IT'S TIME TO GO TO JAPAN !

THE JAPANESE REGULATORY AND MARKET ACCESS ENVIRONMENT

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Shogo NAKAMORI

PAREXEL International

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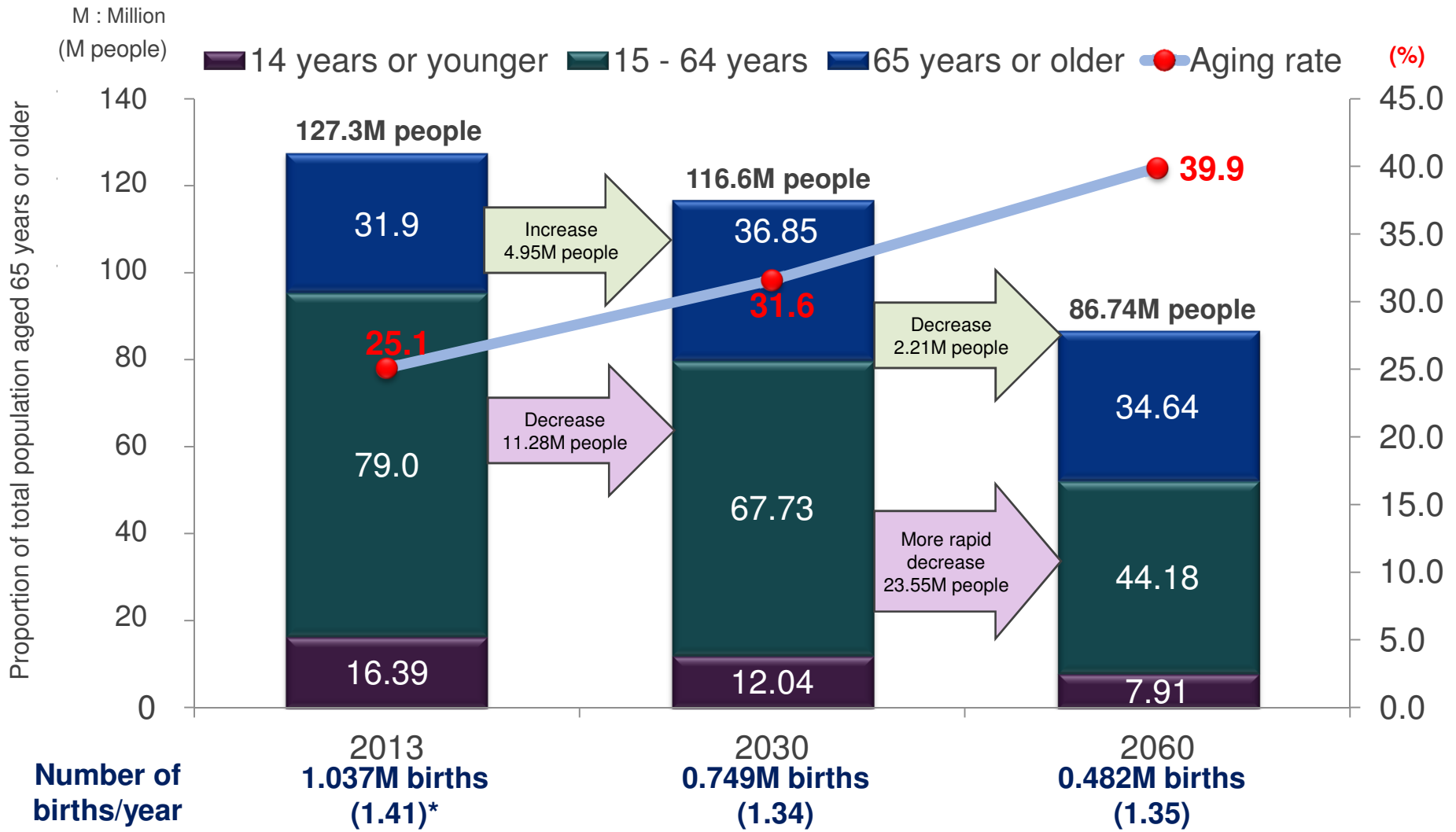
SUDDEN CHANGES IN POPULATION COMPOSITION

