Premarket Submission and Approval Requirements in Japan

Madoka Murakami

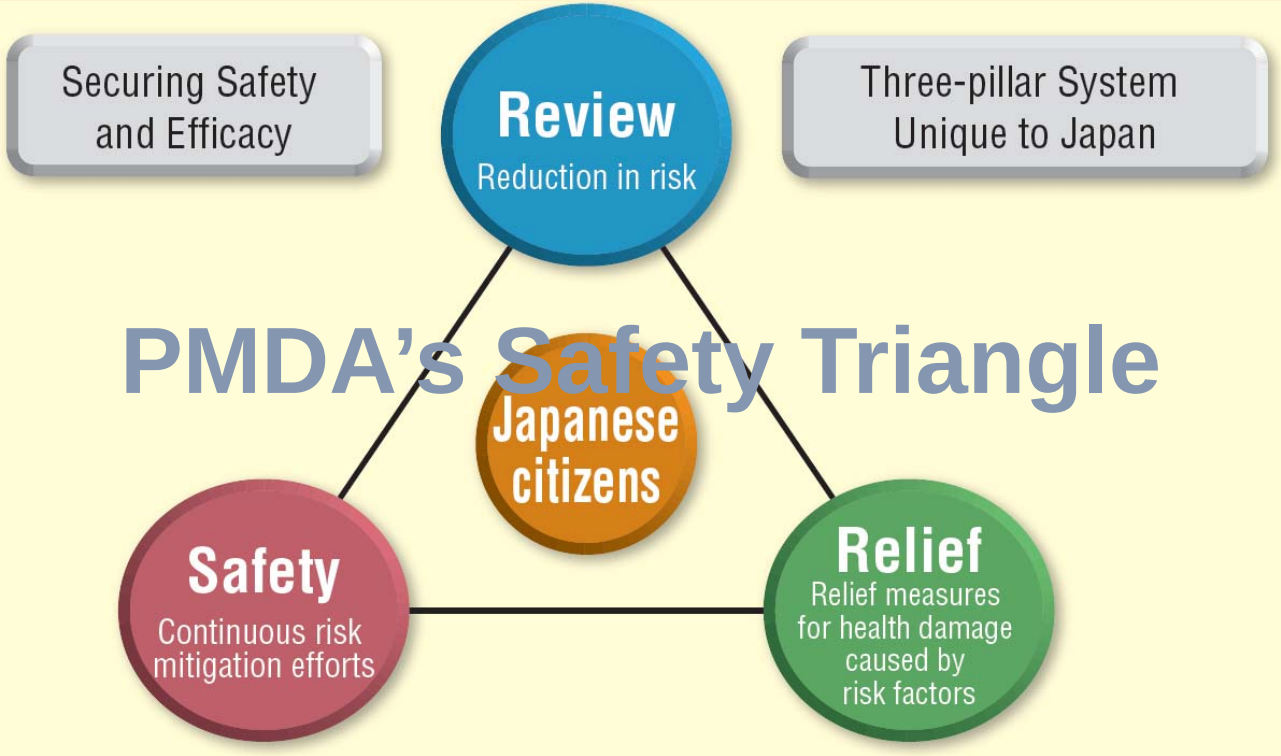
Office of International Programs

Pharmaceuticals and Medical Devices Agency

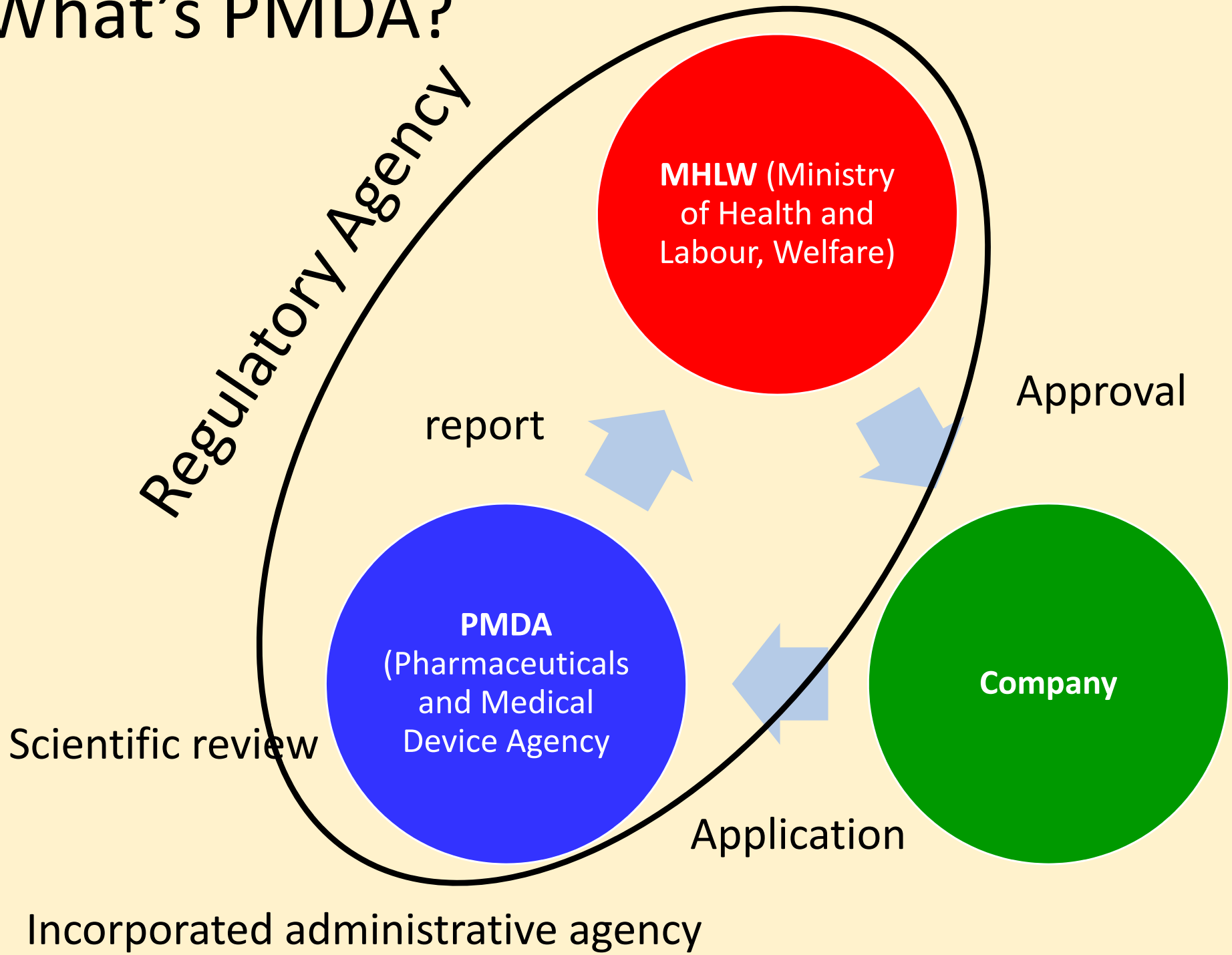
Introduction of PMDA

Pharmaceuticals and Medical Devices Agency (PMDA)

- an Incorporated Administrative Agency (IAA)



What's PMDA?



