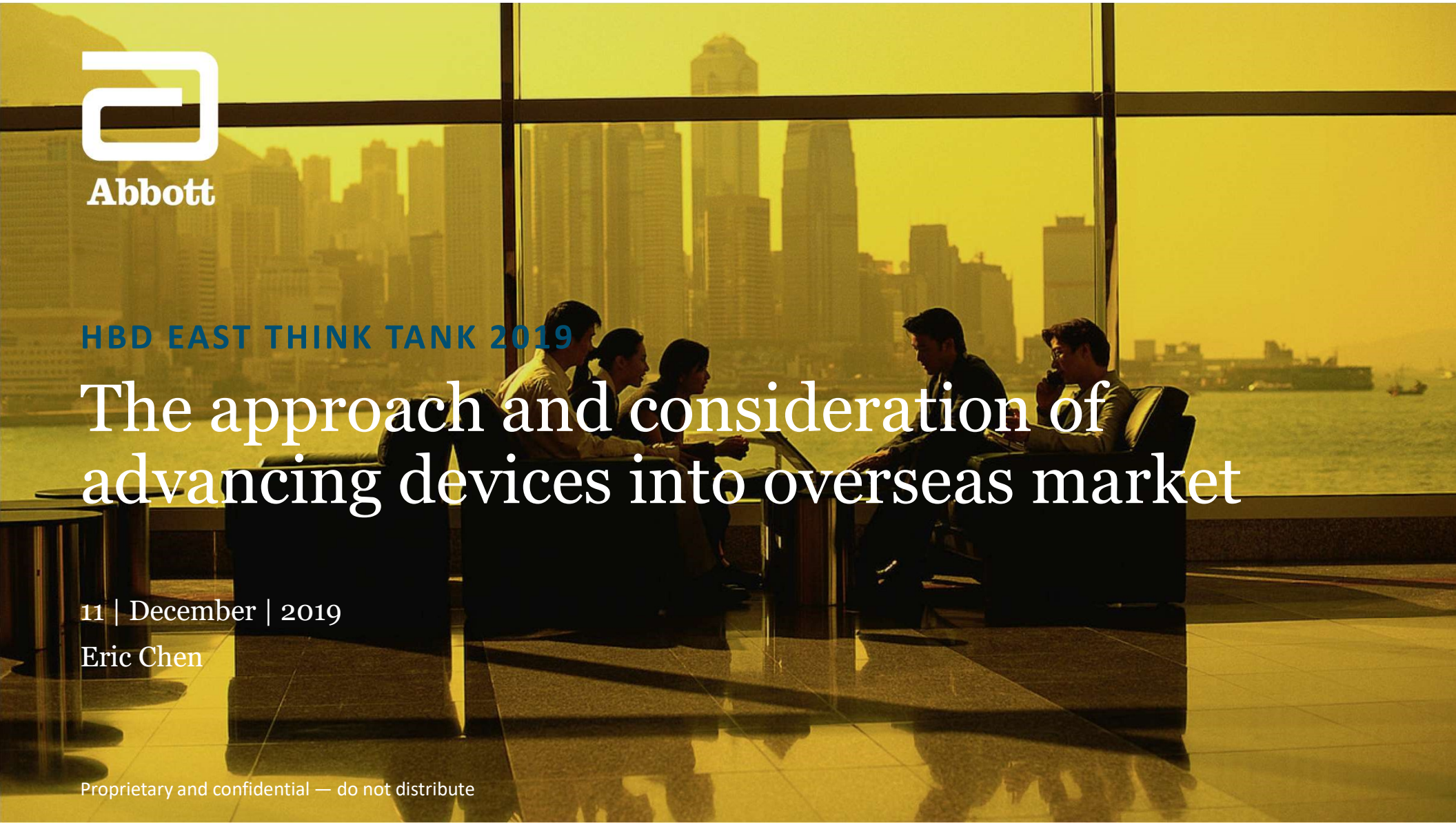


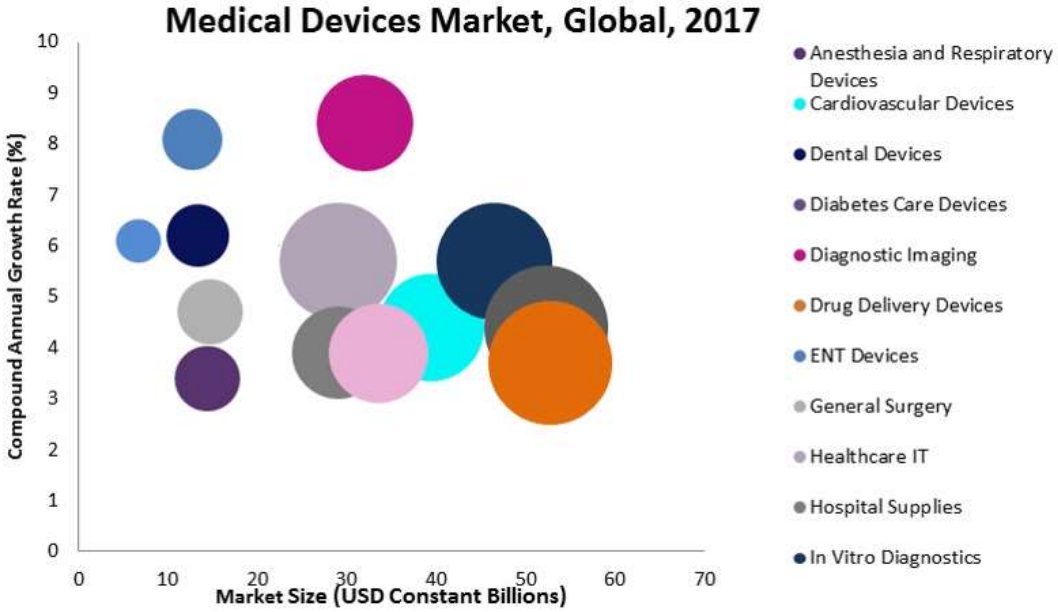
HBD EAST THINK TANK 2019

The approach and consideration of advancing devices into overseas market

11 | December | 2019

Eric Chen

GLOBAL MEDICAL DEVICE MARKET