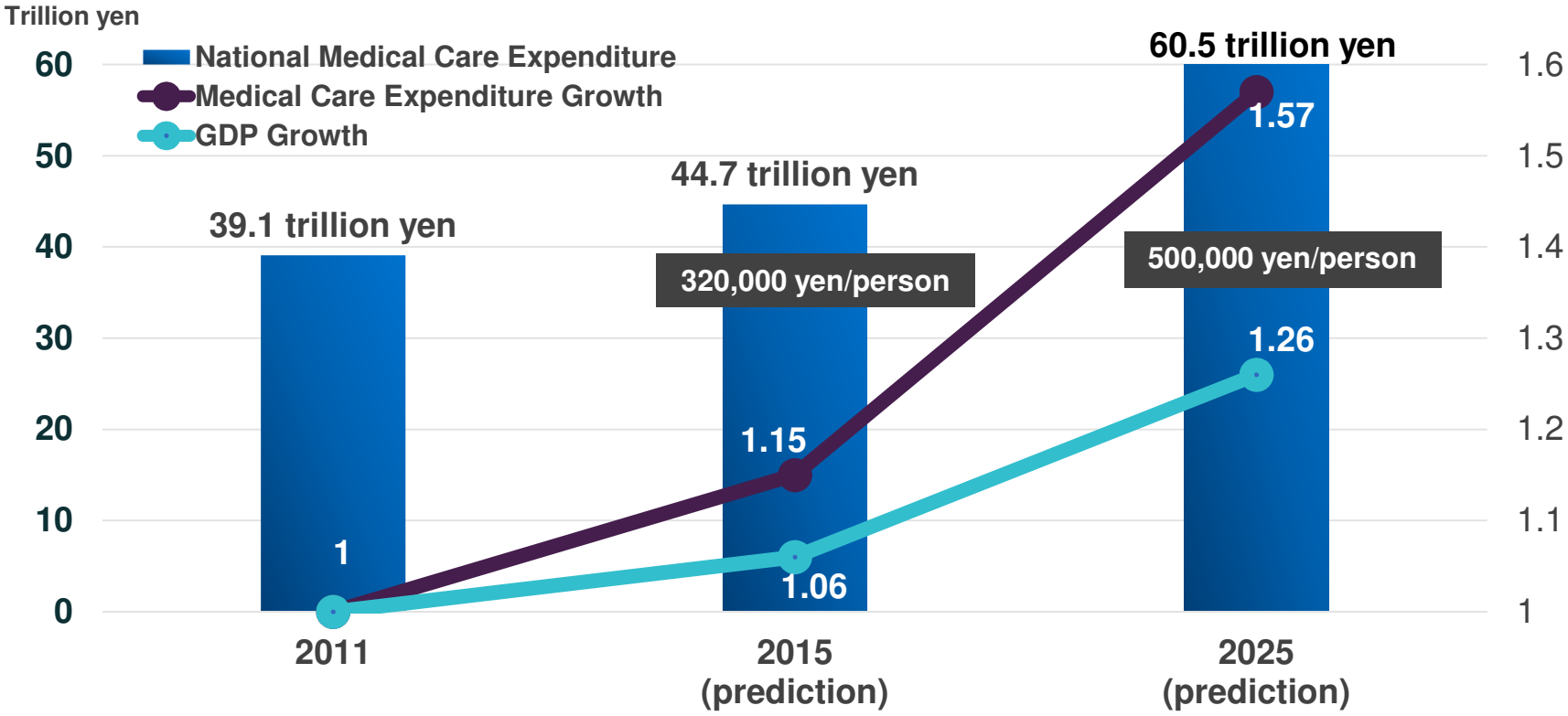


In 2060, 1.3 people will support each elderly person

Source: Ministry of Internal Affairs and Communications "National Census" National Institute of Population and Social Security Research "Population Projection for Japan (January 2012 estimate (median birth/median death estimates" (Current population for October 1 each year)
*Ministry of Health, Labour and Welfare "Demographic Statistics" *1 Source: 2012 Annual Demographic Statistics*

NATIONAL MEDICAL CARE EXPENDITURE FORECASTS

Issue for 2025: All members of the baby boomer generation (born 1947–51) will be "latter-stage elderly" aged 75 years or older (18% of overall) and annual medical care expenditure will reach 920,000 yen.