Incorporated administrative agency

Shared Responsibilities

[MHLW] (Ministry of Health, Labor and Welfare)

Ultimate Responsibilities in policies & administrative measures

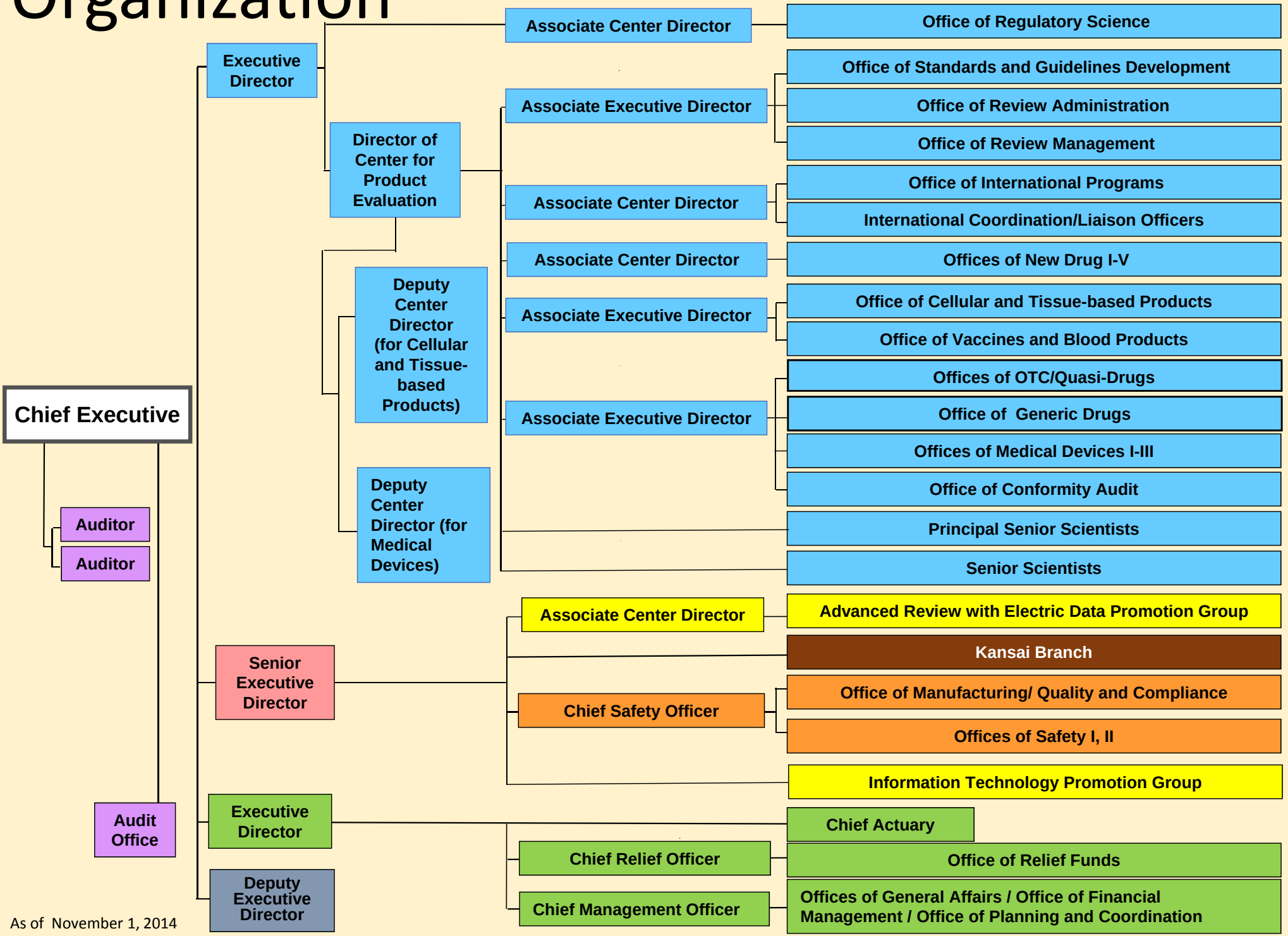
ex. • Final judgment on approval
• Product withdrawal from market

[PMDA]

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

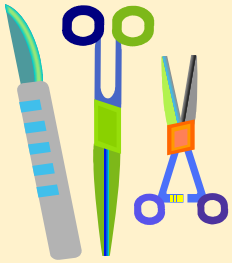
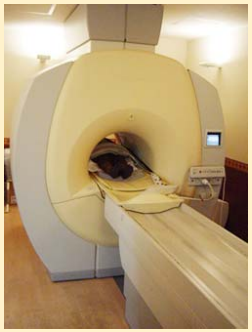
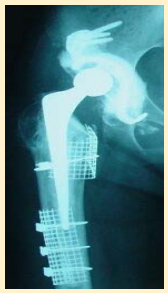
ex. • Approval Review of MDs
• QMS/GLP/GCP inspection
• Collection and analysis of Adverse Event Reports

Organization



As of November 1, 2014

Overview of Medical Device Regulation

Classification	Class I	Class II	Class III	Class IV
	Extremely low risk	Low risk	Medium risk	High risk
Example	X-Ray film 	MRI 	Dialyzer, Artificial bone 	Pacemaker, Artificial heart valve 
Category	General MDs	Controled MDs	Specially controlled MDs	
Review regulation	Self-declaration	Third party certification	Minister's approval (PMDA's review)	
Post-market safety vigilance/surveillance	PMDA and MHLW Re-examination for Brand New MDs, Re-evaluation, AE reporting, Researches, etc.			

