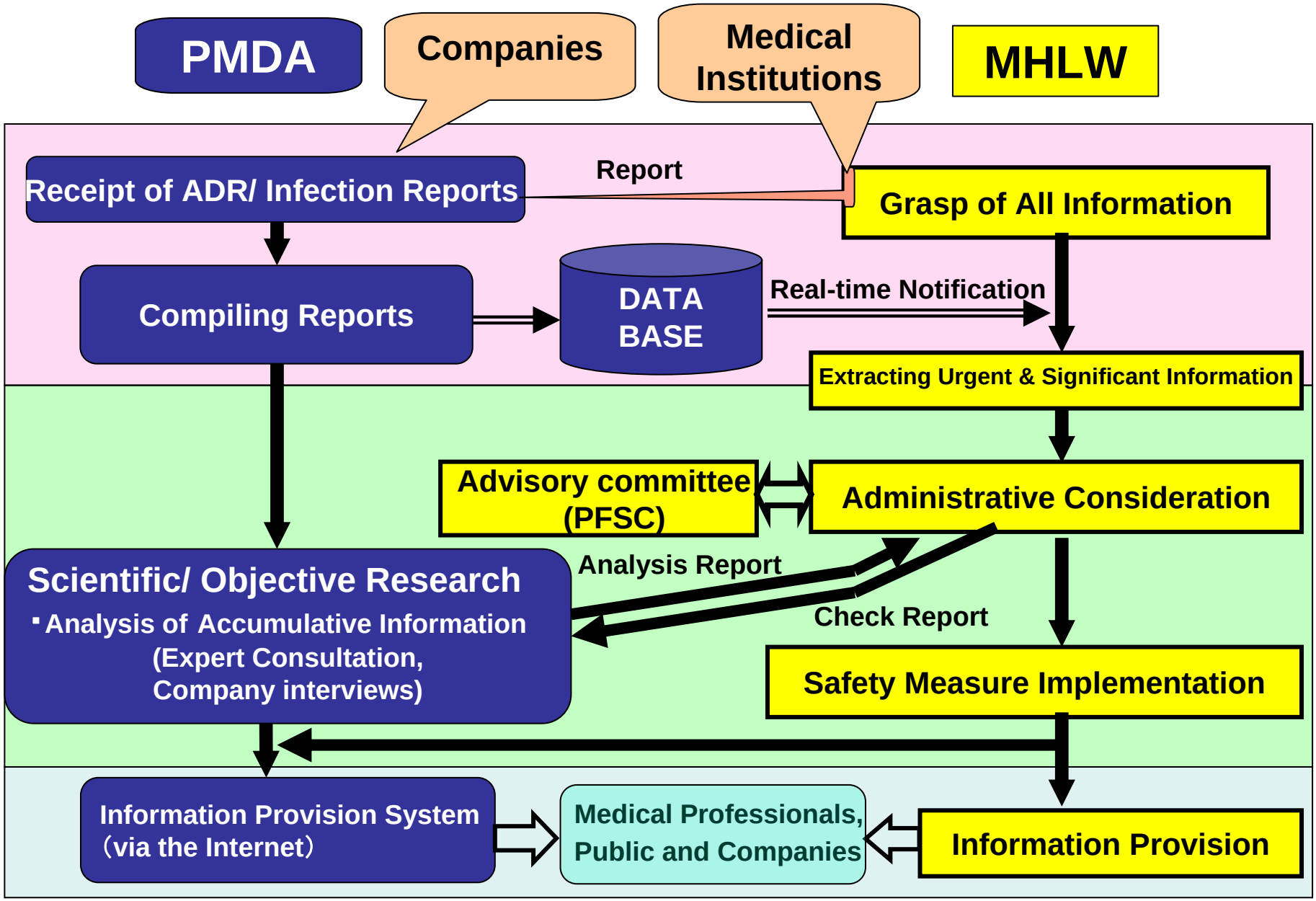


Reported ADR Cases



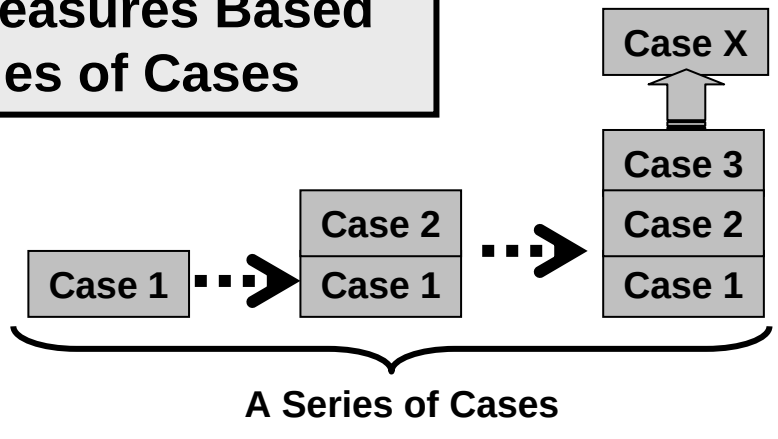
Note :Foreign reports by drug makers are not included in and before FY03'.

Our New Safety Measure (Precautionary Principle)



