



Promotion of Early Patient Access to Medical Devices in the U.S. and Japan – US Regulatory View on Current and Prospective Activities

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December 11, 2019



CDRH Overview

- CDRH's commitment to ensuring patients and providers have timely and continued access to safe, effective, and high-quality medical devices does not occur in a vacuum
- Engage with global regulatory, clinical, and industry stakeholders to leverage available resources and information and promote regulatory consistency and predictability





CDRH Strategic Priorities: 2018 - 2020

- Employee Engagement, Opportunity, and Success
- Simplicity
- Collaborative Communities

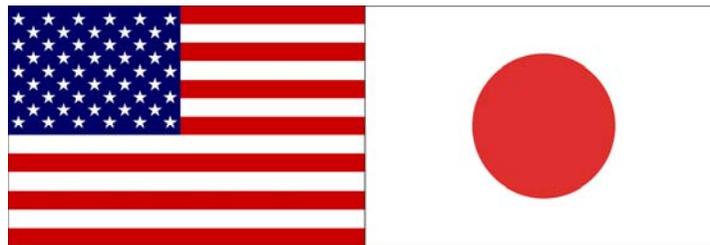
Our Measure of Success:

“By December 31, 2020, more than 50 percent of manufacturers of novel technologies for the U.S. market intend to bring their devices to the U.S. first or in parallel with other major markets.”



What About Japan?

- Similar to US in many ways
 - Large markets
 - Strict regulatory systems
 - Comparable levels of clinical care
- Similar focus on improving the environment for medical device development and access

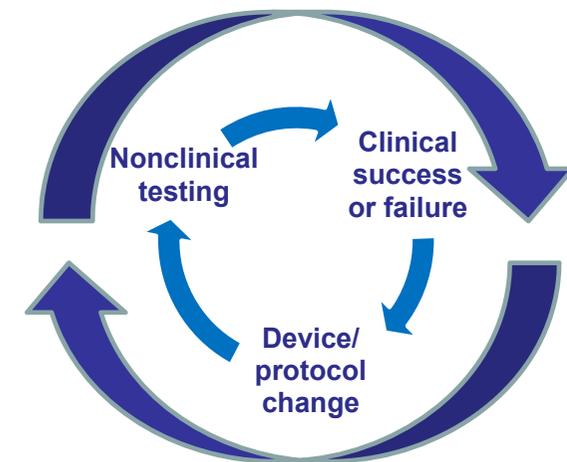




How Can We Promote Patient Access Together Throughout the Total Product Life Cycle?

Early Feasibility Studies

- Promote early-stage clinical research in US
 - Small number of subjects
 - Device design not necessarily final
 - “Just-in-time” non-clinical testing
- Additional focus on streamlining non-regulatory processes
 - IRB approval and site initiation
 - Reimbursement





Early Feasibility Studies

Through HBD, promoted EFS pathway in Japan

4C Medical Plans First Early Feasibility Study For An Implantable In Japan

06 Mar 2019 | NEWS

How can we best utilize multi-national EFS studies and leverage these experiences?

How much do differences in clinical practice, clinical study infrastructure, patient/physician attitudes matter?



Clinical Study Harmonization

- Multiple efforts to enhance the quality and utility of clinical data
 - Acceptance of non-OUS data
 - Standardization of clinical definitions and endpoints
 - Use of real-world evidence (RWE)

Contains Nonbinding Recommendations

**Acceptance of Clinical Data to Support
Medical Device Applications and
Submissions
Frequently Asked Questions**

**Guidance for Industry and
Food and Drug Administration Staff**

Document issued on February 21, 2018.

**Current Considerations
on Real-World Evidence
Use in FDA Regulatory
Submissions**

Examples and decision making from the Center for Devices and Radiological Health's Peripheral
Interventional Devices Branch.

BY ELENI WHATLEY AND MISTI MALONE

**Use of Real-World Evidence to
Support Regulatory Decision-Making
for Medical Devices**

**Guidance for Industry and
Food and Drug Administration Staff**

Document issued on August 31, 2017.



Special Report

State-of-the-Art Review

CLINICAL STATEMENTS

A Consensus Statement on Clinical Trial Design Principles and Endpoint Definitions for Transcatheter Mitral Valve Repair and Replacement: A Consensus Document from the Transcatheter Cardiovascular Interventions (TAVI) Consortium



Consortium

Gibson, MS, MD;
MD;

David Taggart, MD, PhD

Gregg W. Stone, MD, PhD
Jeffrey S. Borer, MD, PhD
Mitchell W. Krucoff, MD, PhD
Robert J. Siegel, MD, PhD
Patrizio Lancellotti, MD, PhD

Update on Mitral Valve Incompetence: A Consensus Document from the European Association of Cardiovascular Imaging and the European Association of Percutaneous Cardiovascular Interventions