Medical Devices Regulation

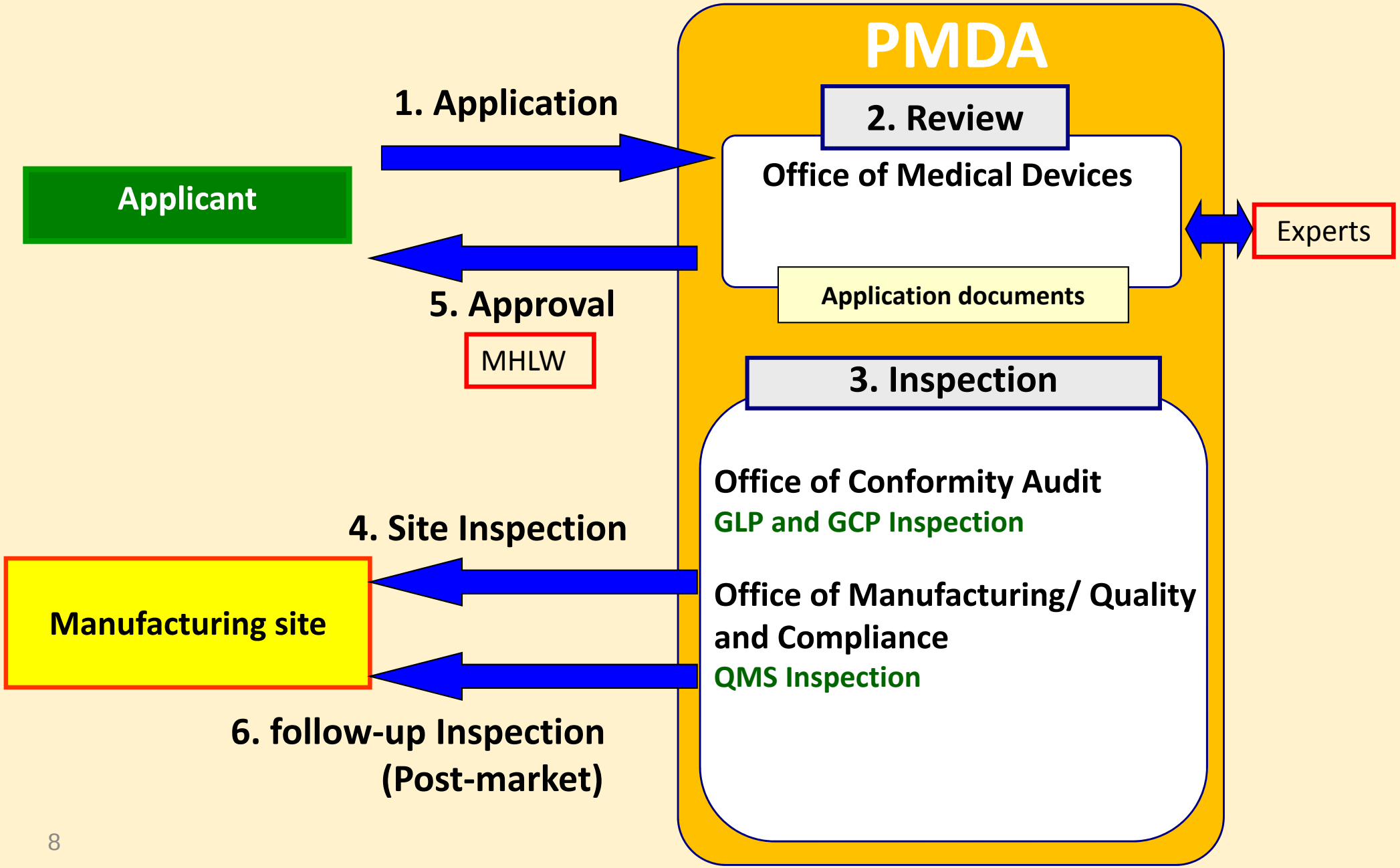
EU	Japan	US
Pre-market review		
Notified body certification (requirements depend on device classification)	Class III, IV: Minister's approval Class II: Notified body certification Class I: Self-declaration	Class III: PMA Approval Class II: 510(k) clearance, Class I: exemption

Governmental approval/license

Notified body review/certification

Self declaration/exemption

Overview of review process



Medical Device Marketing Regulation in Japan

Marketing Regulation

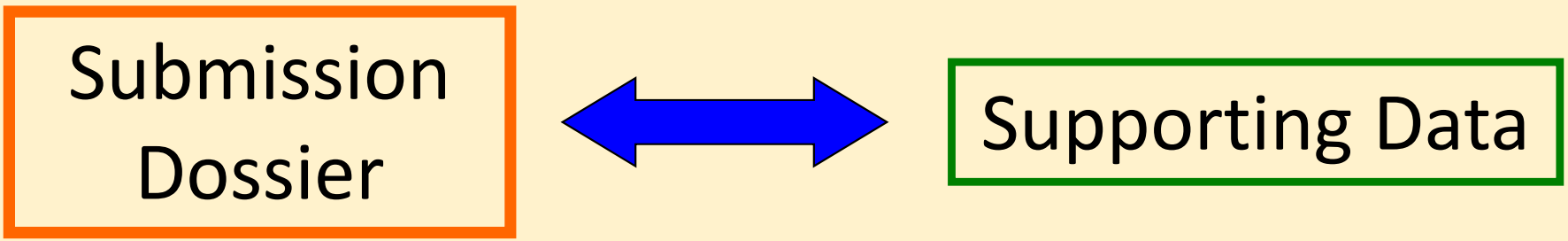
License for Manufacturing
(Accreditation for Foreign Manufacturers)
- Standards of buildings and facilities
- Obligation of QMS regulation compliance

License for Marketing
- GQP (Good Quality System)
- GVP (Good Vigilance Practice)

Marketing Approval
- Review of quality, efficacy and safety
- Compliance with QMS regulation on each manufacturing site

Application document

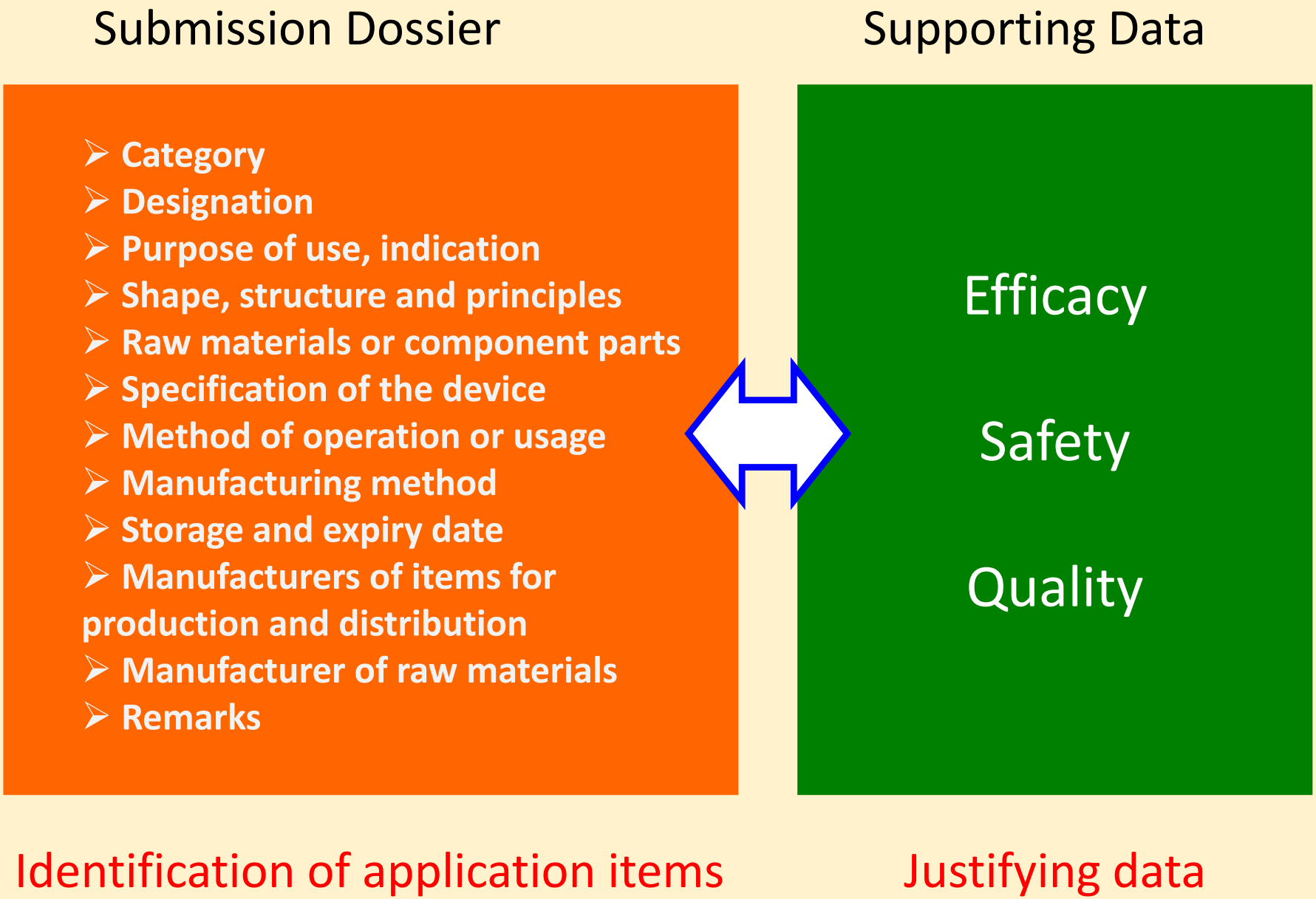
- Submission Dossier
- STED (*Summary Technical Documentation, GHTF SG1N11)
- Supporting Data
- Reference Data