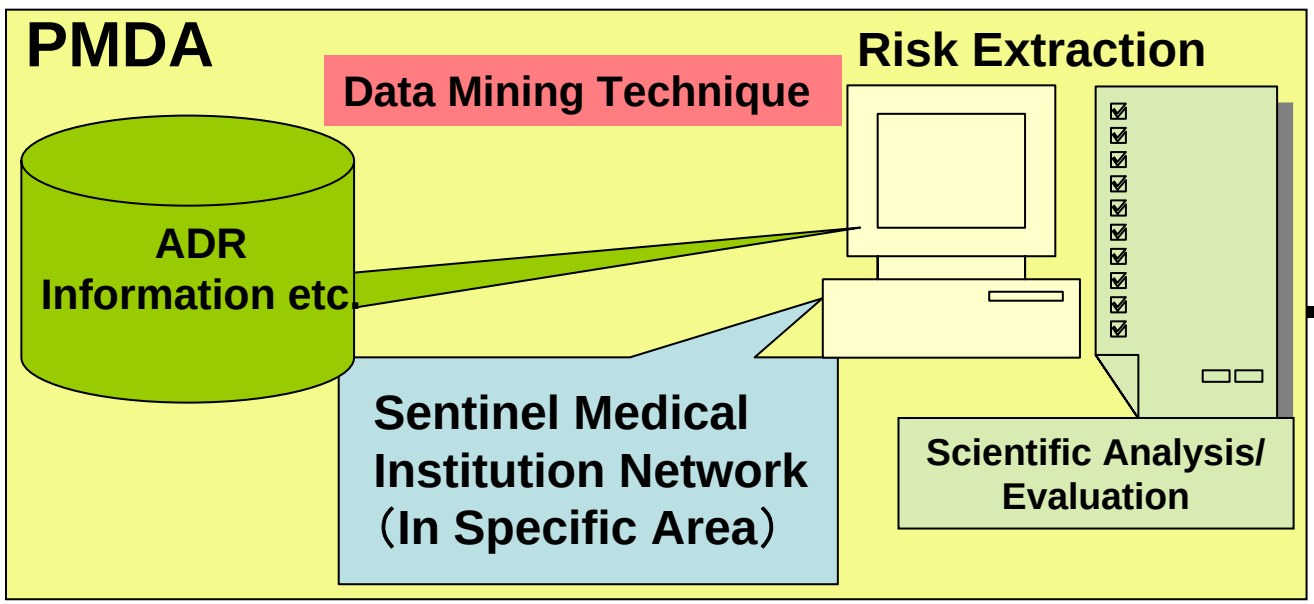
Reform of Safety Measures

Safety Measures Based on a Series of Cases



MHLW
Implementation of Safety Measures

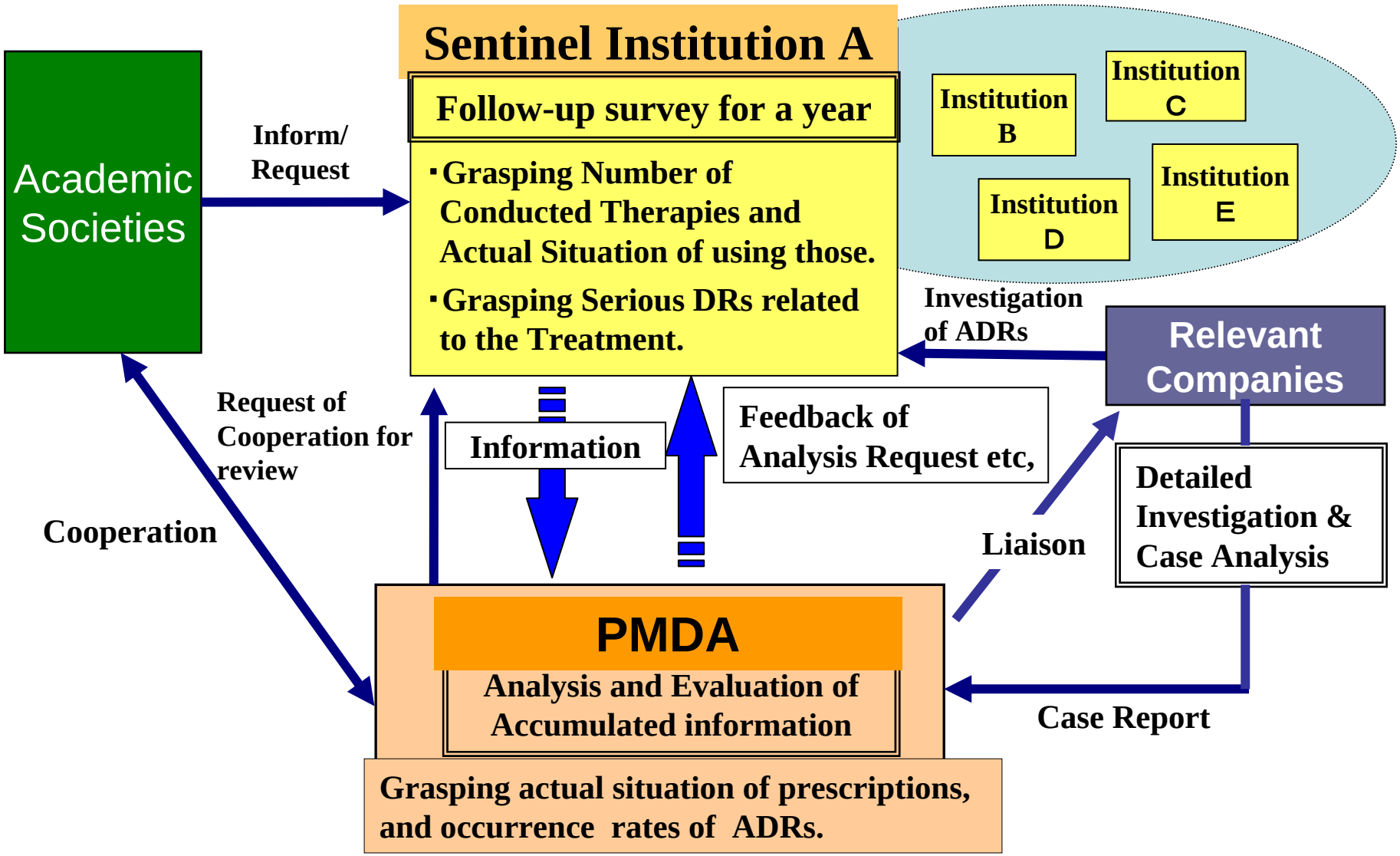
Prospective/ Preventive Safety Measures



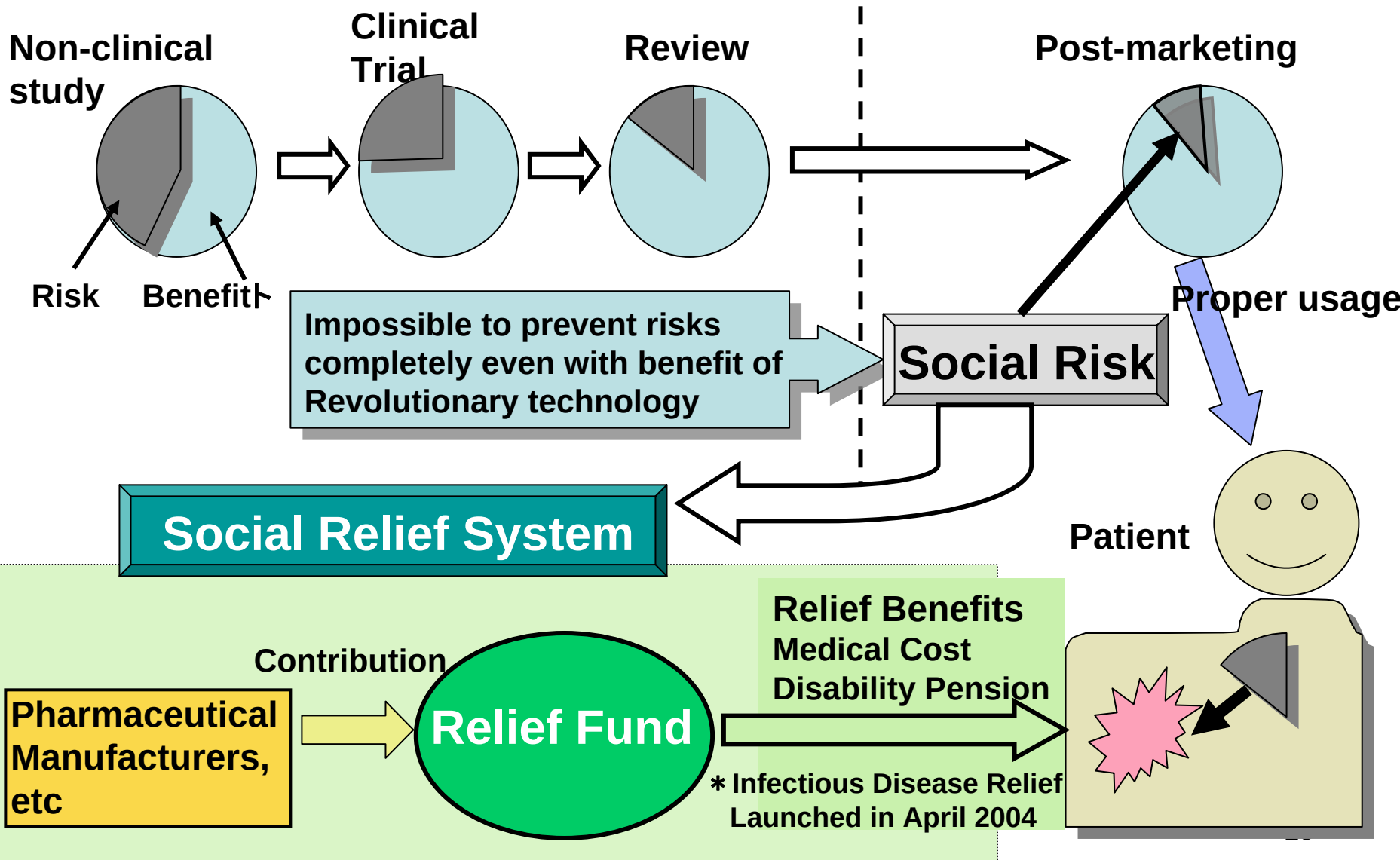
MHLW
Implementation of Safety Measures

Sentinel Medical Institution Network

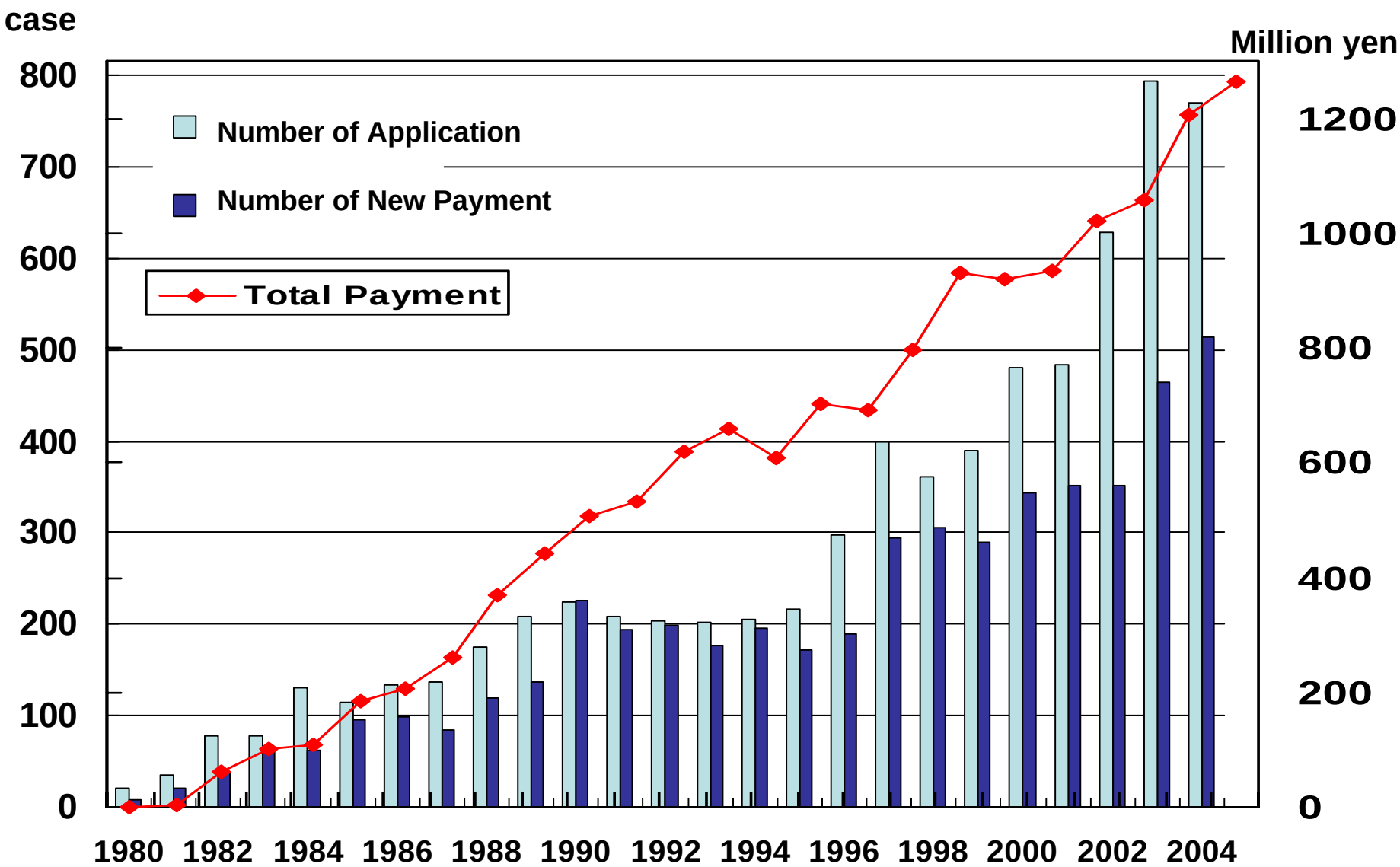
（In FY 05’ ‘the Actual Situation of combined therapies of anti-cancer drugs’ was conducted.）