*Source: *1: Created from future estimate backup data released as documents at an intensive review meeting held on June 2, 2011 regarding social security reform*
**2: Medical Care Expenditure and GDP growth are shown as versus 2011. Source: documents created by the Ministry of Health, Labour and Welfare*

REGULATORY AUTHORITIES IN JAPAN

MHLW

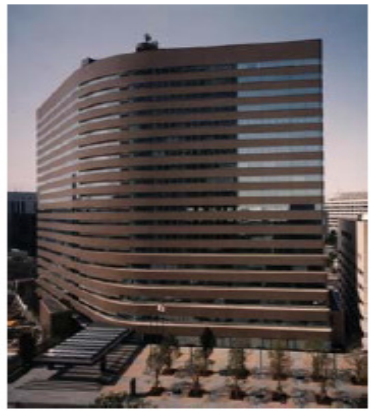
Pharmaceutical and Food Safety Bureau, MHLW

- **Final authorization of applications**
- **Publishing Guidelines**
- **Advisory Committee**
- **Supervising PMDA activities**

PMDA

Pharmaceuticals and Medical Devices Agency

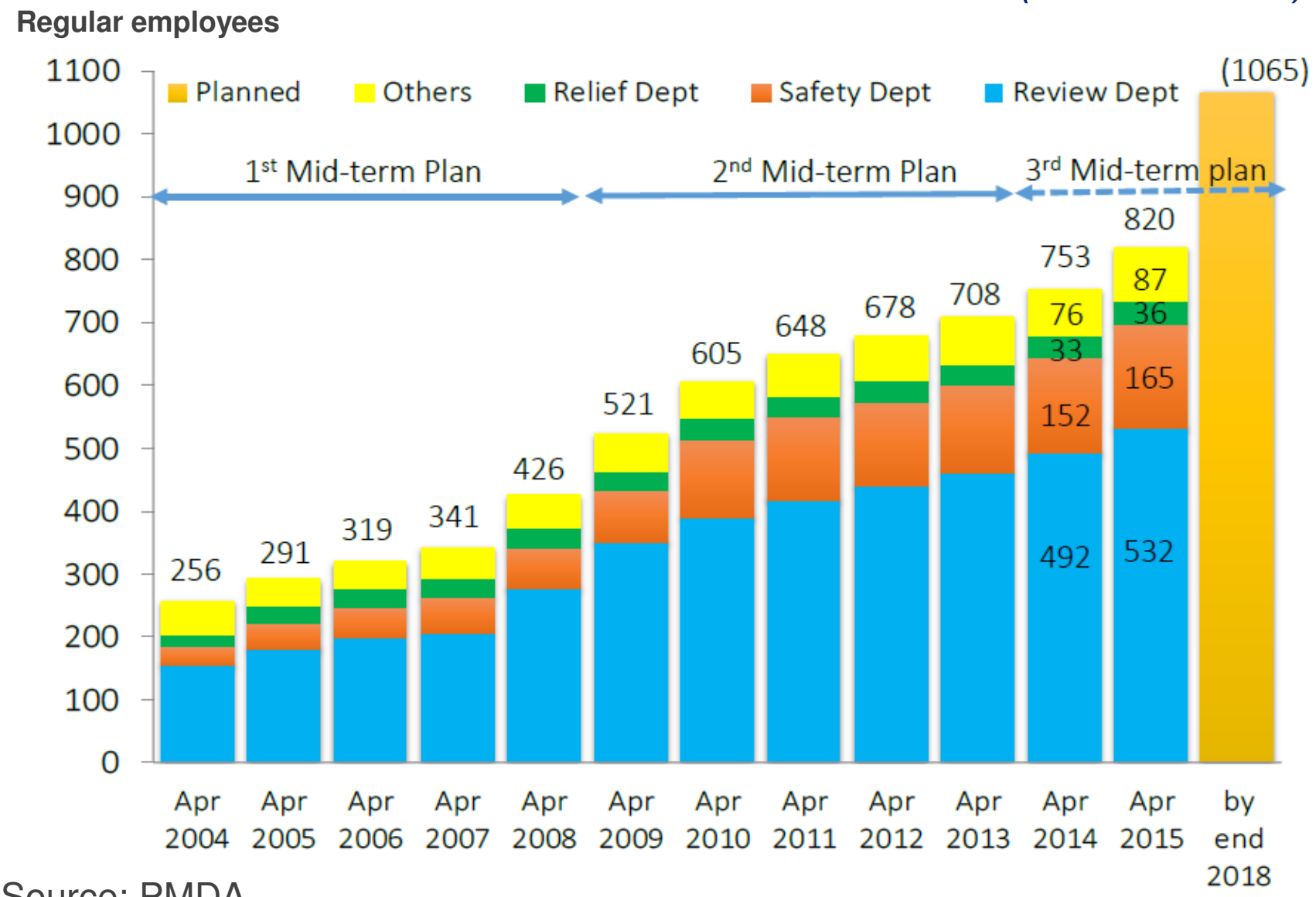
- **Scientific Review for Drugs & Medical Devices**
- **GCP, GMP inspection**
- **Consultation on Clinical Trials etc.**