Identification of application items

Justifying data

Submission Dossier and Supporting Data



Pre-market review

Essential Principles

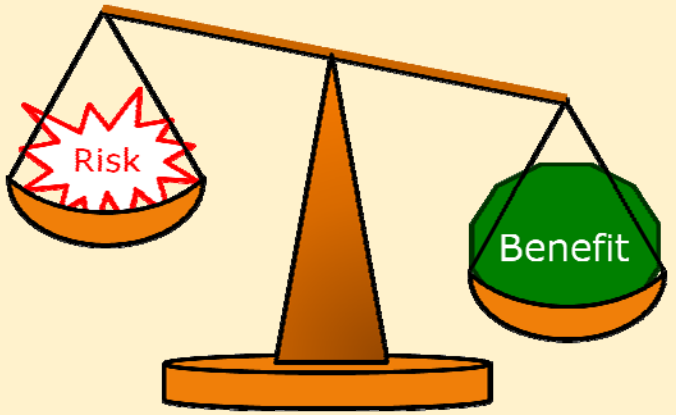
Conformity Assessment

- Standards
- Device Specification
- Design Control
- Design verification and validation
- Clinical Evidence
- STED
- Declaration of conformity

Risk < Benefit

Then,

On the Market



Approval/Certification Standards

Class	Japanese Medical Device Nomenclature (JMDN)
Class I	1,195
Class II	1,800
Class III	756
Class IV	343
Total	4,094

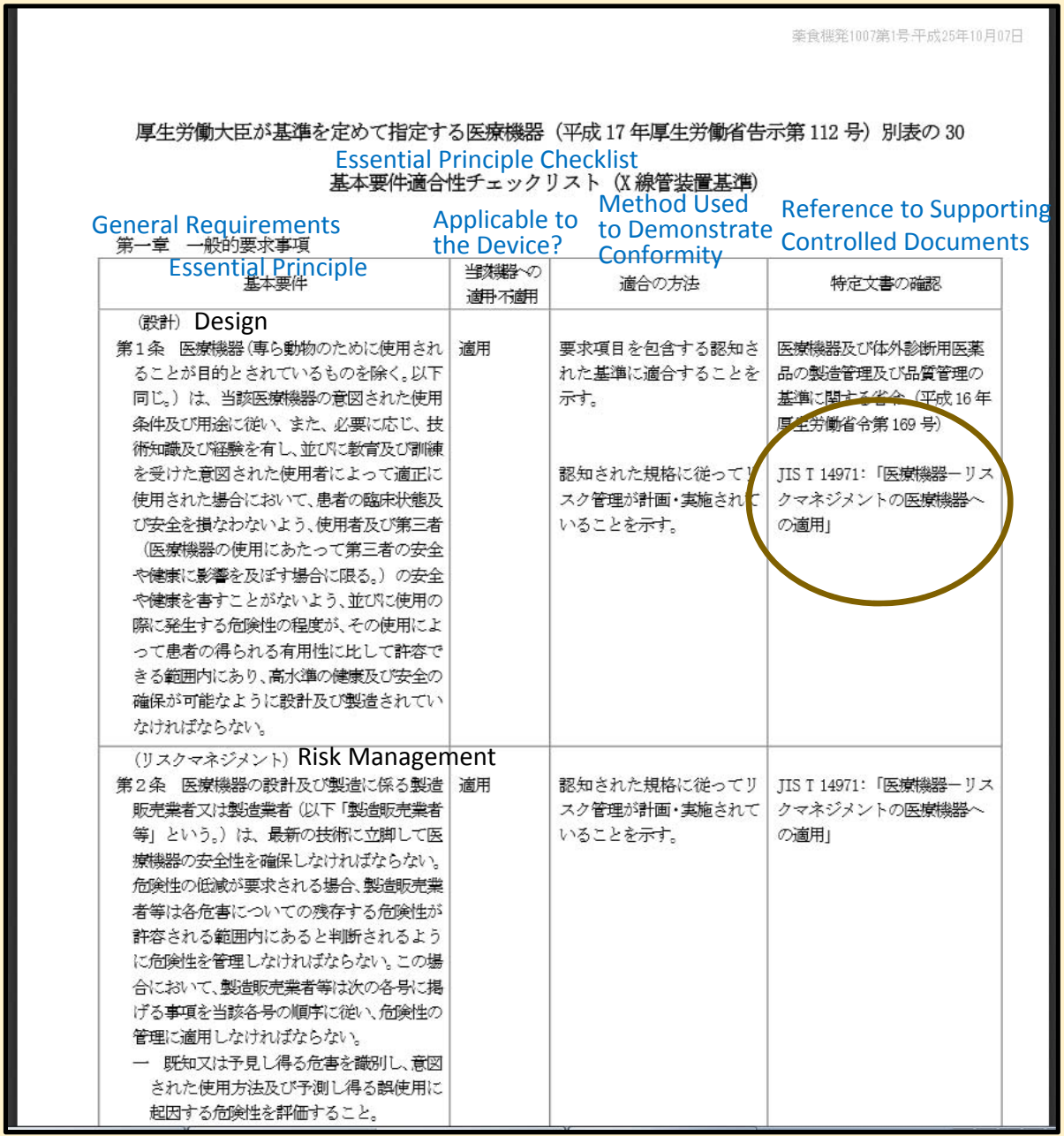
Certification Standards: 827 (JMDN: 1369)

Approval Standards: 44 (JMDN: 90)

As of February 21, 2014

Essential Principle Checklist for Approval/Certification Standards

- Clearly showing requirements for the products in individual standards
- JIS standards are referred but most JIS standards are basically harmonized with ISO, IEC etc standards
- Products which doesn't meet standards can be reviewed via other review process