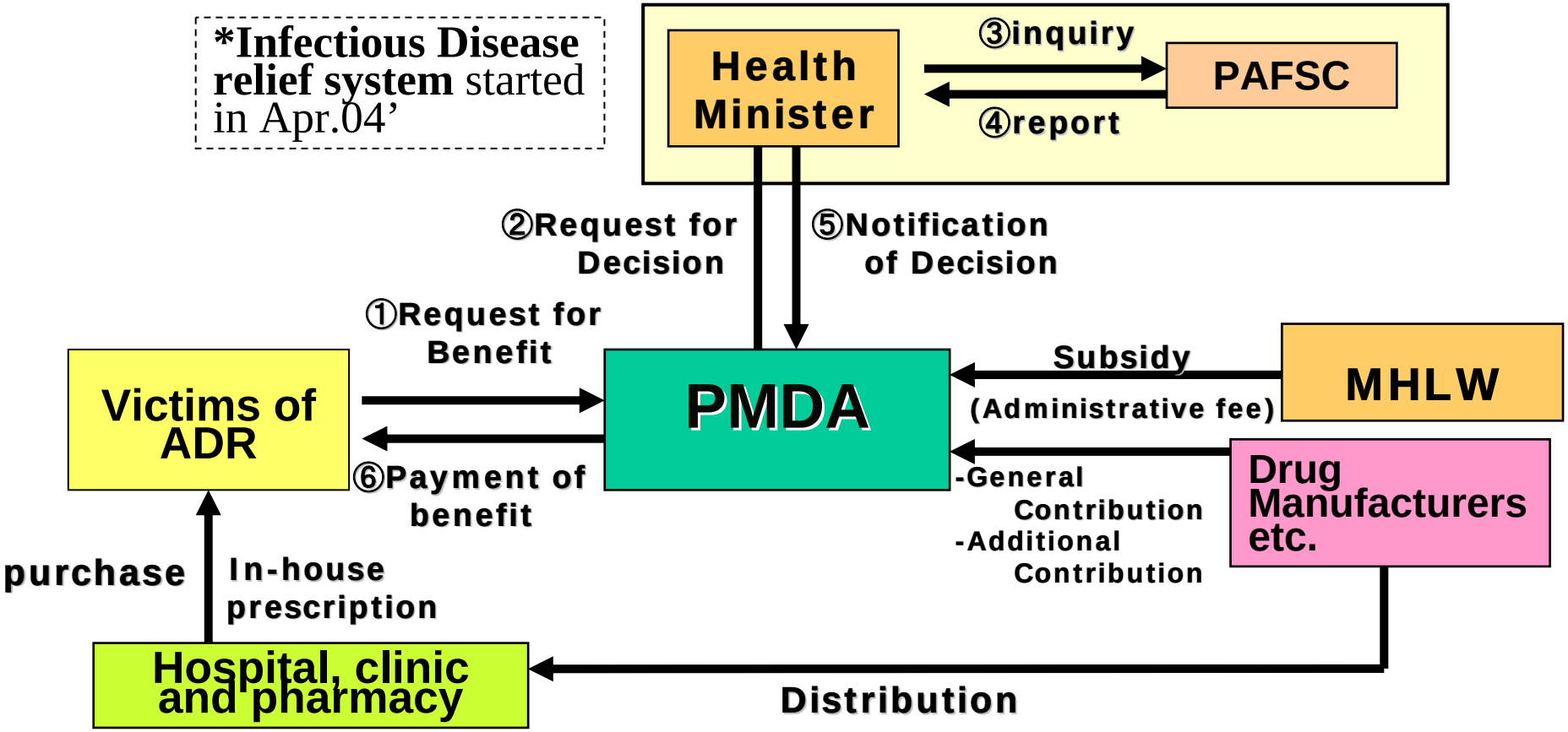
Drug Risk & Relief



Number of Application for Benefits and Amount of Total Benefit



ADR Relief System



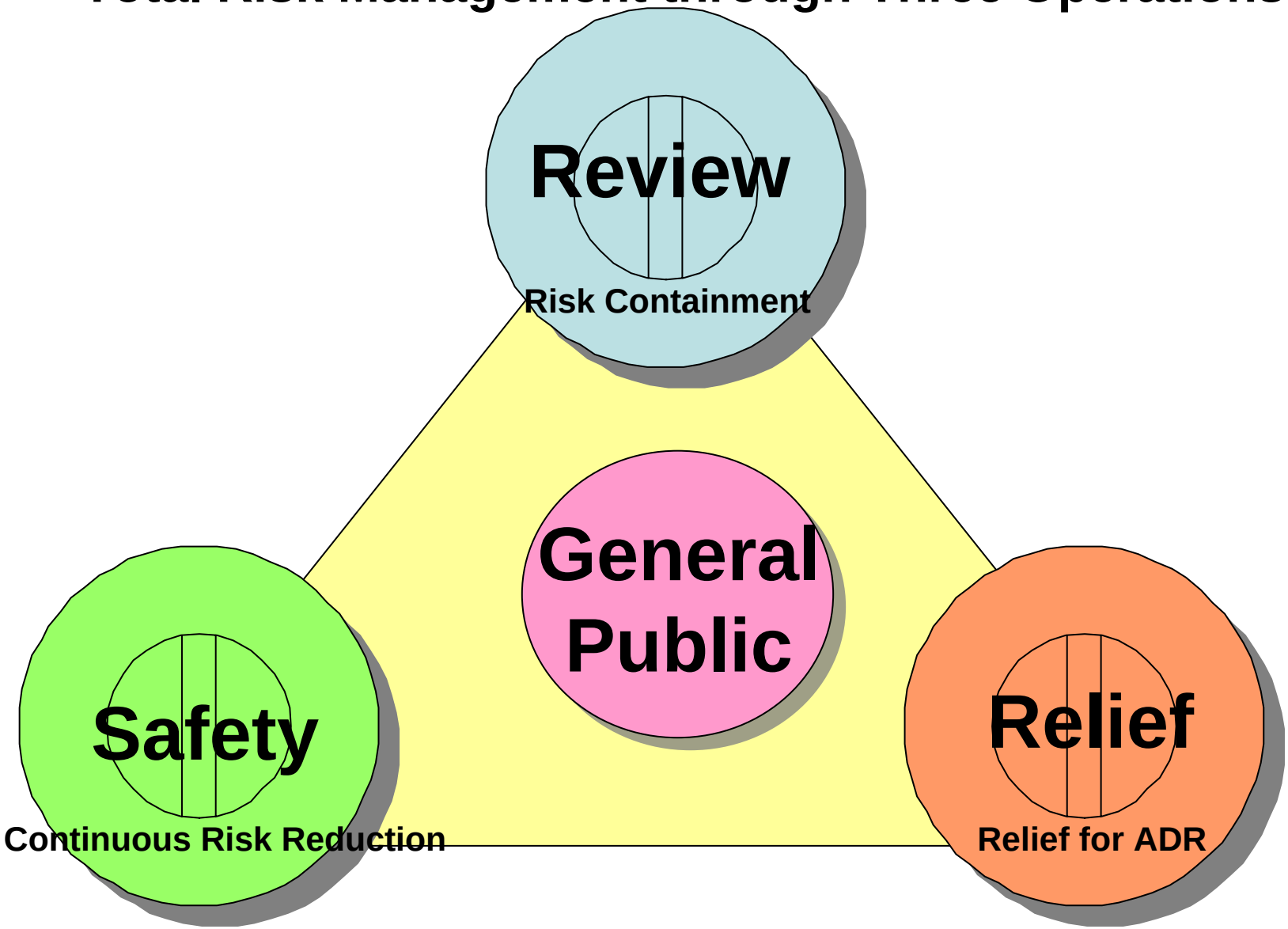
Financial Resources

① Contributions collected from pharmaceutical manufactures, etc
- ●General Contributions：Certain rate of total shipment（0.3/1000at current rate）
- ●Additional Contributions：25％ form manufactures of main cause

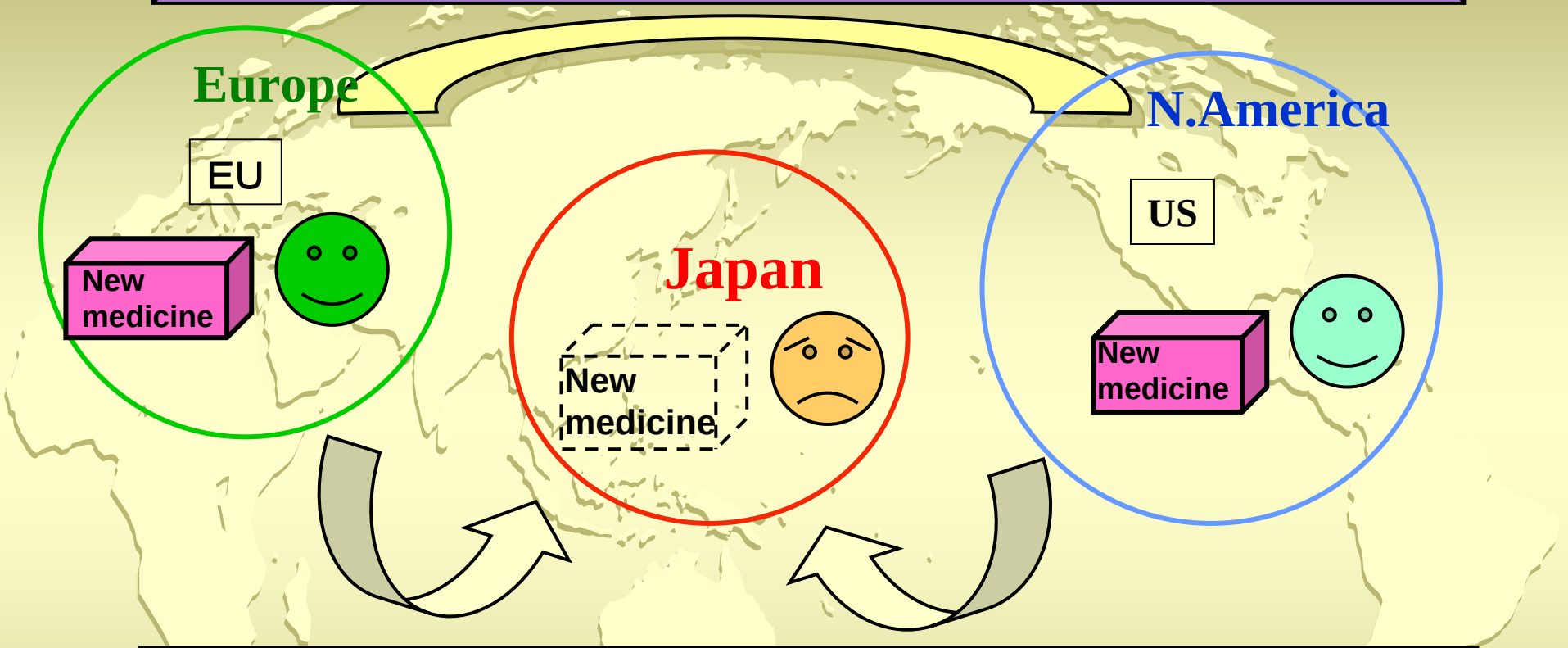
② 50％ of administrative fees at government expenses

Safety Triangle

- Total Risk Management through Three Operations -



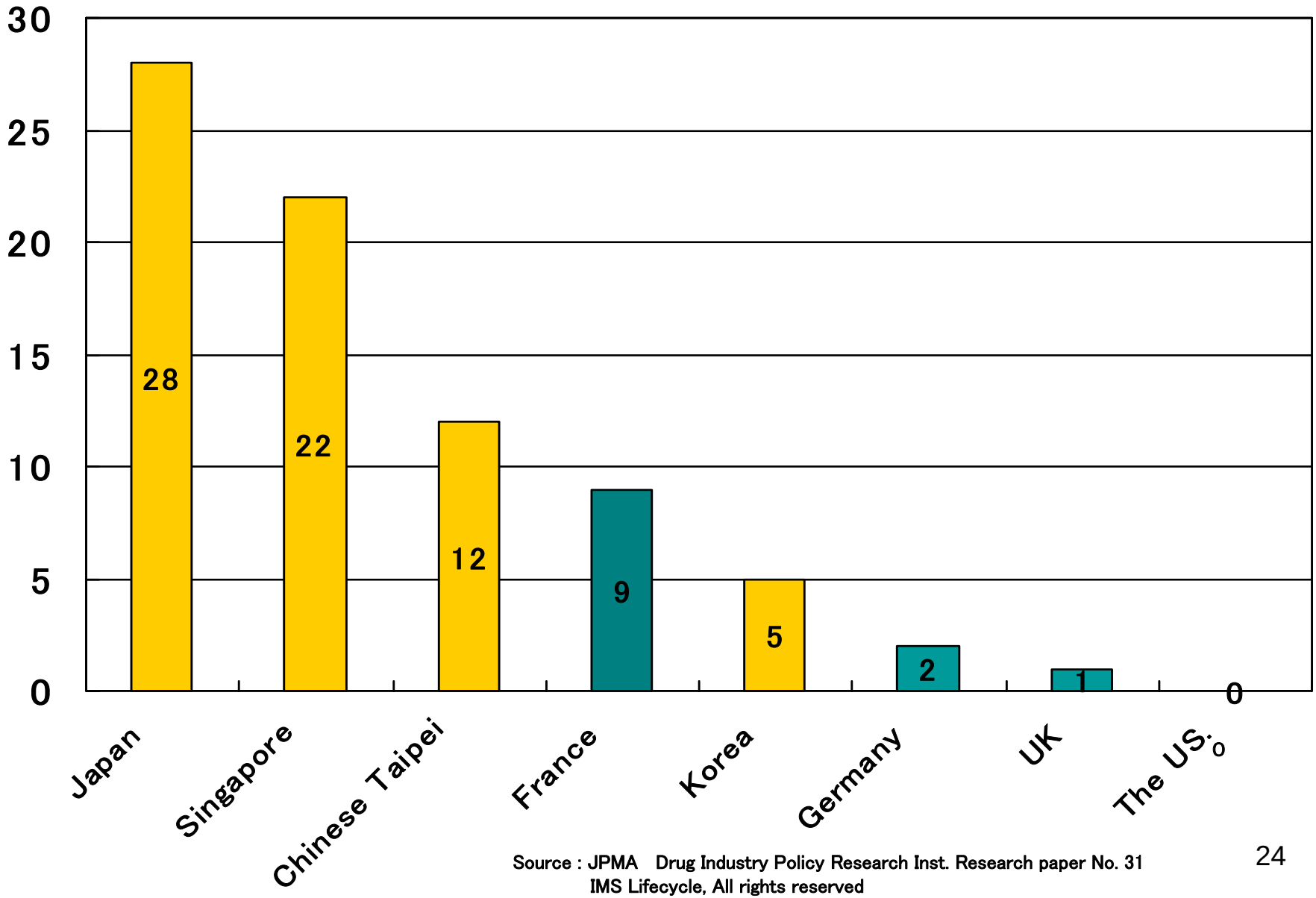
Our Current Issue=“THE DRUG LAG”