https://www.medicaldevice-network.com/research-reports/researchreportrisking-health-for-profit-in-the-medical-devices-industry-5908091/

MEDICAL DEVICE DEVELOPMENT

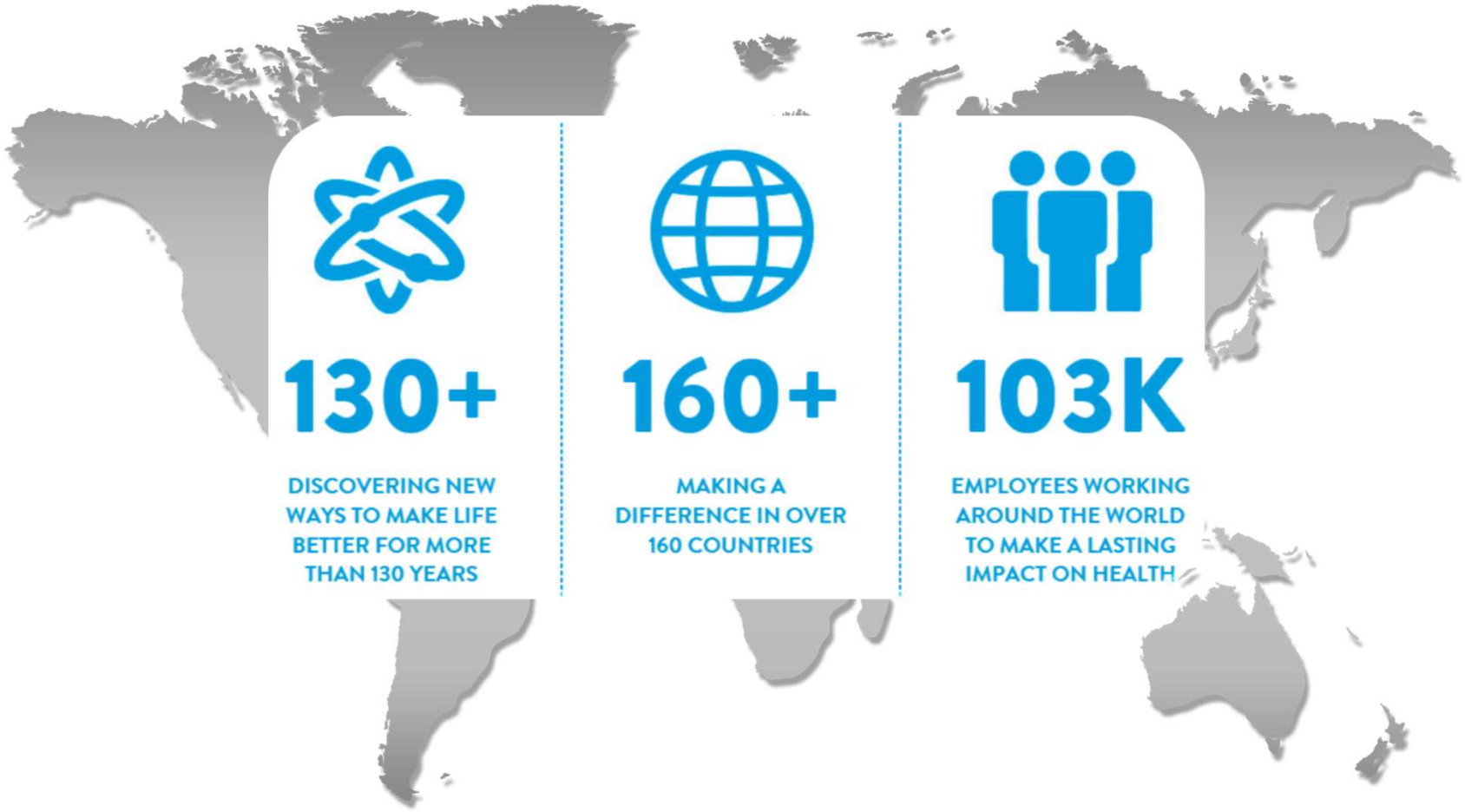
- Global medical device market size was valued at $425 Billion in 2018
- Expected to reach $612 Billion in 2025
- Initial clinical testing of novel medical device has been moving to non-US sites
- Device innovation may follow overseas
- Devices are being developed exclusively for non-US markets