RECOMMENDED SEQUENCE OF STEPS TO REACH THE JAPANESE MARKET

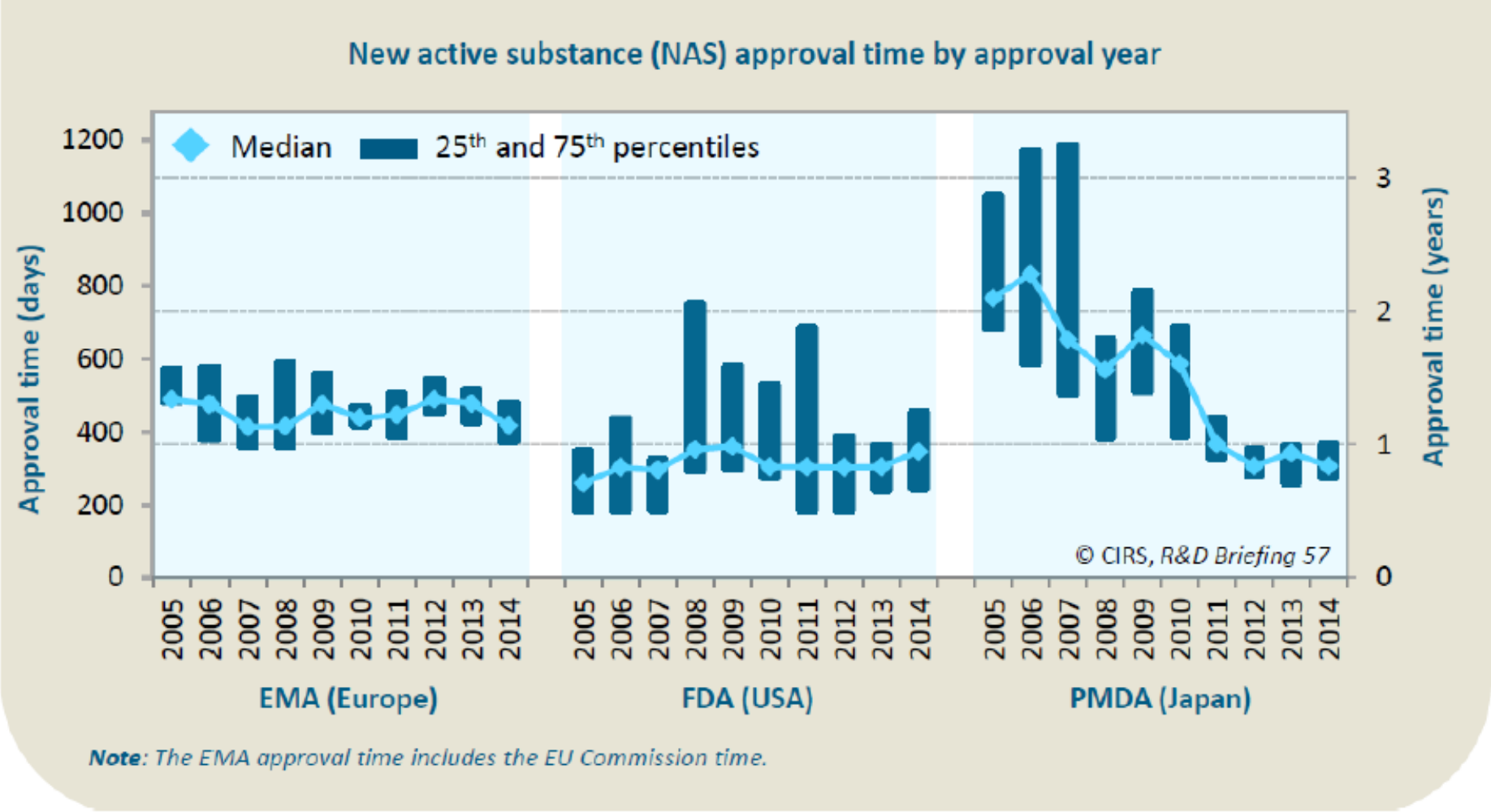
ACTION	PURPOSE
1. Key Opinion Leader (KOL) Interviews	Define unmet medical need; obtain support
2. Pre-Consultation Meeting with PMDA	Set stage for consultation and questions/discussions
3. Consultation Meeting with PMDA (clinical; may also need CMC or others)	Obtain consensus on registration strategy and required studies
4. Clinical Trial Notification (CTN)	Approval to conduct studies
5. Orphan Drug Designation Application (if appropriate)	Obtain ODD and Priority Review status; consider grant application
6. Clinical Trials	Collect clinical evidence in Japanese patients
7. Pre-JNDA Consultation with PMDA	Set stage for JNDA approval
8. JNDA Submission (by local MAH holding a Marketing Business License)	Obtain marketing approval
9. Pricing dossier	Negotiate price and reimbursement