Two disadvantages

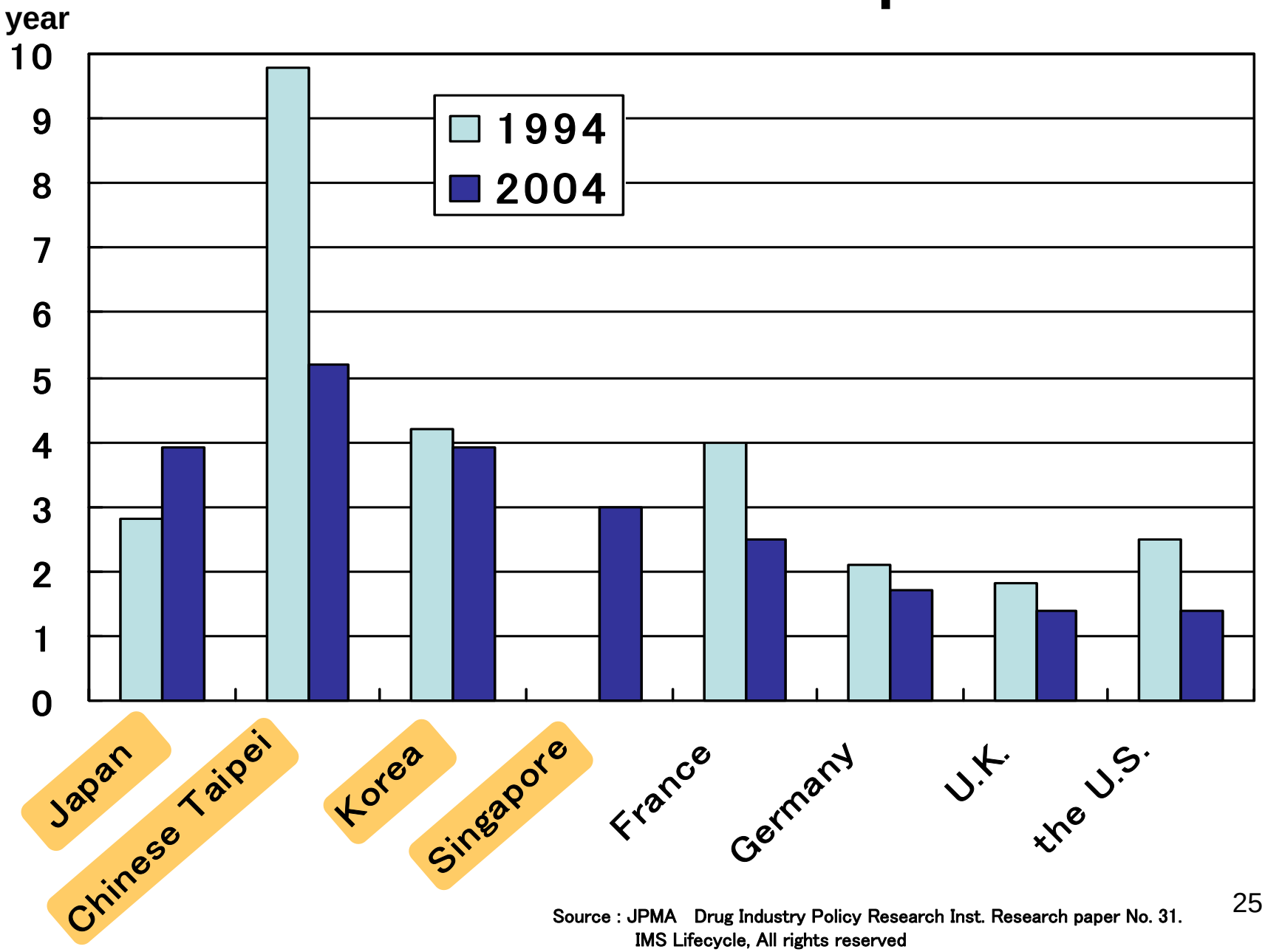
1 Patients = No benefit from leading edge medical treatment
2 Manufactures = Inaccessible to Japanese market

Number of products waiting for marketing
Among World's top 88 selling-products in 2004



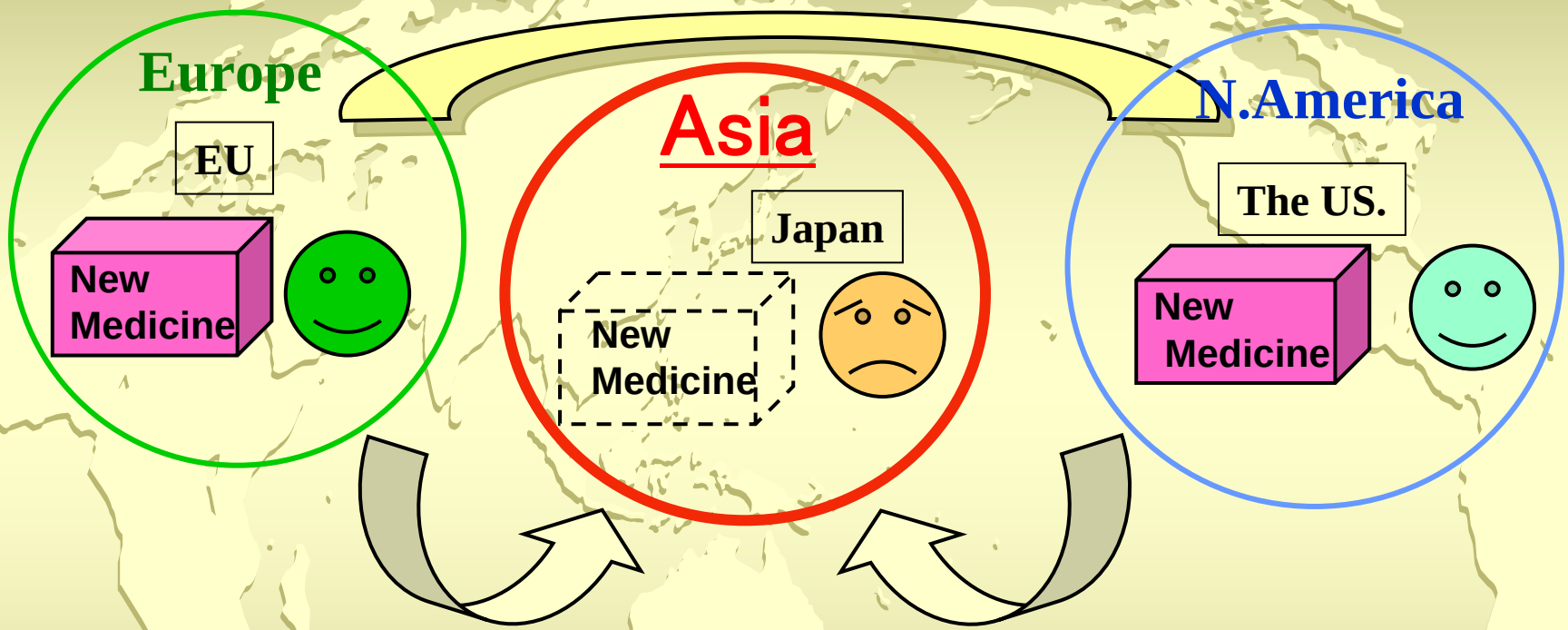
Source : JPMA Drug Industry Policy Research Inst. Research paper No. 31

How soon to release a product?



Source : JPMA Drug Industry Policy Research Inst. Research paper No. 31.

Asian (including Japan) Current Issue ="THE DLUG LAG"