Slide from Philippe Auclair

ABBOTT CREATES

…breakthrough products – in diagnostics, medical devices, nutrition and branded generic pharmaceuticals – that help you, your family and your community lead healthier lives, full of unlimited possibilities.

BROAD AND BALANCED GEOGRAPHIC PRESENCE



HISTORICAL DEVICE DEVELOPMENT PATTERN

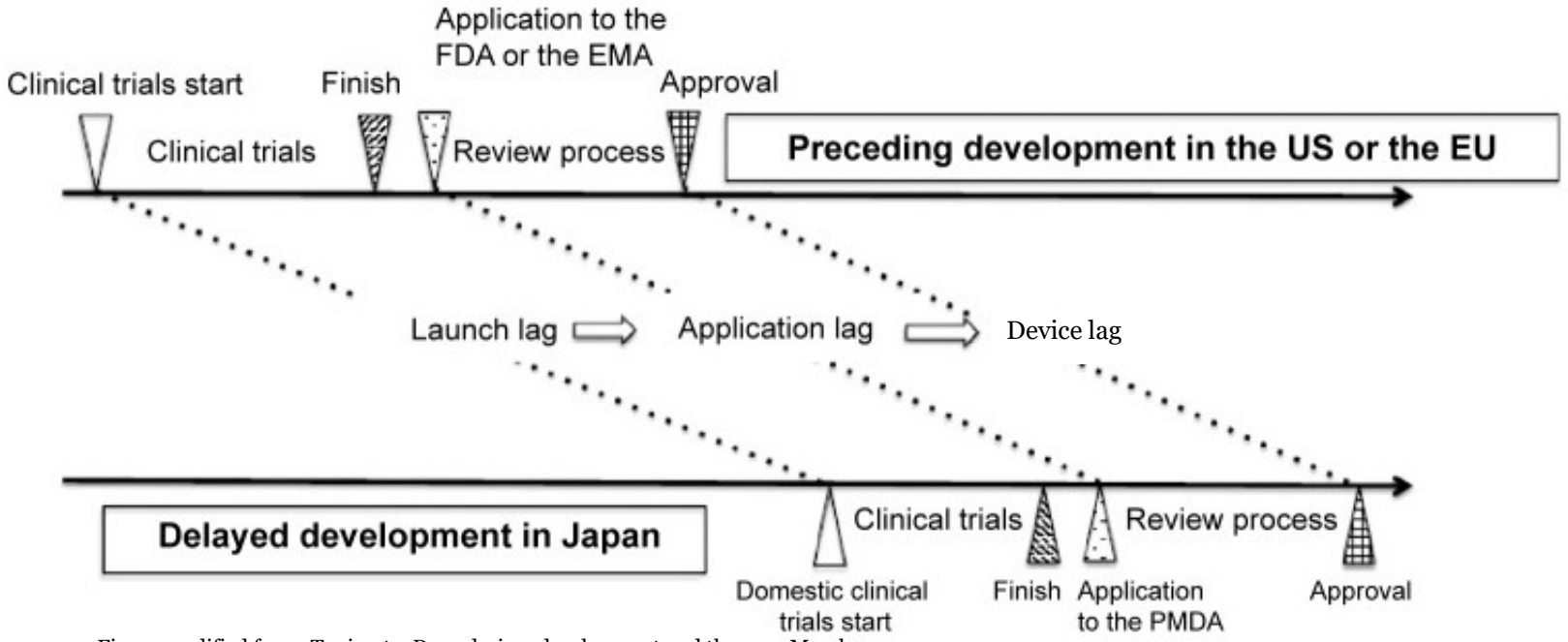
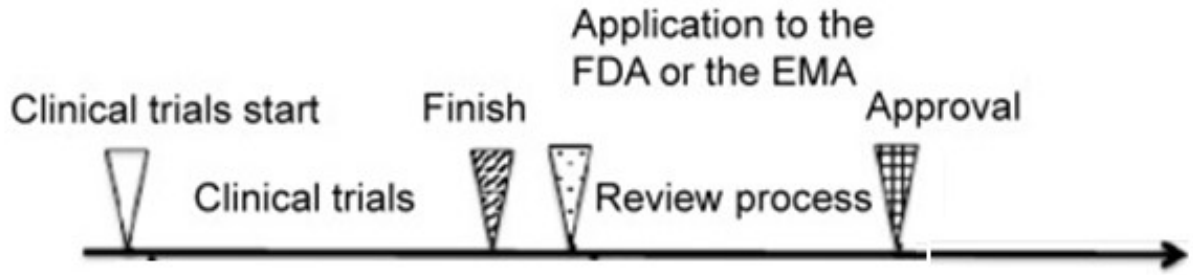


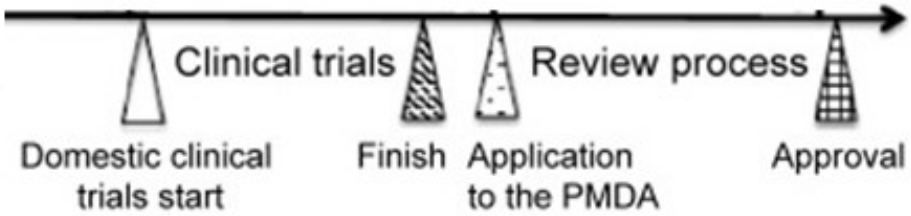
Figure modified from: Tanimoto, Drug design, development and therapy, March 31, 2015

Note: Not all devices have required domestic clinical trials in Japan

CURRENT DEVICE DEVELOPMENT PATTERN



PMDA initiatives have shortened the premarket evaluation such as Sakigake and Conditional Early Approval System