A. Pieter Koster, MD, PhD
Eugene H. Black, MD, PhD
Rebecca T. Hahn, MD, PhD
Josep Rodés-Gabriel, MD, PhD

Evaluation and Treatment of Patients With Lower Extremity Arterial Disease: A Consensus Document from the International Working Group on Peripheral Arterial Disease

Consensus Document on Research Core Data Elements for Registry Assessment of Peripheral Interventional Devices (RAPID)

Manesh R. Patel, MD, PhD
William Gray, MD, PhD
Michael R. Jaff, DO, PhD
Roxana Mehran, MD, PhD
Thomas J. Povsic, MD, PhD
James Tcheng, MD, PhD
Bret N. Wiechmann, MD, PhD

Registry Assessment of Peripheral Interventional Devices (RAPID)
— Registry Assessment of Peripheral Interventional Devices Core Data Elements —

W. Schuyler Jones, MD; Mitchell W. Krucoff, MD; Pablo Mora-Rebecca W. Wilgus, RN, MSN; Anne H. Heath, BA; Mary F. Wilgus, MD; James E. Tcheng, MD; J. Danica Marinac-Dabic, MD, PhD; Misti L. Terrie L. Reed, MS; Rie Fukaya, MMedSc; Robert Lookstein, MD; Nobuyoshi Azuma, MD, PhD; Herbert D. Aronow, MD, MPH; Daniel J. Bertges, MD; Michael R. Jaff, DO, PhD; Thomas T. Tsai, MD, MSc; Joshua A. Smale, BS; Margo J. Zauberman, MD, PhD; Robert J. Thatcher, MBA; Jack L. Cronenwett, MD; Durham, NC; Sifeng Wang, MD; Tokyo, Japan; New York, NY; Providence, RI; Burlington, Vt; Newton, MA; Tempe, Ariz; Santa Clara, Calif; Minneapolis, Minn; Lebanon, NH



Circ J 2018; 82: 2233–2239
doi:10.1253/circj.CJ-18-0014

REVIEW

Design Strategies for Global Clinical Trials of Endovascular Devices for Critical Limb Ischemia (CLI)

— A Joint USA-Japanese Perspective —

Hiroyoshi Yokoi, MD; Mami Ho, MD; Shin Iwamoto, PhD; Yuka Suzuki, PhD; Gary M. Ansel, MD; Nobuyoshi Azuma, MD; Nobuhiro Handa, MD; Osamu Iida, MD; Koji Ikeda, PhD; Fumiaki Ikeno, MD; Norihiko Ohura, MD; Kenneth Rosenfield, MD; John Rundback, MD; Hiroto Terashi, MD; Takahiro Uchida, MD; Yoshiaki Yokoi, MD; Masato Nakamura, MD; Michael R. Jaff, DO

REVIEW



Circ J 2018; 82: 2233–2239
doi:10.1253/circj.CJ-18-0817

LETTER TO THE EDITOR

Harmonization by Doing Proposal for Global Clinical Trial Designs for Endovascular Devices for Treatment of Critical Limb Ischemia: The United States Food and Drug Administration Perspective

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Circ J 2018; 82: 2233–2239
doi:10.1253/circj.CJ-18-1066

AUTHOR'S REPLY

Harmonization by Doing Proposal for Global Clinical Trial Designs for Endovascular Devices for Treatment of Critical Limb Ischemia: The United States Food and Drug Administration Perspective — Reply —

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Office of Medical Devices III (M.H.);
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Pharmaceuticals and Medical Devices Agency, Tokyo, Japan



Clinical Study Harmonization

Japan and US moving in similar directions



Circ J 2018; 82: 636–643
doi:10.1253/circj.CJ-17-0533

REVIEW

Rapid Globalization of Medical Device Clinical Development Programs in Japan
— The Case of Drug-Eluting Stents —

Madoka Murakami, PhD; Yuka Suzuki, PhD; Toshiyoshi Tominaga, PhD

GLOBAL PERSPECTIVES



New Regulatory Framework for Medical Devices in Japan: Current Regulatory Considerations Regarding Clinical Studies

Akihide Konishi, MD, PhD, Soichiro Isobe, PhD, and Daisaku Sato, PhD

COMMENTARY

The MIHARI project: establishing a new framework for pharmacoepidemiological drug safety assessments by the Pharmaceuticals and Medical Devices Agency of Japan[†]

Chieko Ishiguro*, Yoshinori Takeuchi, Yoshiaki Uyama and Tomiko Tawaragi

Office of Medical Informatics and Epidemiology, Pharmaceuticals and Medical Devices Agency, Tokyo, Japan

What additional steps can be taken to promote US-Japanese clinical collaboration?