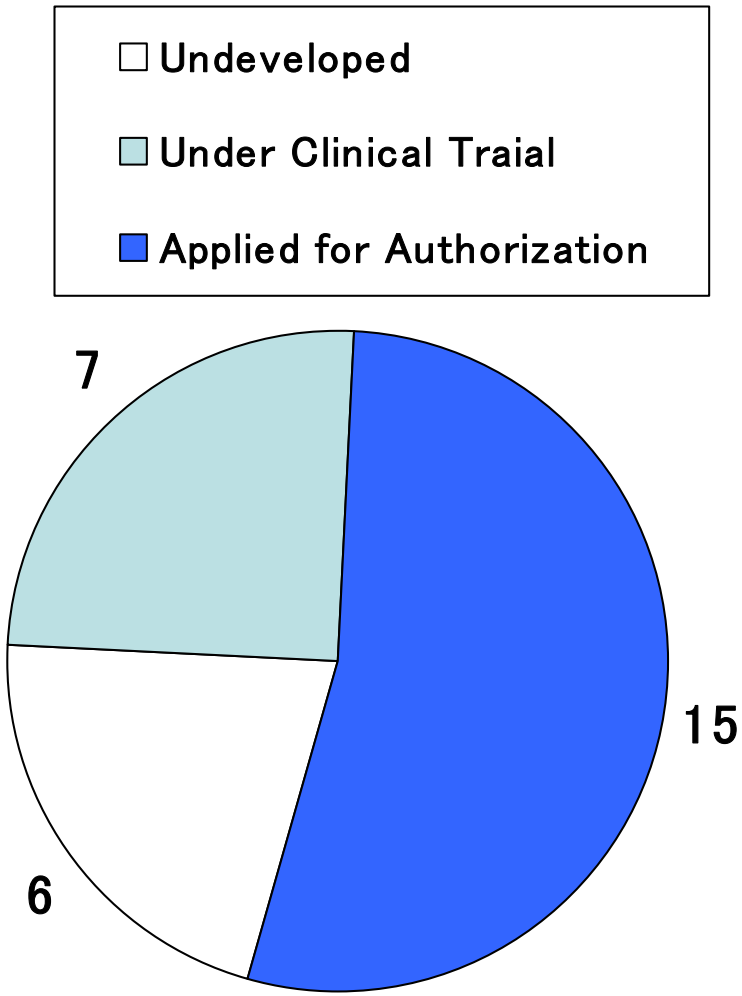


Two disadvantages

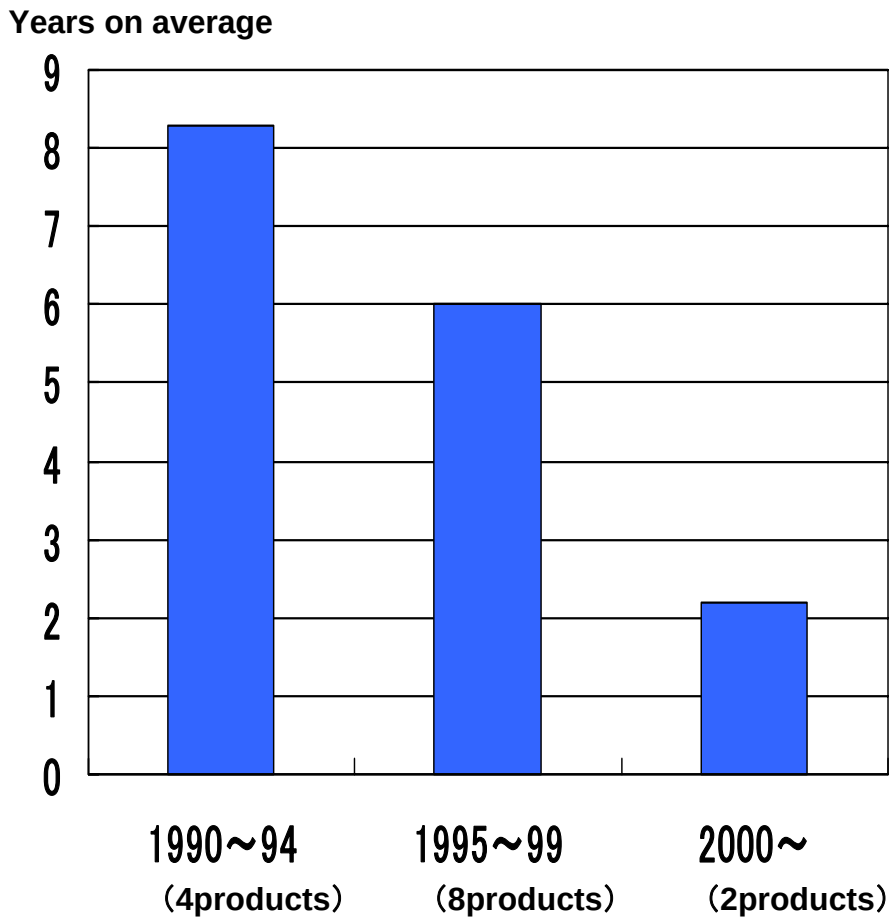
1. Patients=No benefit of leading-edge medical treatment
2. Manufacture=inaccessible to Asian market

Delayed Drug Application to Japan

Situation of 28 popular products

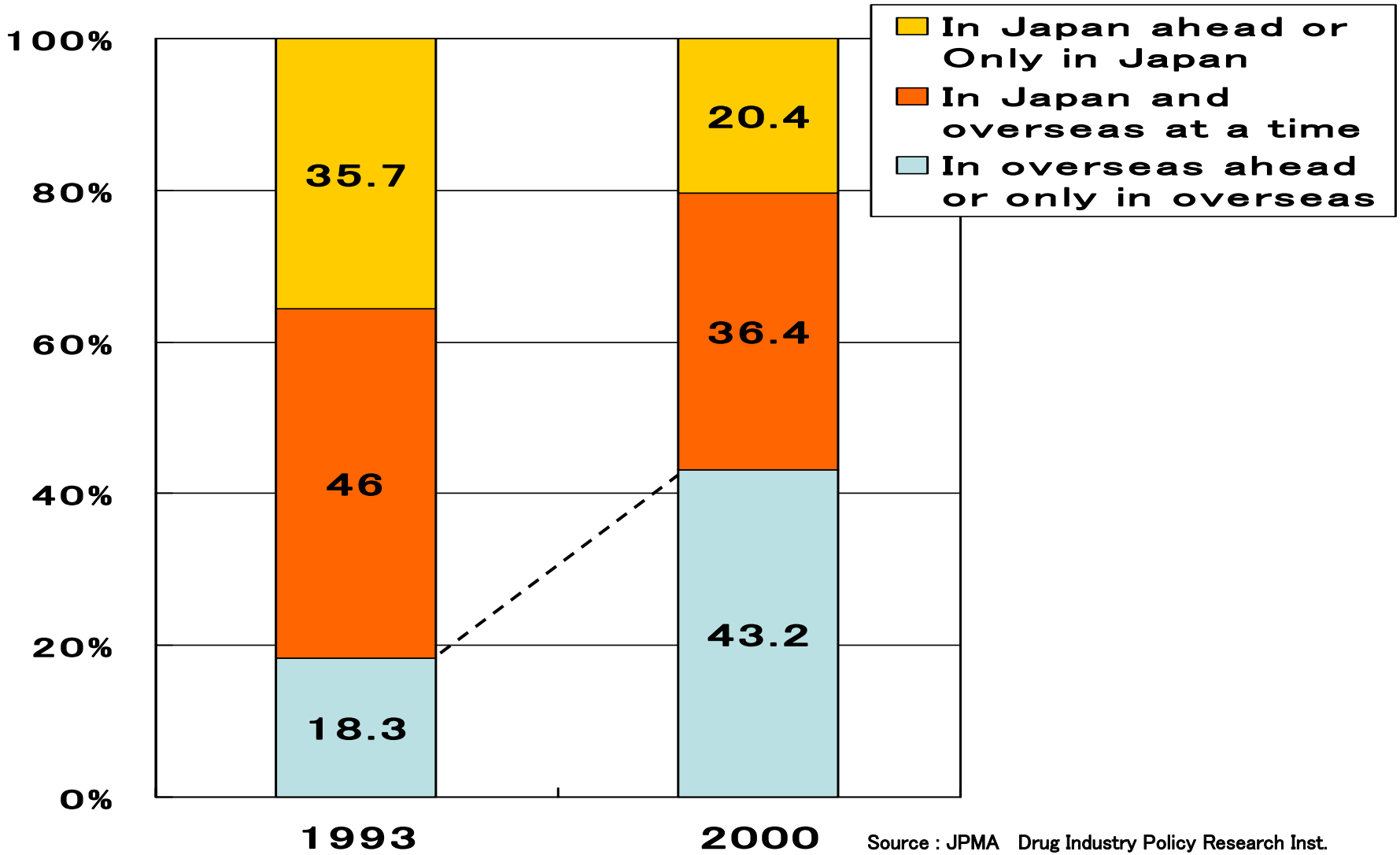


Length from world first release to application in Japan (about 15products under application)



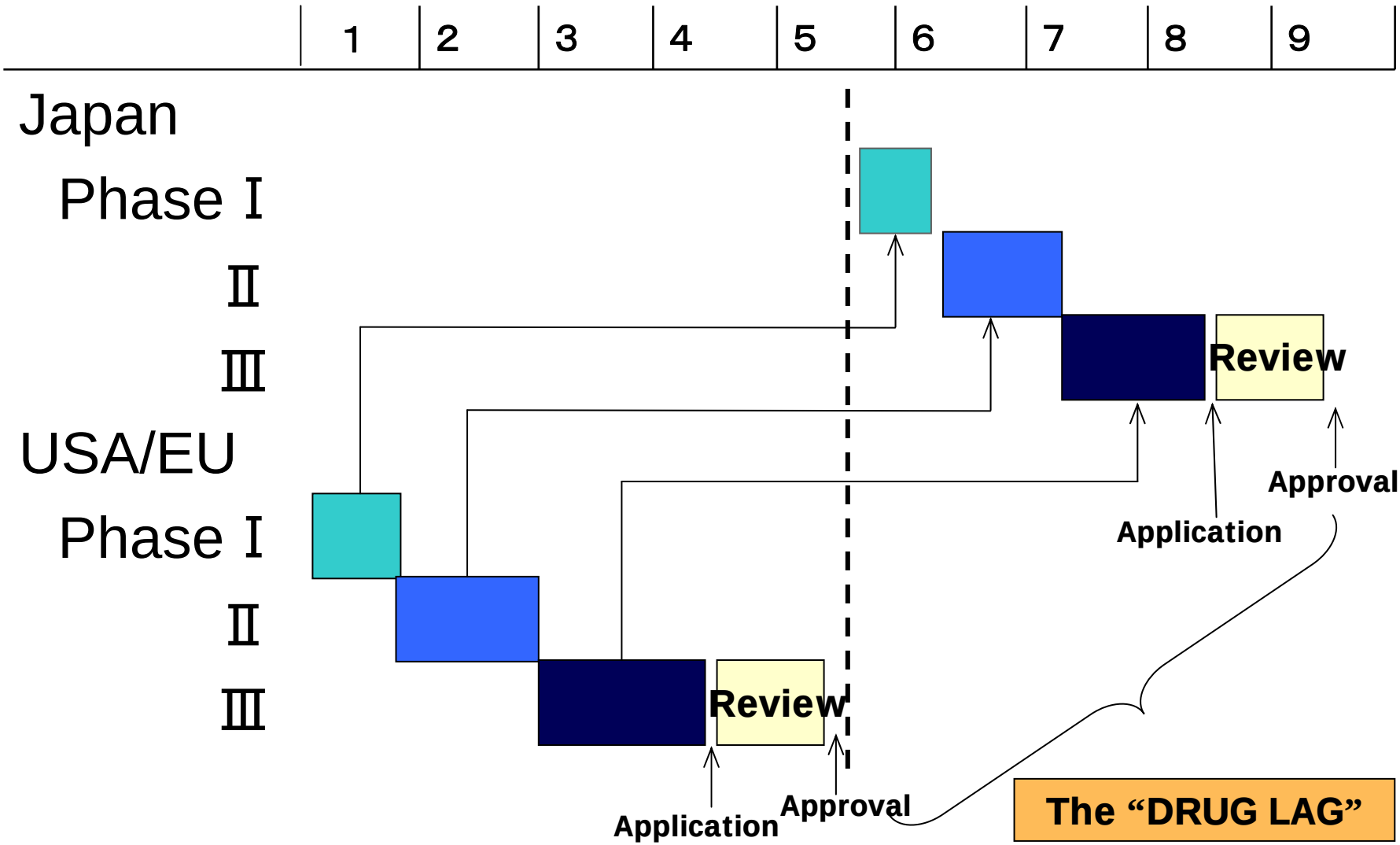
Source : JPMA Drug Industry Policy Research Inst. Research paper No. 31