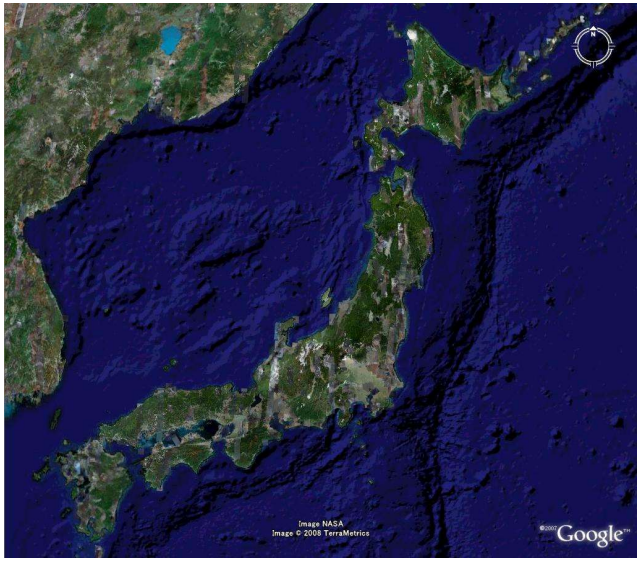


Note: Not all devices have required domestic clinical trials in Japan

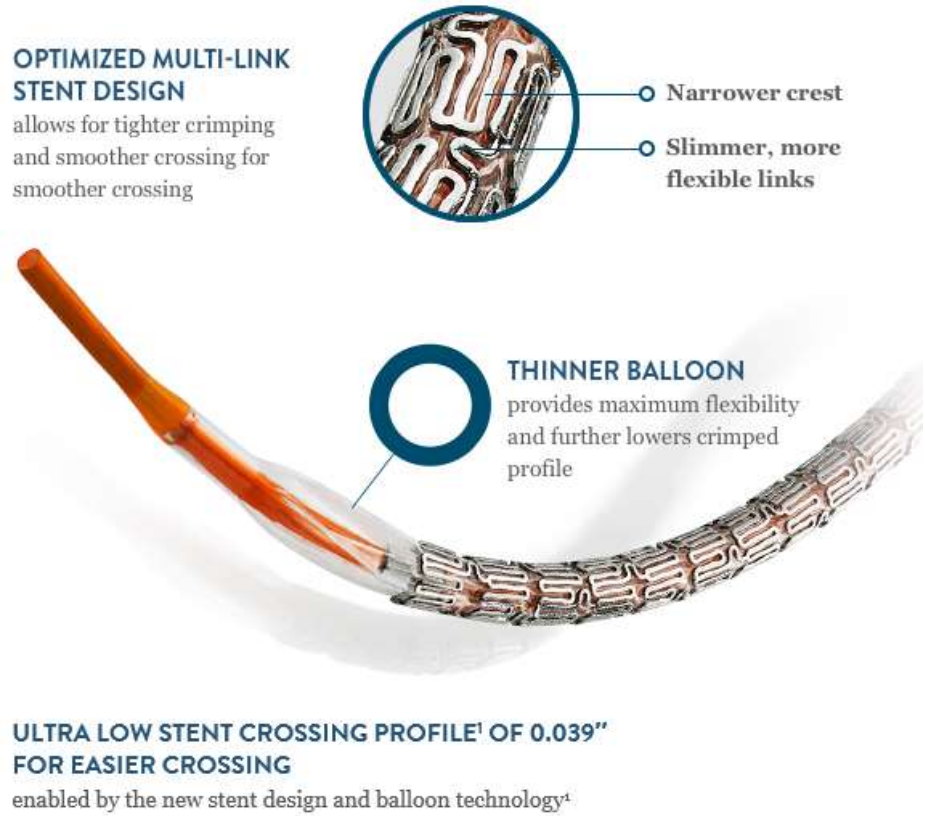
JAPAN

CURRENT AND FUTURE

- PMDA continues to improve the medical devices review process
  - Earlier submission opportunities
  - Faster review times (includes regulatory + applicant) – FY17 (April 2017-March 2018) for Shin, Kairyo, and Kohatsu
    - 8.3 total months for new medical devices with priority review (goal 10 months)
    - 11.9 total months for new medical devices with standard review (goal 14 months)
    - 8.8 total months for improved medical devices with clinical data (goal 10 months)
    - 5.8 total months for improved medical devices without clinical data (goal 6 months)
    - 3.6 total months for generic medical devices (goal 4 months)
  - Enhanced harmonization of clinical trial standards and review



ABBOTT XIENCE SIERRA STENT



BACKGROUND

- CE mark on October 2017
- FDA approval on May 2018
- **Approved in Japan on April 2018**
  - Total review time – 6 months
  - Supported by foreign and Japanese clinical study results
  - National reimbursement granted by MHLW on May 2, 2018

ABBOTT XIENCE XPEDITION 48mm STENT

BACKGROUND

- CE mark on May 2013
- Not FDA approved
- **Approved in Japan on April 2018**
  - Total review time – 8 months
  - Consultations with physicians, societies, and PMDA and MHLW prior to submission
  - Supported by foreign clinical study for the additional model