Are there non-regulatory issues to consider, such as international collaborations between medical societies?



Breakthrough Devices / Safer Technologies (STEP) Programs

- Intended to facilitate access to devices that:
 - Offer advantages compared to existing treatments for a debilitating or life-threatening disease (BD)
 - Treat less serious disease and offer an improved safety profile (STEP)
- Incorporate more frequent discussions, novel clinical and non-clinical approaches, pre/post-market data shifts, ...

Breakthrough Devices Program
Guidance for Industry and
Food and Drug Administration Staff

Document issued on December 18, 2018.

Safer Technologies Program for
Medical Devices

Draft Guidance for Industry and
Food and Drug Administration Staff

DRAFT GUIDANCE



Breakthrough Devices / Safer Technologies (STEP) Programs

In Japan, similar “Sakigake” program exists

Strategy of SAKIGAKE by MHLW

On June 17th, 2014, the Ministry of Health, Labour and Welfare (MHLW) announced the “Strategy of SAKIGAKE” to lead the world in the practical application of innovative medical products.

The “Strategy of SAKIGAKE” covers from basic research to clinical research/trials, approval reviews, safety measures, insurance coverage, improvement of infrastructure and the environment for corporate activities, and global expansion.

One of the major policies of the “Strategy of SAKIGAKE” is the “SAKIGAKE Designation System,” which promoting R&D and early clinical research/trials in Japan aiming at early practical application for innovative medical products with prospective significant efficacy by conducting priority consultations, prior assessment, and priority reviews.

Together with MHLW, PMDA will work towards implementation of the strategy.

December 15, 2017

Marketing Approval Granted for TITANBRIDGE™

First SAKIGAKE Designated Medical Device

to Treat Adductor Spasmodic Dysphonia

Can these programs be complementary for companies seeking both U.S. and Japanese approval?

Can lessons learned from one program be applied to the other?



Regulatory Decision-Making

- 510(k): Alternative pathway for clearance based not on substantial equivalence, but on:
 - Intended use/technology equivalent to predicate
 - Performance testing following FDA-specified methods/criteria
 - Based on recognized standards or historical performance of comparable products

Contains Nonbinding Recommendations

Safety and Performance Based Pathway

Guidance for Industry and Food and Drug Administration

Document issued on September 20, 2019.



Regulatory Decision-Making

- Least Burdensome principle: the minimum amount of information necessary to address a regulatory issue through the most efficient manner, at the right time
 - Benefit-risk considerations
 - Acceptable of uncertainty
 - Pre-market/post-market balance

Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications

Guidance for Industry and Food and Drug Administration Staff

Document issued on August 30, 2019.

Consideration of Uncertainty in Making Benefit-Risk Determinations in Medical Device Premarket Approvals, De Novo Classifications, and Humanitarian Device Exemptions

Guidance for Industry and Food and Drug Administration Staff

Document issued on August 30, 2019.

Balancing Premarket and Postmarket Data Collection for Devices Subject to Premarket Approval

Guidance for Industry and Food and Drug Administration Staff

Document issued on April 13, 2015.

Innovation in Regulation Applied to Descending Thoracic Aortic Endografts

FDA Regulatory Review Scientist Dorothy B. Abel discusses what led to the unique expanded approval of a thoracic endograft and a landmark postapproval study.



Regulatory Decision-Making

- Very similar principles developed and implemented in Japan
- IMDRF developing a process for recognition of third-party marketing decisions



Circ J 2018; 82: 1487–1490
doi:10.1253/circj.CJ-17-1425

REVIEW

First Approval of Improved Medical Device Conditional on Use-Result Survey in Japan
— Regulatory Review of Polymer-Free Drug-Coated BioFreedom Coronary Stent —

Akihide Konishi, MD, PhD; Mami Ho, MD, PhD; Yuko Shirai, BSc; Haruki Shirato, PhD



IMDRF International Medical
Device Regulators Forum

Title: Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews

Authoring Group: IMDRF GRRP Working Group

*Can we exploit the synergies between U.S./Japanese review approaches?
Are there additional opportunities for bilateral collaboration and reviews?*



Points to Consider/Discuss



- Are there opportunities to optimize EFS use in each country?
- Can we develop best practices for collecting/analyzing RWE?
- Is there value in post-market collaboration/information-sharing?
- What infrastructure/non-regulatory issues can we address?
- Are HBD and other collaborations practical for small businesses?
- ??



Conclusions

- In recent years, both U.S. and Japan have taken steps to facilitate patient access throughout the product life cycle
- Further US-Japanese collaborations make particular sense now
- Consider opportunities to use previous learnings and initiate new projects as part of your regulatory and clinical strategies
- How can HBD build on its successes and enter new areas?



Thank You!

ご清聴ありがとうございます！