薬食機発1007第1号 平成25年10月07日

厚生労働大臣が基準を定めて指定する医療機器（平成17年厚生労働省告示第112号）別表の30

Essential Principle Checklist

基本要件適合性チェックリスト（X線管装置基準）

General Requirements

第一章　一般的要求事項

Essential Principle 基本要件	Applicable to the Device? 当該機器への適用・不適用	Method Used to Demonstrate Conformity 適合の方法	Reference to Supporting Controlled Documents 特定文書の確認
（設計）Design 第１条　医療機器（専ら動物のために使用されることが目的とされているものを除く。以下同じ。）は、当該医療機器の意図された使用条件及び用途に従い、また、必要に応じ、技術知識及び経験を有し、並びに教育及び訓練を受けた意図された使用者によって適正に使用された場合において、患者の臨床状態及び安全を損なわないよう、使用者及び第三者（医療機器の使用にあたって第三者の安全や健康に影響を及ぼす場合に限る。）の安全や健康を害することがないよう、並びに使用の際に発生する危険性の程度が、その使用によって患者の得られる有用性に比して許容できる範囲内にあり、高水準の健康及び安全の確保が可能なように設計及び製造されていなければならない。	適用	要求項目を包含する認知された基準に適合することを示す。 認知された規格に従ってリスク管理が計画・実施されていることを示す。	医療機器及び体外診断用医薬品の製造管理及び品質管理の基準に関する省令（平成16年厚生労働省令第169号） JIS T 14971：「医療機器－リスクマネジメントの医療機器への適用」
（リスクマネジメント）Risk Management 第２条　医療機器の設計及び製造に係る製造販売業者又は製造業者（以下「製造販売業者等」という。）は、最新の技術に立脚して医療機器の安全性を確保しなければならない。危険性の低減が要求される場合、製造販売業者等は各危害についての残存する危険性が許容される範囲内にあると判断されるように危険性を管理しなければならない。この場合において、製造販売業者等は次の各号に掲げる事項を当該各号の順序に従い、危険性の管理に適用しなければならない。 一　既知又は予見し得る危害を識別し、意図された使用方法及び予測し得る誤使用に起因する危険性を評価すること。	適用	認知された規格に従ってリスク管理が計画・実施されていることを示す。	JIS T 14971：「医療機器－リスクマネジメントの医療機器への適用」

Acceptance of Foreign Clinical Data

- MHLW/PMDA have accepted foreign clinical data for years if it is good enough to evaluate a device's clinical safety and efficacy on Japanese population under Japanese medical practice/environment.

Number of devices approved after review with clinical trial data

	FY2009	FY2010	FY2011	FY2012	FY2013
Foreign clinical study results	32	29	38	23	34
Domestic and foreign clinical study results	6	2	5	3	8
Domestic clinical study results	14	19	14	23	24

*Source: PMDA annual report FY2013.

Action Program for Acceleration of Medical Device Reviews (issued in Dec. 2008)

MHLW / PMDA will accelerate the Medical Device review processes and reduce total review time* for approval,

- **on the premise of ensuring quality, efficacy, and safety of medical devices**
- **paying due consideration to minimize burdens to applicants**
- **under combined efforts by both the regulatory side and the applicants side**
- **by taking scientific and reasonable measures**

(* Total elapsed time from submission to approval)

Action program for Acceleration of Medical Device Reviews

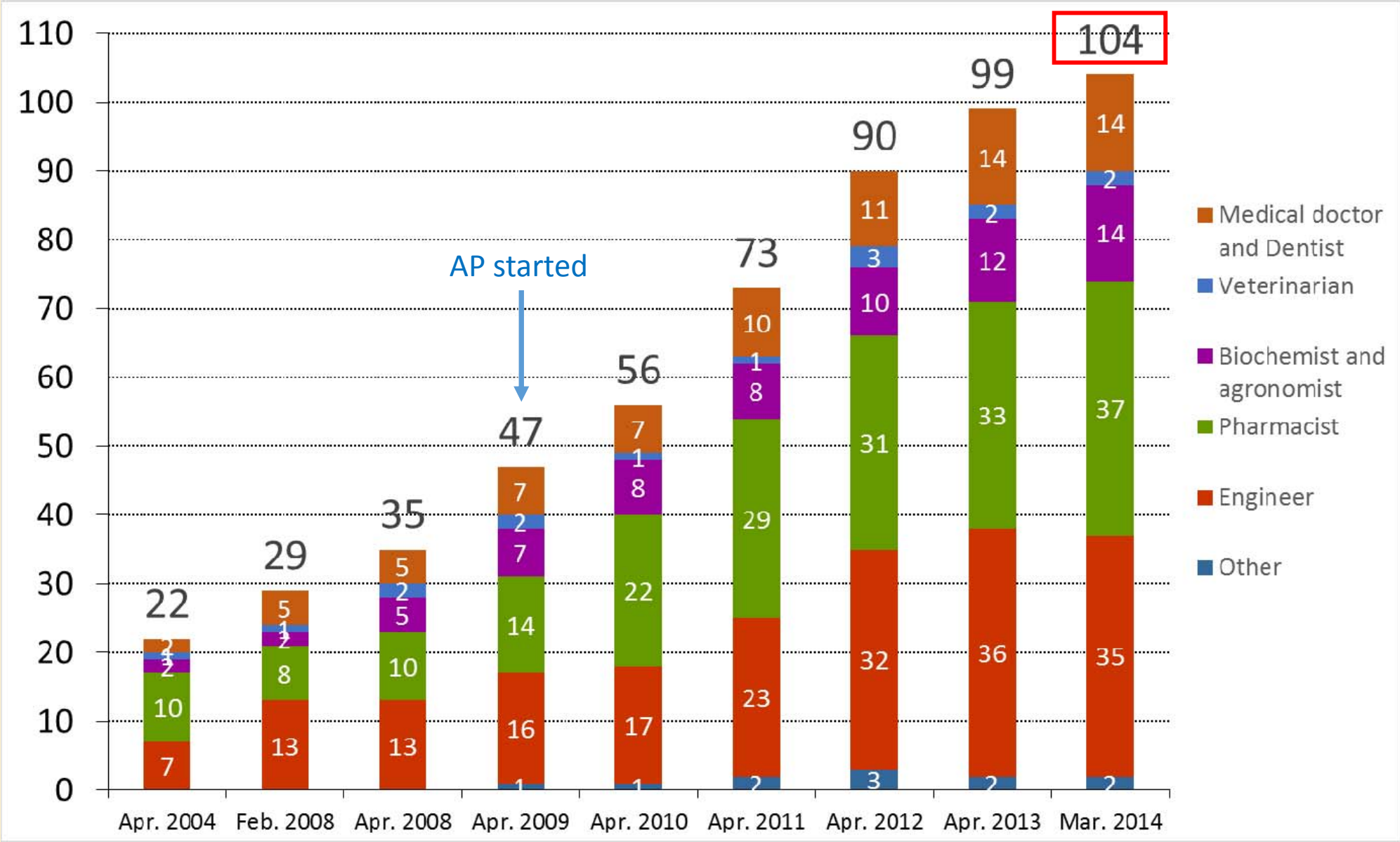
	FY2009	FY2010	FY2011	FY2012	FY2013
Improve quality by increasing the number of staff and enhancing training	Increase staff 35 → 104 (FY2013)				
Introduce 3-Track system			3-track Review System		
Clarify review criteria	Formulate Approval standards/ Good Review Guideline				
Set review time goals	•New Medical Devices (Standard 14 mos. Priority 10 mos.) •Improved MD with clinical data: 10 mos. w/o clinical data: 6 mos. •Generic MD 4 mos. (FY2013)				
Full transition to Third-party Certificate of class Ⅱ Medical Devices	Transit by FY2011				
Progress management	Government & Industry Dialogue 2/year（from FY2009）				