RAPID INCREASE IN PMDA REVIEW STAFF REFLECTS INTEREST IN INDUSTRY CONSULTATIONS (400+/YEAR)



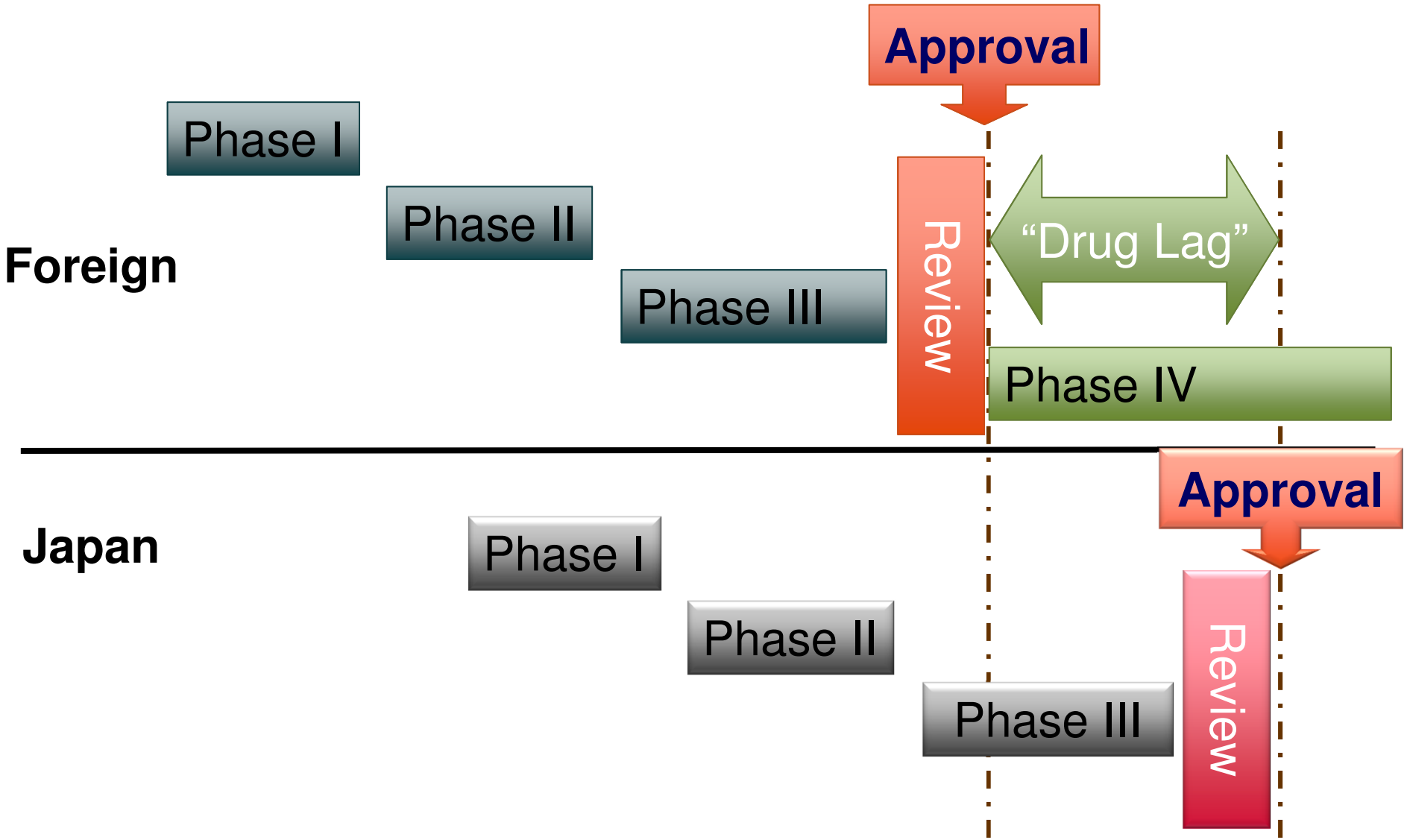
Source: PMDA

NEW DRUG APPROVALS IN ICH COUNTRIES 2005-2014: JAPAN IS NOW ON PAR WITH EMA AND FDA

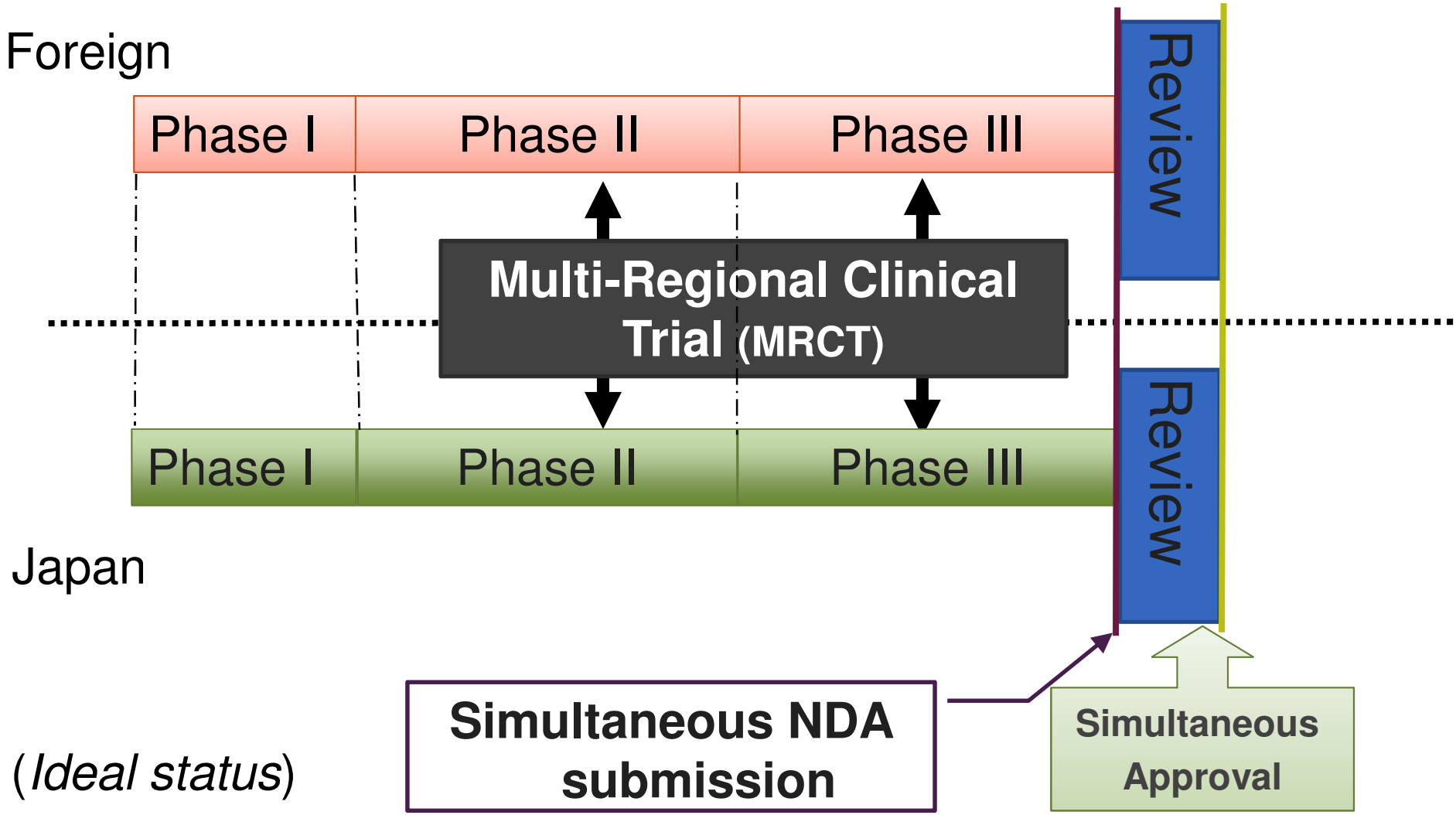


Source: R&D Briefing 57, July 2015, Centre for Innovation in Regulatory Science Ltd.

JAPAN HAS SUFFERED FROM A "DRUG LAG" : TRADITIONAL STANDALONE CLINICAL MODEL



ELIMINATING THE DRUG LAG: GLOBAL SIMULTANEOUS CLINICAL DEVELOPMENT MODEL



(*Ideal status*)

JAPAN-APPROVED NEW DRUGS BASED ON GLOBAL CLINICAL TRIALS THAT INCLUDE JAPANESE PATIENTS