Clinical trial sites of Japanese drug companies

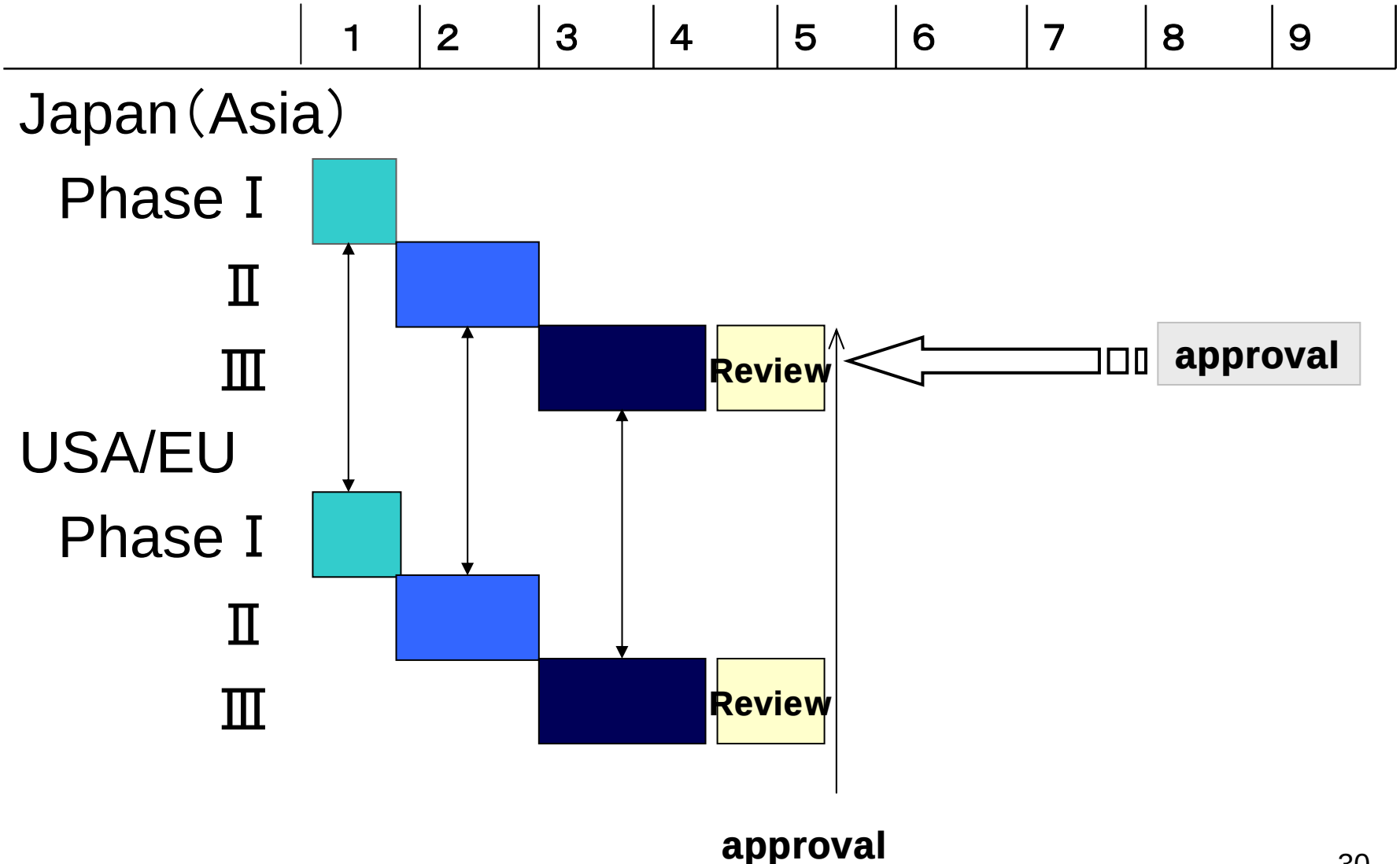


Source : JPMA Drug Industry Policy Research Inst. Research paper.

Clinical Study Package of Bridging Studies



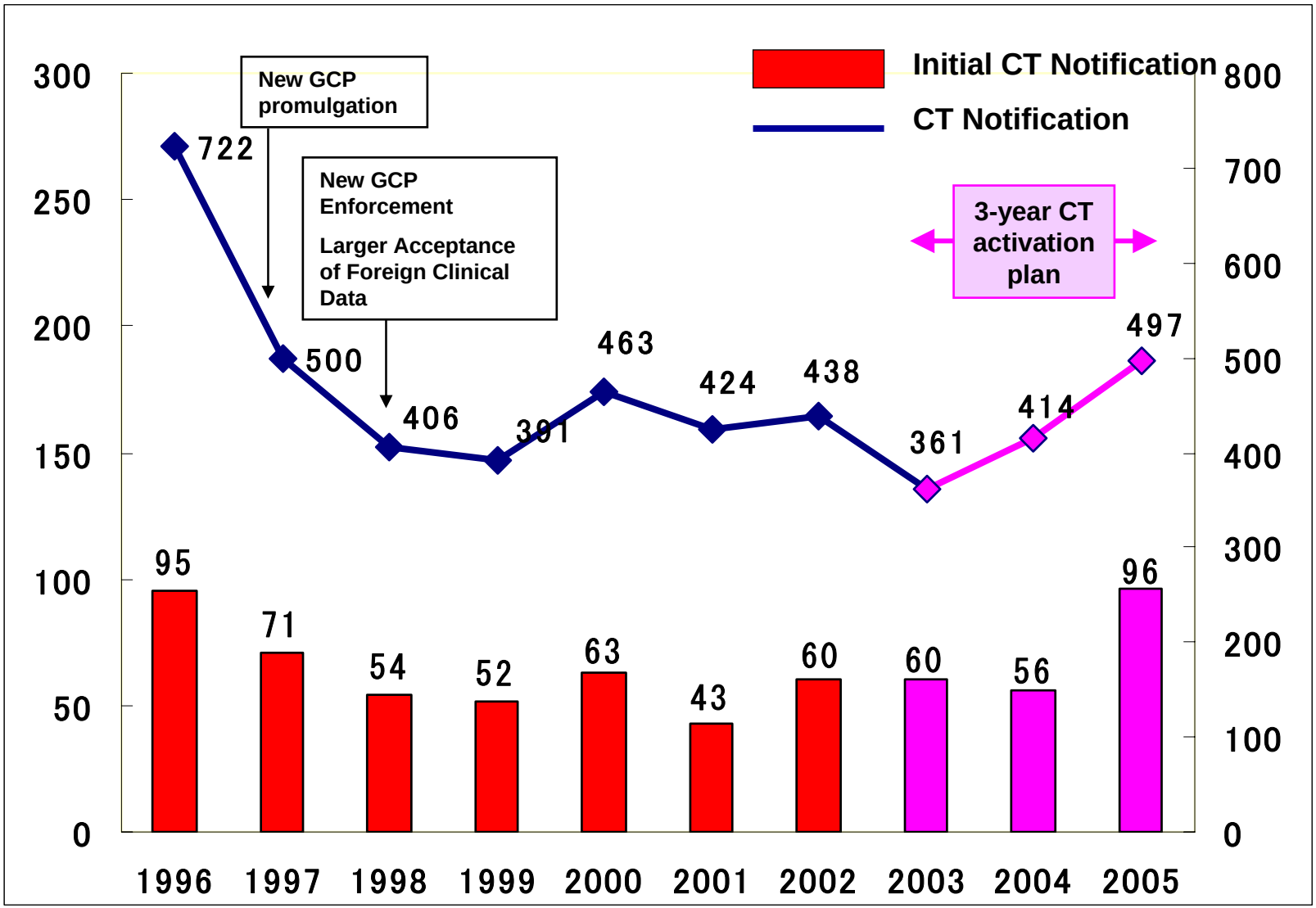
Involvement in Global Clinical Study



Initial CT notification

Number of Notified Clinical Trials

CT notification



（Source;：MHLW）

Development of Basic Clinical Study including CT

1 Reinforcement of CT Operation for Medical Institution

・**1170** Medical Institutions registered in large-scale **CT network**

2. Cultivation of Staff

・**4524** staffs completed **CRD** training

3. Promotion of participation in CT

・Illuminating measures and information supplement（Clinical Study Registration System）

4. Promotion for Drug Maker

・Introduction of IT and adoption of fixed format

5.Promotion of Product Research and Development

3-year CT activation plan（2003-2005）

（the Health Policy Bureau）

Development of System or CT ,Approval, review

1.Summary

・Participation in Global Clinical Trial and Promotion of Concurrent Application

・Development of CT Environment of Asia

2. Clinical Trial System

・Reform of CT procedure

・Operation of GCP ordinance for Globalization

・Improvement of Quality and Function of IRB including consideration of Central IRB

・Rationalization of call for subject

・GCP operation under consideration of Medical Devices

・Compensation program

3. Review and approval system

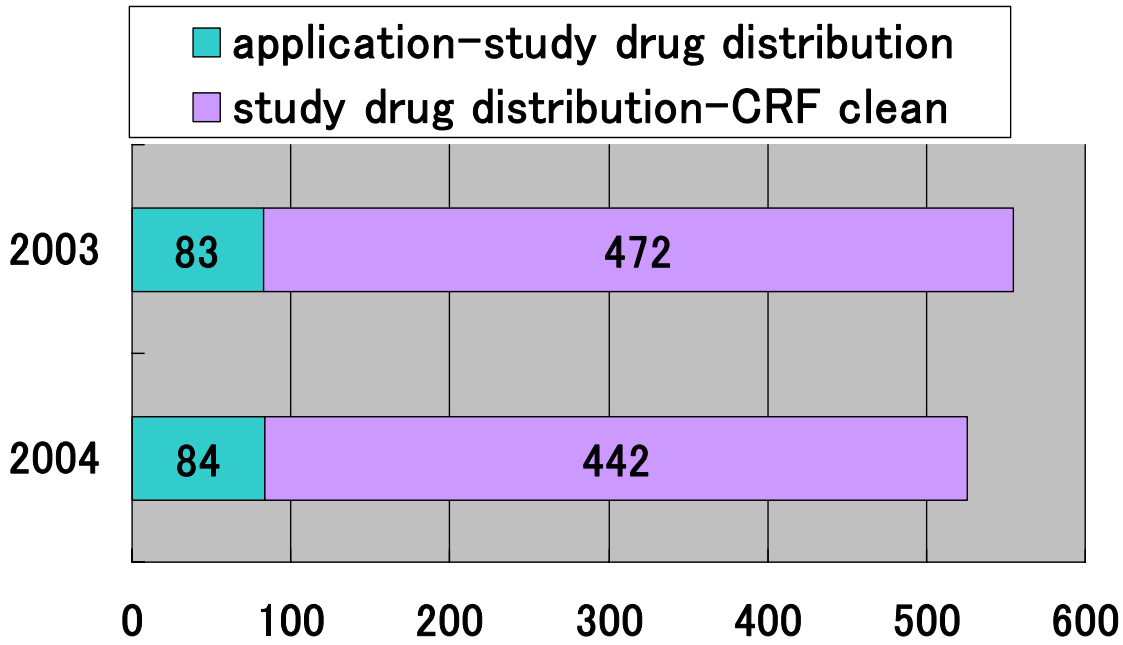
・Improvement of Review system in PMDA

・Modification of approval system for Medical Devices.