Performance Goal of the Time Period of Review

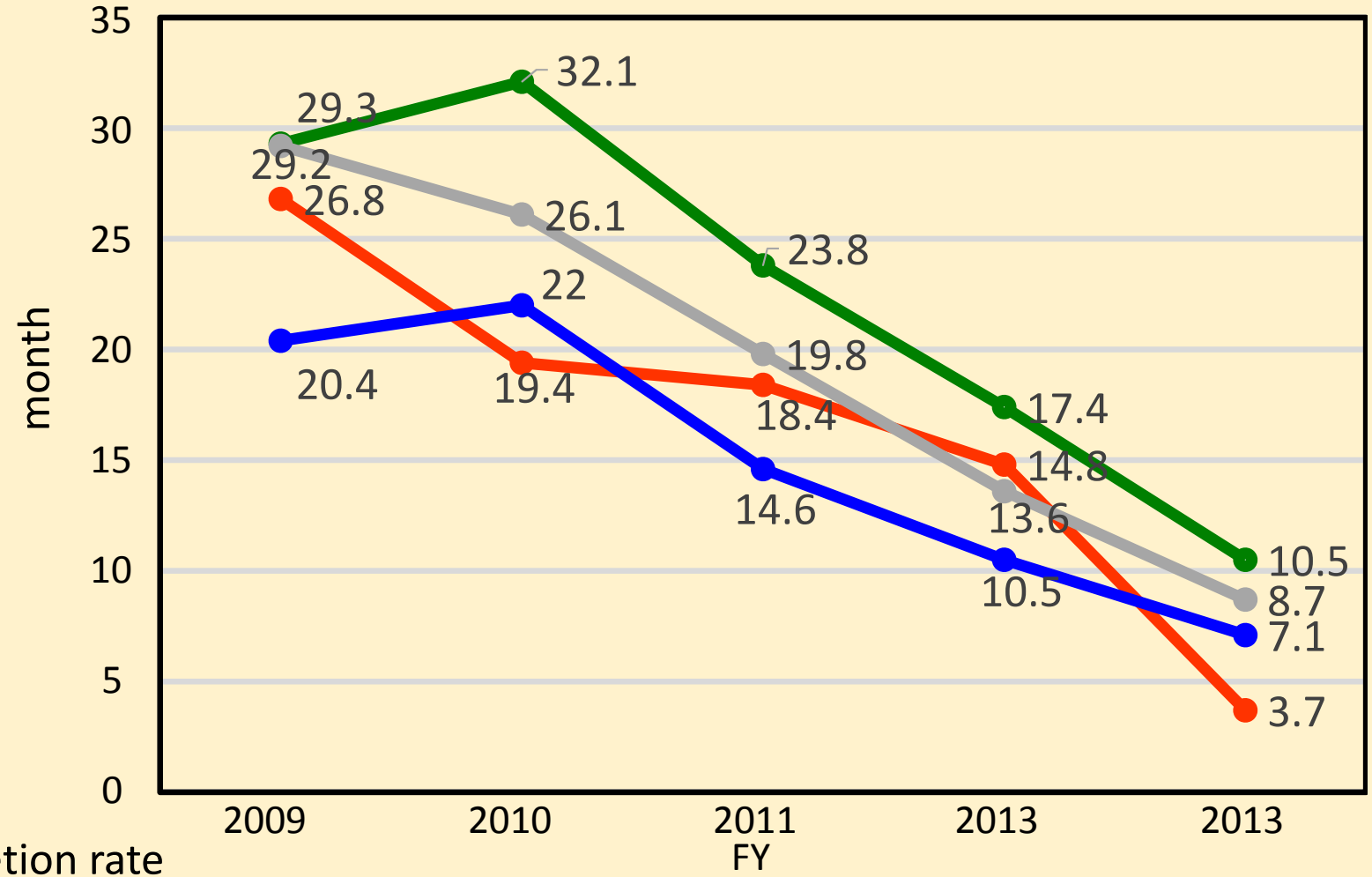
With combined efforts by both regulatory & applicants, total review time should be reduced to the below goal:

Performance Goal: total review time (median, unit: months)			~ FY2008	FY2009	FY2010	FY2011	FY2012	FY2013
New MD (Shin)	Standard items	total time	~ 21	21	21	20	17	14
		for agency	~ 8	8	8	8	7	7
		for applicant	~ 14	14	14	12	10	7
	Priority items	total time	~ 16	16	16	15	13	10
		for agency	~ 9	8	8	7	7	6
		for applicant	~ 9	9	9	8	6	4
Improved MD (Kairyo)	with clinical data	total time	~ 16	16	16	14	12	10
		for agency	~ 9	8	8	7	7	6
		for applicant	~ 7	7	7	6	5	4
	w/o clinical data	total time	~ 11	11	11	10	9	6
		for agency	~ 6	6	6	6	5	4
		for applicant	~ 5	5	5	5	4	2
Generic MD (Kohatsu) (with specific criteria)		total time	~ 8	8	6	5	4	4
		for agency	~ 5	5	4	4	3	3
		for applicant	~ 3	3	2	1	1	1