MARKET ACCESS FOR DEVICES

PREVAILING CURRENTS

- Market access for medical device manufacturers is more difficult than ever
- New global compliance requirements and payer demands compel companies to be good communicators
- Overcoming obstacles
  - Plan ahead for clinical studies
  - Collaborate with industry influencers
  - Adopt flexible technology
  - Work with regulatory agencies
  - Understand available innovative programs

Figure from https://www.mddionline.com/overcome-these-market-access-challenges

GLOBAL CLINICAL TRIALS

Figure from: https://www.clinicalleader.com/doc/major-challenges-with-global-clinical-trials-and-how-to-overcome-them-0001

ADVANTAGES

- Lower costs and patient access
- Shorten the duration of the clinical trial
- Allow for testing slight differences in treatment protocols
- Experimenting new way to use existing devices
- Allow for large studies in multiple regions of the world or even small studies in one or two countries
- Companies still need to plan early and thoroughly to meet local requirements

CLINICAL DEVELOPMENT STAGES

Regulatory Status	**Pre-Market**		**Post-Market**	
Clinical Development Stage	Pilot stage	Pivotal stage	Post-market stage	
Purpose	Exploratory	Confirmatory		Observational
Types of Clinical Trial Designs	First in Human Early Feasibility Study Traditional Feasibility Study	Pivotal Study	Post-Approval Study	Registry
Location	US OUS	US OUS	US OUS	US OUS

JAPAN-US MEDICAL DEVICE HARMONIZATION BY DOING

POINTS TO CONSIDER FOR JAPAN-US CLINICAL TRIALS

- Ensure that differences in culture and perceptions are addressed
- Need for training and support for clinical trial investigators
- Development of guidelines for good clinical practices
- Pre-trial community engagement and open dialogues between regulators and industry
- Ensure the reliability of the data submitted to the regulatory bodies
- Improving the quality of clinical data

RECENT ADVANCEMENTS FROM PMDA

SHORTENING PREMARKET EVALUATION AND IMPROVE PATIENT ACCESS

- Sakigake designation
  - Strategy to put innovative medicines/devices/regenerative medicines into practice
  - 9 devices have been selected in the past 4 years

SAKIGAKE Designation System

SAKIGAKE is a system to put innovative medicines/medical devices/regenerative medicines originated from Japan into practice.

Designation Criteria

Medical products for diseases in dire need of innovative therapy and satisfies the following two conditions:

1. Having developed firstly in Japan and anticipating an application for approvals (desirable to have PMDA consultation from the beginning of R&D)
2. Prominent effectiveness (i.e. radical improvement compared to existing therapy), can be expected based on the data of mechanism of action from non-clinical study and early phase of clinical trials (phase I to II)

Designation Advantage

: To shorten the time to approval

: To facilitate R&D

①Prioritized Consultation
[Waiting time: 2 months→1 month]
Shortening a waiting time for a clinical trial consultation from the submission of materials.

② Substantial Pre-application Consultation
[de facto review before application]
Accepting materials in English

③Prioritized Review
[12 months → 6 months]
Striving to conclude review within 6 months
* Accept the result of phase III study after the application on a case-by-case basis to shorten the time from R&D to approval

④Review Partner
[PMDA manager as a concierge]
Assign a manager as a concierge to take on overall management for the whole process toward approval including conformity assurance, quality management, safety measures, and review

⑤Substantial Post-Marketing Safety Measures
[Extension of re-examination period]
Strengthening post-marketing safety measures such as extension of re-examination period as well as facilitating coalition with scientific societies, and transmission of information globally.