2006～2009	2010	2011	2012	2012	2013	2014
Tolterodine	Peramivir	Dabigatran	Denosumab	Insulin - Degludec	Paclitaxel	Riociguat
Losartan	Everolimus	Trastuzumab	Aripiprazole	Glycopyrronium	Pregabalin	Tadalafil
Trastuzumab	Panitumumab	Pramipexole	Olanzapine	Pazopanib	Tofacitinib	Afatinib
Insulin - Glulisine	Travoprost/ Timolol	Edoxaban	Exenatide	Everolimus	Regorafenib	Turoctocog alfa
Tadalafil	Temsirolimus	Dasatinib	Crizotinib	Fesoterodine	Bevacizumab	Ranibizumab
	Laninamivir	Indacaterol	Budesonide/ Formoterol	Everolimus	Pertuzumab	
	Nilotinib	Linagliptin	Esomeprazole	Apixaban	Lixisenatide	
		Gefitinib	Formoterol	Insulin-Degludec+Aspart	Regorafenib	
		Everolimus	Axitinib		Indacaterol/ Glycopyrronium	
			Budesonide/ Formoterol		Paliperidone	
			Atomoxetine		Vilanterol/ Fluticasone	
			Aflibercept		Bevacizumab	
					Aflibercept	

Red: Asian Clinical Trial

Guidance: “Basic Principles on Global Clinical Trials”

Guidance RC: “Basic Principles on Global Clinical Trials –Reference Cases”

59 applications were approved as of March 1, 2014

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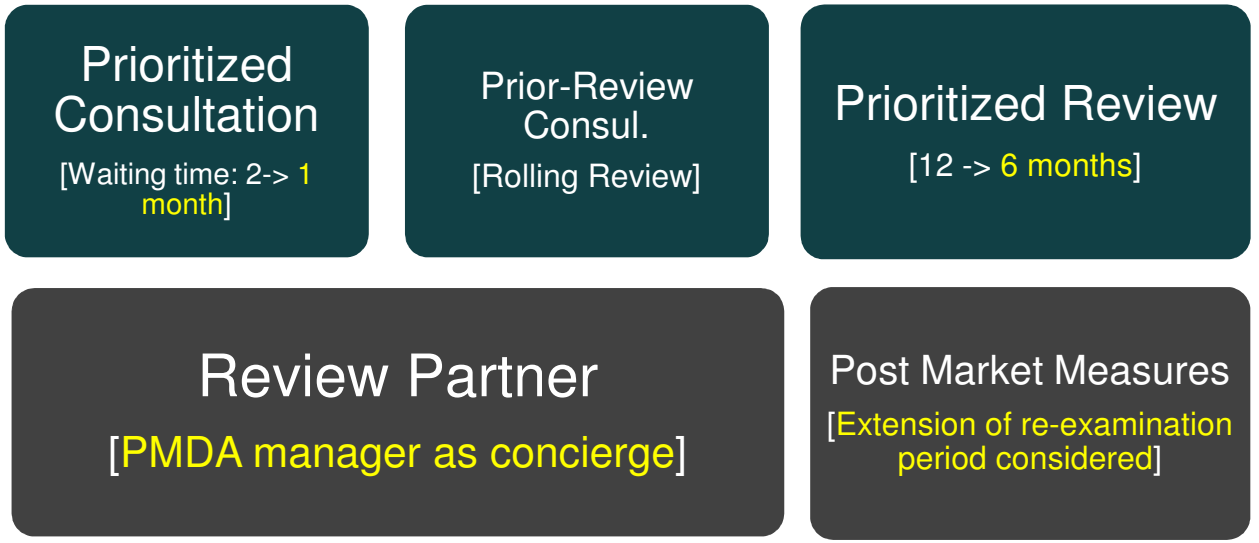
ACCELERATED PATHWAY FOR PRODUCT DEVELOPMENT: SAKIGAKE ("BREAKTHROUGH") FRAMEWORK