Quantitative Increase and Background of Medical Device Reviewers



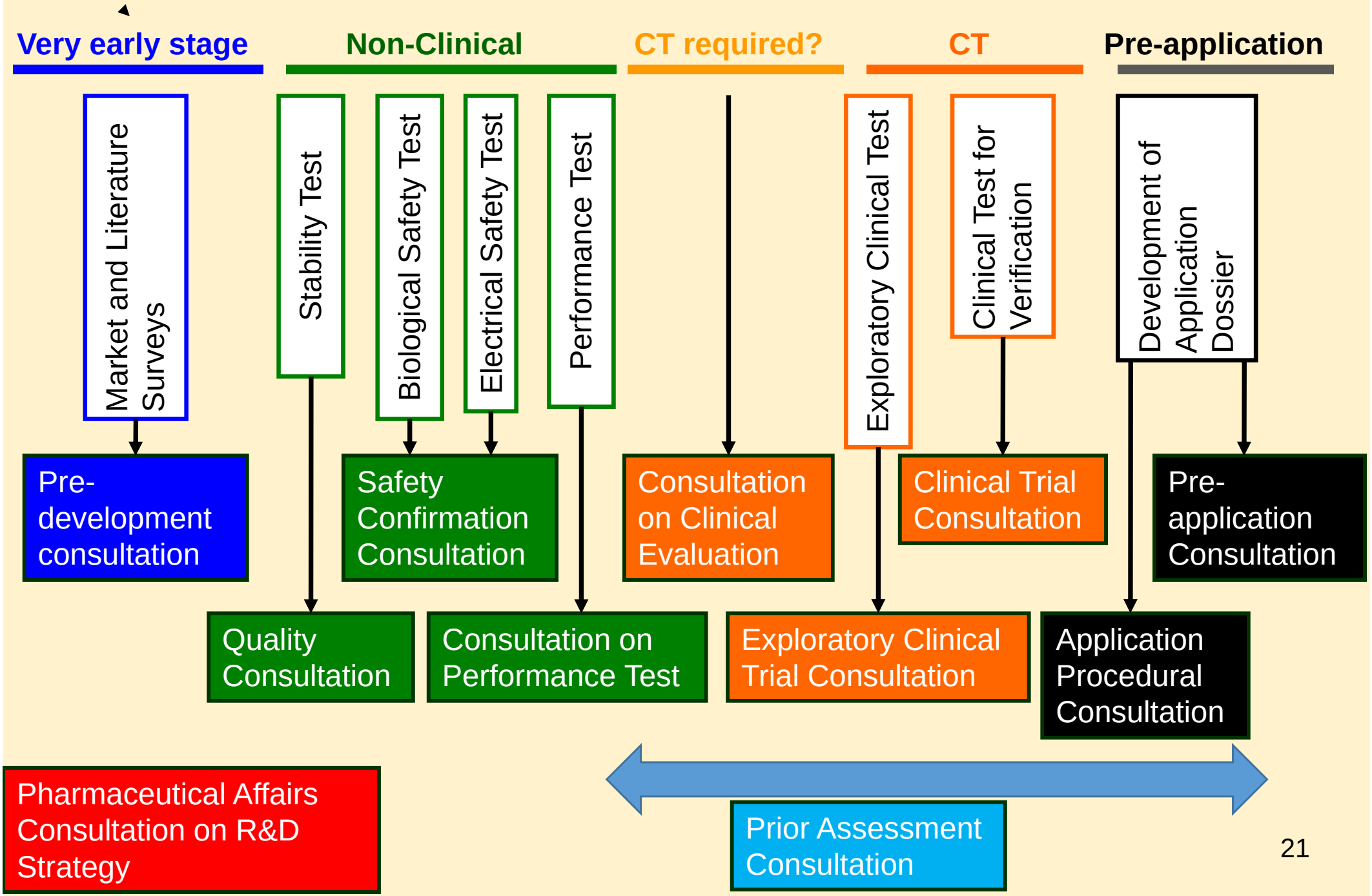
90% Tile Review Times for Medical Devices
(Total time in submission cohort)



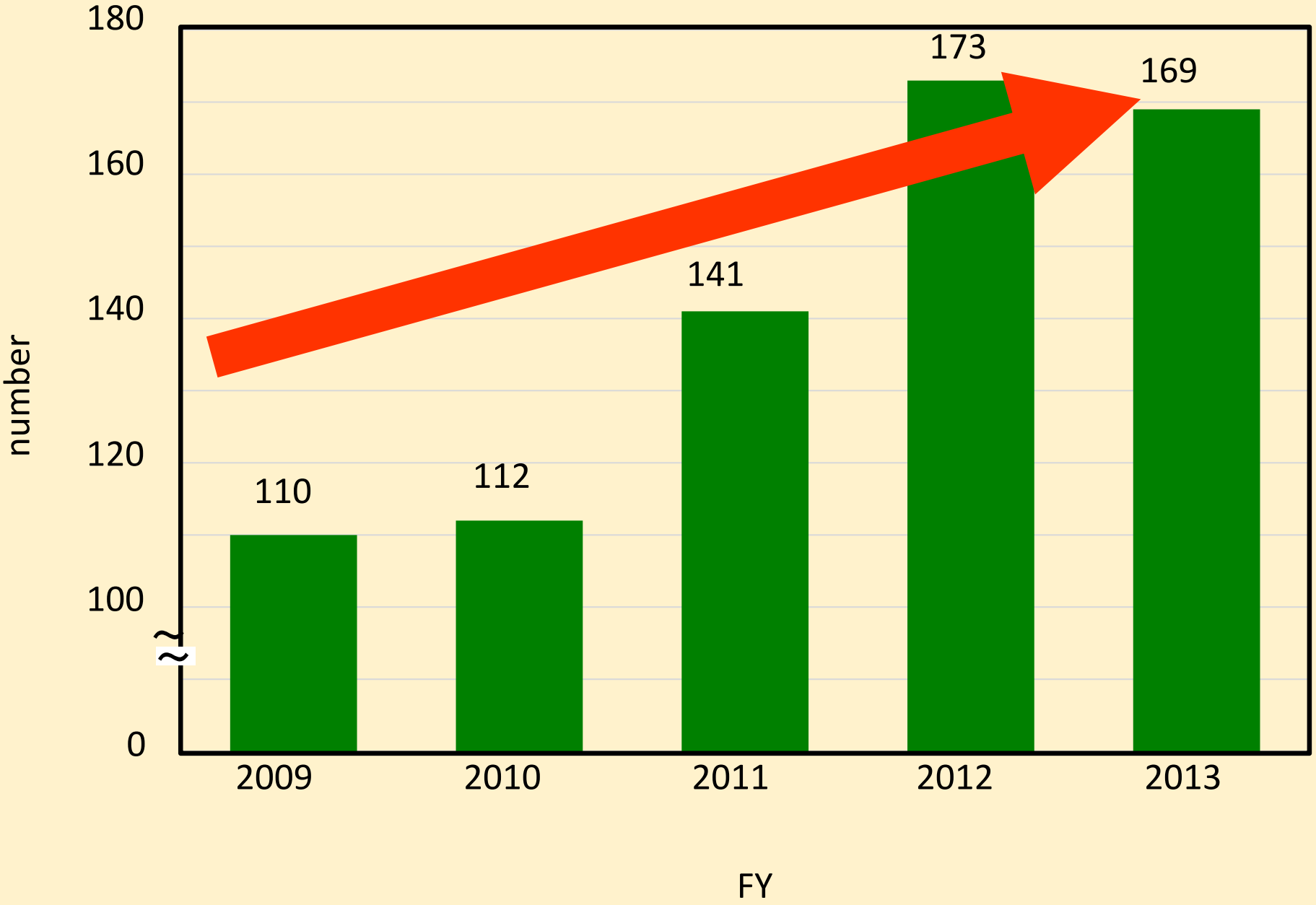
Completion rate

Category	FY	2009	2010	2011	2012	2013
New		100%	92.0%	95.2%	96.3%	46.9%
Improved (w clinical data)		100%	96.1%	96.0%	100%	75.0%
Improved (w/o clinical data)		100%	95.7%	94.2%	88.9%	44.8%
Generic		98.4%	96.2%	97.2%	95.6%	63.9%

PMDA's Consultation Menu



Number of consultations for Medical Devices



Collaboration Plan for Acceleration of Medical Device Review（FY2014～FY2018）

（issued on Mar. 31, 2014）

Quality concerns in the review process of medical devices need to be improved by both administration and applicants, and both parties should work together towards the following measures to further shorten the period required for approval of medical devices and to promote standardization.