（PFSB）

Decision by Clinical Trial Issue Committee, MHLW in July 05'

Clinical Trial Environment



***Comparison of period of CT**

2003 555days on average

↓ ↓

2004 526days on average

Source: JPMA

***Comparison of average days**
(form application to case report)

2004 → 2005

622 days → 558 days

***Comparison of cost for Medical Institution**
(Including R&D expenses, CRC expenses, SMO expenses)

1.95 m yen → 1.678 m yen

(on average)

Source; Research on Clinical Cost / R&D Head Club cost research working group

Our Recent Approach to Important Issues

1. Appraisal of Necessary Clinical Trial Data and Evaluation Methods in Review

1) To Promote Japan's Participation in Global Development and International Clinical Study

2) To Consider Positioning of Japanese Domestic Data among International Clinical Study Data obtained in Other Asian Countries

3) To Introduce Evaluation Methods focusing on Cutting-edge Technologies such as Pharmacogenomics

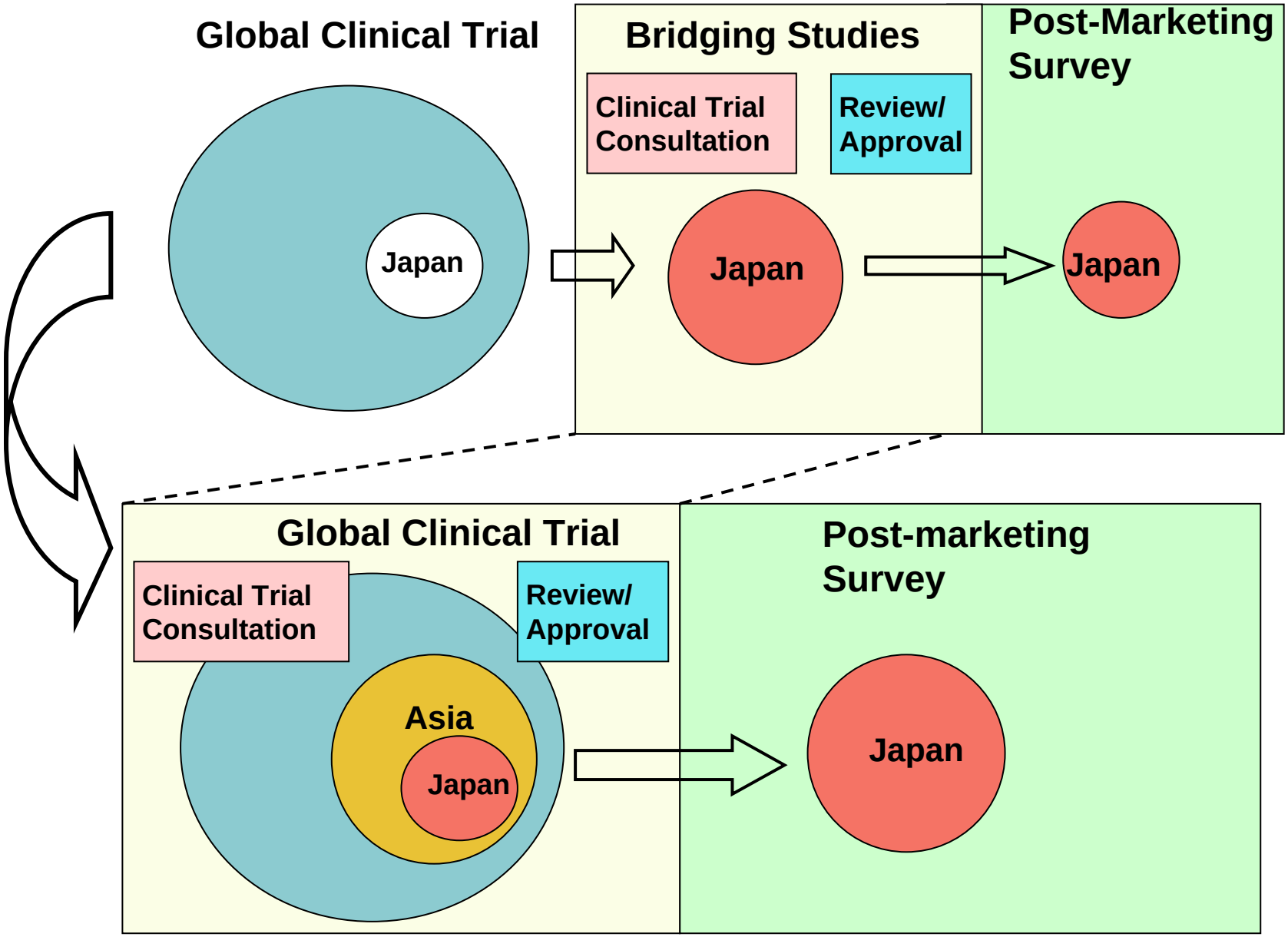
4) To Strengthen Risk Management by Reinforcement of Post-marketing Safety Measures Coordinated with Pre-market Review in Introduction of International Clinical Study and Cutting-edge Technologies

2. To Assist Improvement of Clinical Trial Environment by reinforcing On-site GCP Audit

3. Active Support of Development of Cutting-edge Biotechnologies through Clinical Trial Consultations and Other Measures

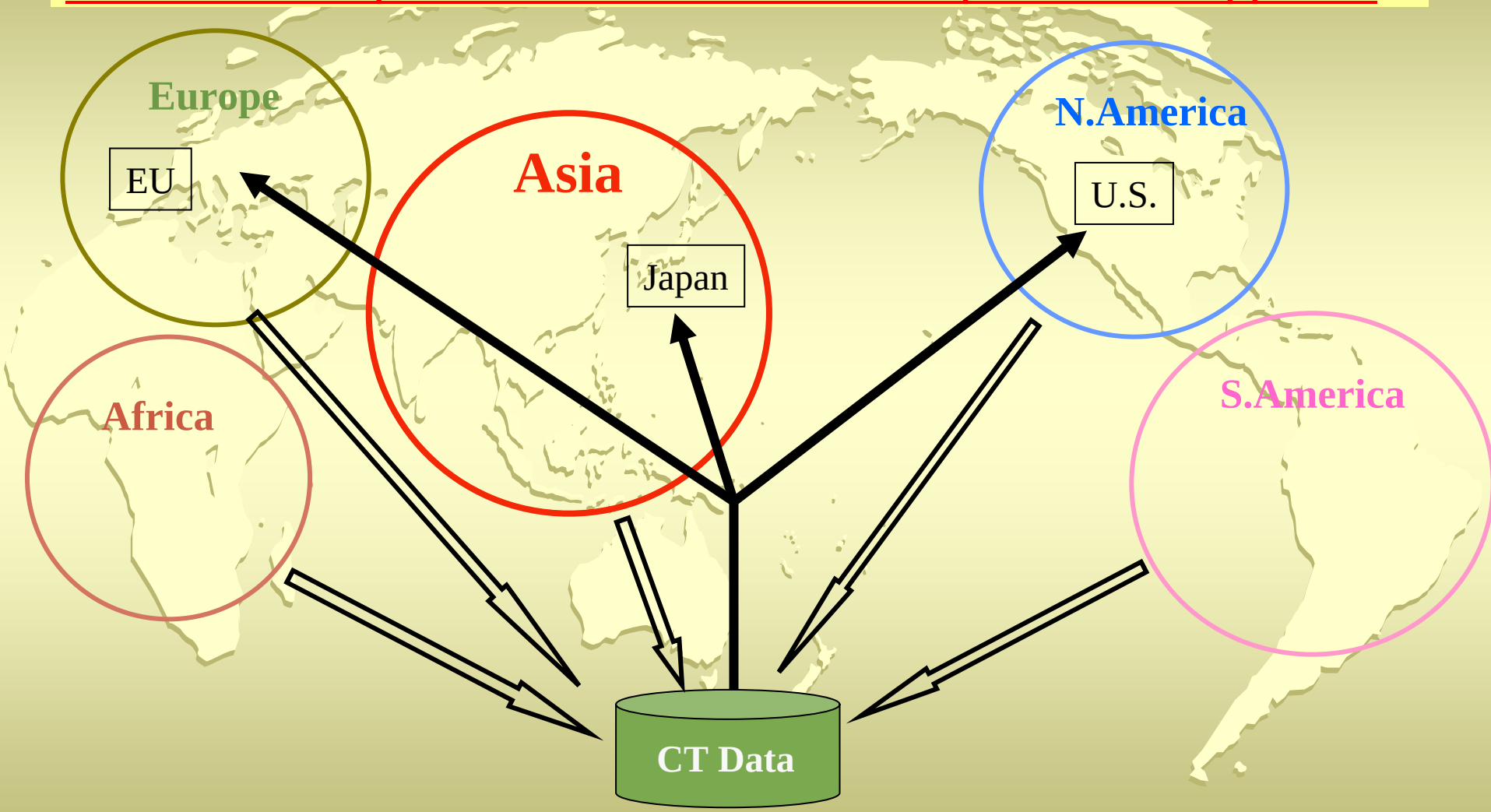
4.Increse number of experts and developing their ability