- **Criteria**
  - Medical products (drugs, devices, regenerative therapies) for diseases in dire need of innovative therapy
  - Applied for approval first in Japan or simultaneously in Japan and other countries
  - Prominent effectiveness can be expected based on non-clinical study and early phase of clinical trials

- **Advantages for Designated Products**



EVIDENCE OF JAPAN'S APPETITE FOR INNOVATION – DOMESTIC AND FOREIGN

- Investment in PMDA staffing
- Priority Review of J-NDAs available
- *Sakigake* framework for breakthrough products
- Orphan Drugs framework
- Reduced "drug lag"
- Regenerative Medicine Law
- 7 Biosimilars approved (vs 1 in US and 22 in EU)
- PMDA Outreach to Academic Scientists to promote innovation
- Creation of AMED (NIH-like Agency for Medical Research and Development)
- Premium prices granted to innovative medicines, including 10-20% premium pricing for *sakigake*

IT'S TIME TO GO TO JAPAN !

- Conditions in Japan are now favorable for:
  - ✓ Productive **early and direct communications** with Japanese Regulators and KOLs
  - ✓ **Inclusion of a subset of Japanese patients** in East Asian or global clinical studies as part of a global development program
  - ✓ Achievement of timely **registration** (comparable timelines to FDA and EMA) for NMEs, biosimilars and generics
  - ✓ **Attractive pricing,** and premiums for innovative therapies – including *sakigake* products

BOSTON, MASSACHUSETTS

INTRODUCTION OF PAREXEL INTERNATIONAL

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FULL RANGE OF EXPERTISE

PAREXEL Clinical Research Services

- Early Phase Services
- Phase II-III Services
- Clinical Trial Supplies and Logistics
- Quantitative Clinical Development

PAREXEL Informatics

- Clinical Data Management (DataLabs® EDC)
- Randomization and Trial Supply Management (ClinPhone® RTSM)
- Electronic Patient-Reported Outcomes (ePRO)
- Perceptive MyTrials® Platform and Infrastructure
- Study Management and Monitoring (IMPACT® CTMS)
- Medical Imaging
- Regulatory Information Management (LIQUENT InSight®, LIQUENT SmartDesk™)

PAREXEL Consulting

- Regulatory Strategy and Operations
  - Regulatory Outsourcing Services
  - Integrated Product Development
- Strategic Compliance and Risk Management

PAREXEL Access

- Late Phase Interventional
- Observational Research
- Drug Safety
- Market Access Consulting
- Medical Communications

PAREXEL JAPAN OVERVIEW

Tokyo Office

Osaka Office

Kobe Office

- **Chairman and CEO：Josef H. von Rickenbach**
- **Established in 1995/7 and incorporated in 1997/10.**
- **General Manager：Shogo Nakamori**
- **More than 1,000 full-time employees.**
- **Office Locations：Tokyo, Osaka, Kobe**
- **Membership of professional institutions：**
  - Japan CRO Association Full Member
    - Shogo Nakamori is “Executive Director of JCROA”
  - Osaka Pharmaceutical Manufacturers Association (OPMA)

THANK YOU

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