1. Initiatives for quality enhancement during review process
2. Establishment of regular review periods
3. Progress management, etc.

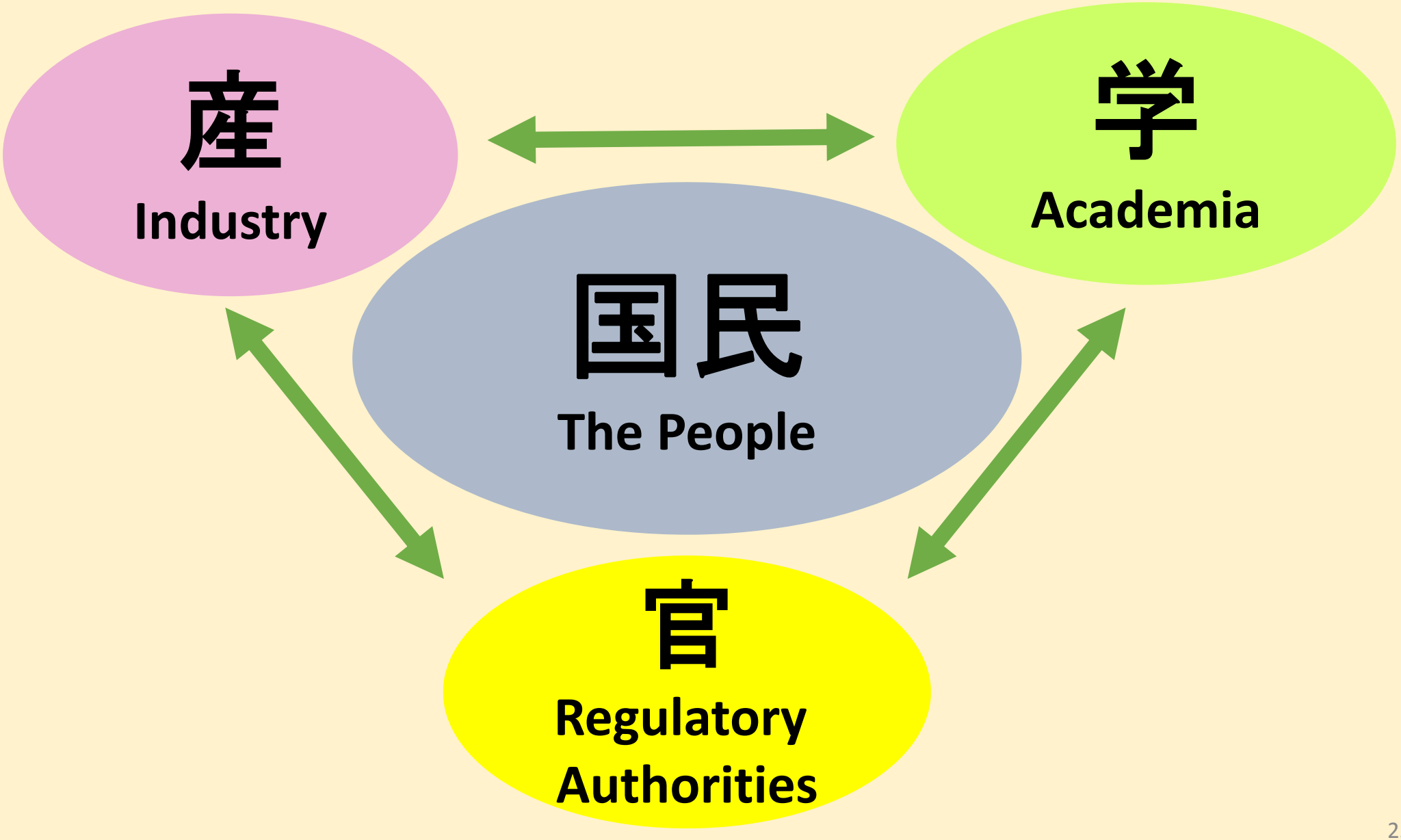
New Performance Goal towards FY2018*

(Total Time)

- New Medical Device
  - Standard items: 12 months
  - Priority items: 9 months
- Improved Medical Device
  - With clinical data: 9 months
  - Without clinical data: 7 months
- Generic Medical Device
  - New application: 5 months
  - Partial change application: 4 months

* In order to set higher target, 80 percentile figures are adopted instead of median

Industry-Government-Academia: National Obligation and Accountable Collaboration



IMDRF

IMDRF International Medical Device Regulators Forum

International Medical Device Regulators Forum

Established in October 2011

Management Committee member

Founding member of GHTF

Brazil China Russia

World Health Organization

APEC Asia-Pacific Economic Cooperation

Life Science Innovation Forum

AHWP Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

Pan American Health Organization
Regional Office of the World Health Organization

2nd PMDA MD training seminar
(regulators only)

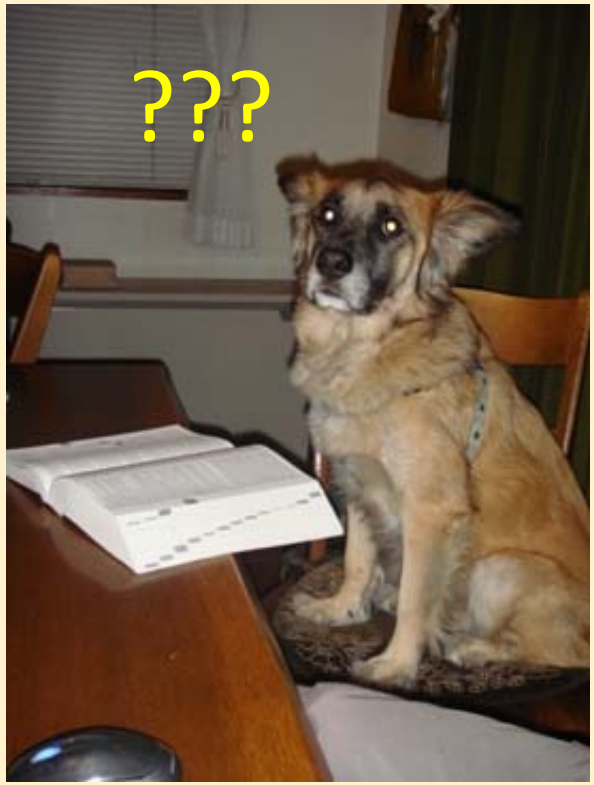
- Date: February 2 – 6, 2015
- Venue: PMDA (Tokyo, JAPAN)
- Fee: Free
- Topics
  - ✓Pre-market review
  - ✓QMS
  - ✓Clinical trials
  - ✓Case study
  - ✓Post-market surveillance system
  - ✓Facility Tour

1st PMDA MD Training Seminar 2014

Make it GLOBAL

(Win-Win Relationship)

Any questions?



Contact Information
URL: http://www.pmda.go.jp/english/contact/index.html

Thank you!!

Pharmaceuticals and Medical Devices Agency

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