Our Efforts toward Global Clinical Trial



Global Clinical Trial

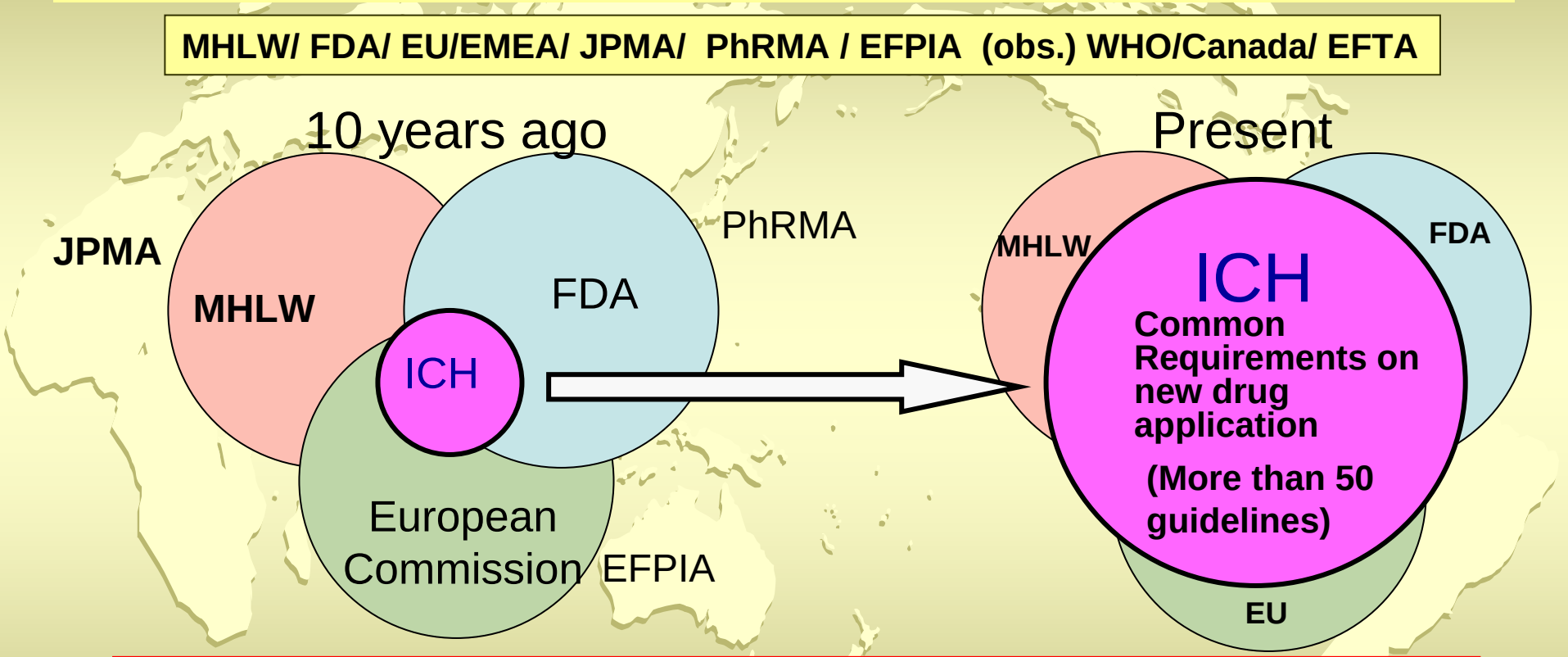
To Achieve Tripartite Simultaneous Development and Approval



Development of International Harmonization in review operation

「International Conference on Harmonization (ICH)」（Founded in 1991）

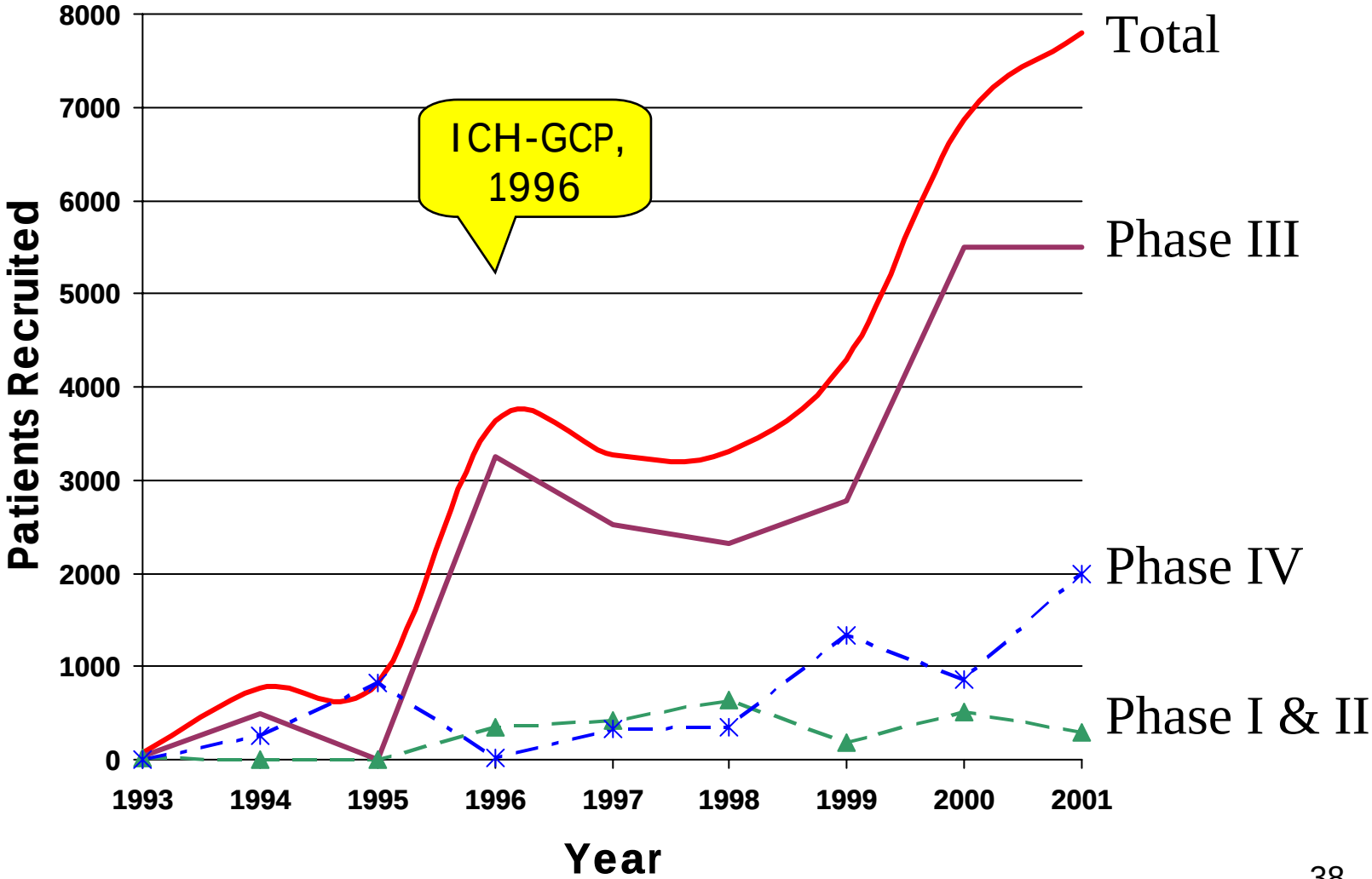
MHLW/ FDA/ EU/EMEA/ JPMA/ PhRMA / EFPIA (obs.) WHO/Canada/ EFTA



Goal＝Simultaneous Submission & Approval In the World

（Reference）”The Global Harmonization Task Force (GHTF)”since 1992

Growth of Clinical Development in Asia

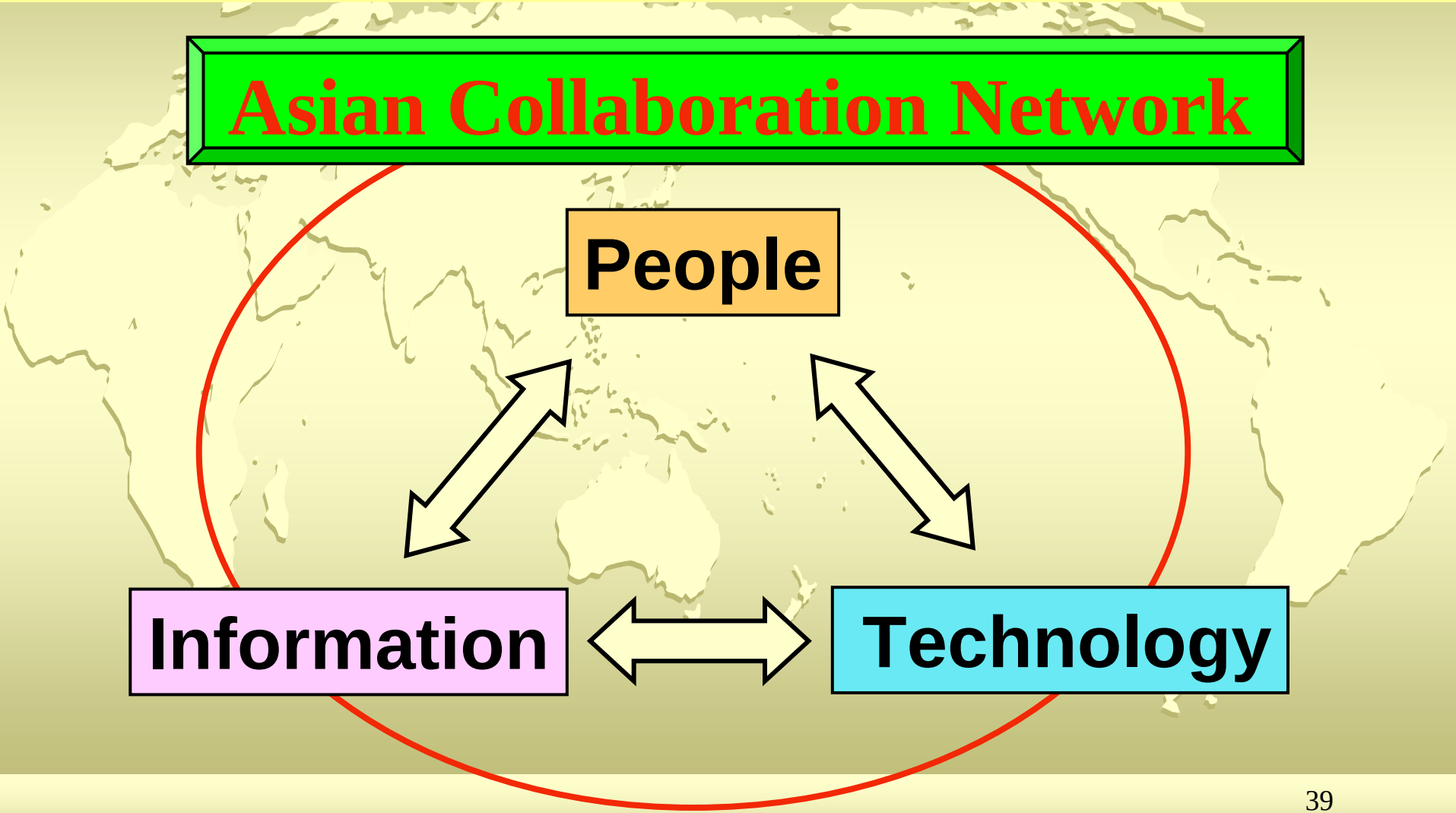


From JPMA Report of Asian CT Study Team

Source: Quintiles Translational

Asia in Global Development

-To ensure faster access to superior drugs for Asian people-



Summary Report APEC 2006

Satoshi Toyoshima, Ph.D

Executive Director

Pharmaceuticals & Medical Devices Agency (PMDA)

Japan

A drug for world wide populations