Designation Procedure

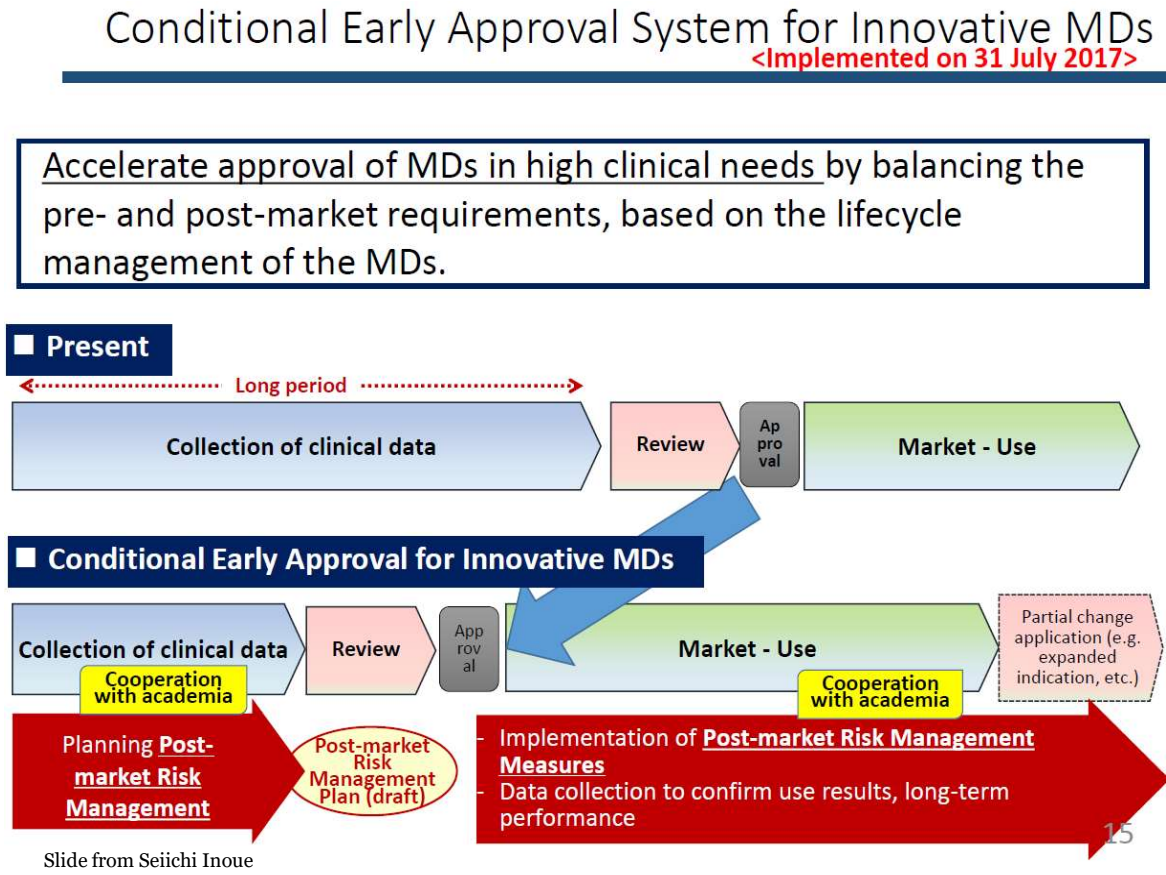
1. **Initiation by applicant:** Application is to be submitted to Evaluation and Licensing Division (ELD) and to be reviewed at PMDA. The result is to be notified within 60 days.
2. **Initiation by ELD:** ELD is to approach a potential applicant. The result is to be notified within 30 days after the submission, if agreed by the applicant.

https://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/dl/140729-01-01.pdf

RECENT ADVANCEMENTS FROM PMDA

SHORTENING PREMARKET EVALUATION AND IMPROVE PATIENT ACCESS

- Conditional early approval system
  - Devices that fulfill great and unmet medical need for which limited data exists
  - Balances pre- and post-market requirements based upon the lifecycle management of the device
  - Designed to accelerate patient access to innovative devices intended to treat life-threatening diseases for which no therapies exist



Slide from Seiichi Inoue

THE FUTURE OF PMDA – The "4 Firsts"

PRIORITY AREAS

- Patient First – communicating well with healthcare professionals and giving highest priority to patient satisfaction
- Access First – accelerating access to innovative medical products and ensure appropriate benefit-risk balance
- Safety First – implement efficient post-market data collection
- Asia First – promoting regulatory harmonization and improving public health across Asian countries or regions

A FOUNDATION OF TRUST

BUILDING BLOCKS TO ENGAGE AND COLLABORATE WITH REGULATORS

- Transparency
- Clarity
- Reliability
- Proactivity
- Collegiality

Figure from https://www.turfmagazine.com/business-management/building-the-foundation/


Abbott