CRT23 CARDIOVASCULAR RESEARCH TECHNOLOGIES

The Pros and Cons of Global Clinical Studies

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Reviewer

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CRTonline.org

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I have no relevant financial relationships

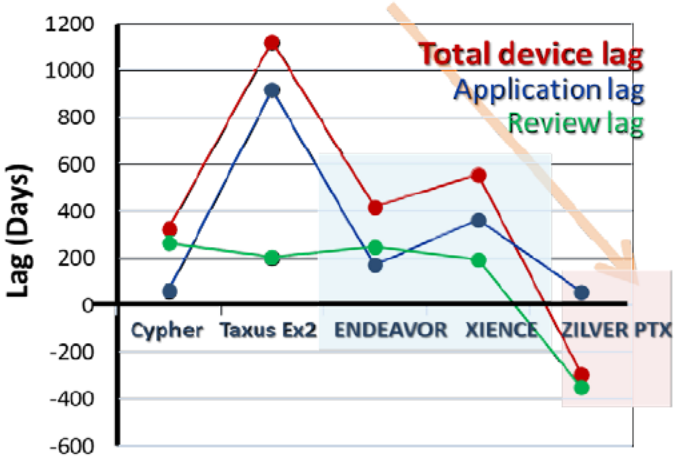
The US – Japan Device Lags for Drug Eluting Stents

2003 **Establishment of Harmonization By-Doing (HBD) Working Group**

- Conducted the US-Japan joint clinical trials for two drug eluting stents
  - ENDEAVOR (Medtronic Japan Co., Ltd.)
  - XIENCE V (Guidant Japan K.K. (former name))

2005 **First Think Tank meeting in Tokyo**

2010 **Simultaneous application for marketing approval of Zilver PTX in the US and Japan**



Circ J 2018; 82: 636-643

Proof of Concept (POC) project

- Target: Specific medical devices under development
- Purpose: To identify issues in simultaneous development in Japan and the US and find solutions.

What can we do for accelerating introduction of innovative medical devices into both the US and Japan?

HBD-WG helps developers to

- efficiently collect clinical evidence by conducting global clinical trials.

  ＜Examples＞
  - Drug-eluting peripheral stent, "Zilver®" produced by Cook Medical
  - Bare metal peripheral stent, "Misago®" produced by Terumo Corporation
  - （HBD-for-Children) Transcatheter pulmonic valve, “Harmony™ TPV system” produced by Medtronic Inc.
- understand differences in regulations between the US and Japan
- build and use a solid relationship among academia, industry, and regulatory agency.

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Scientific papers will be issued!

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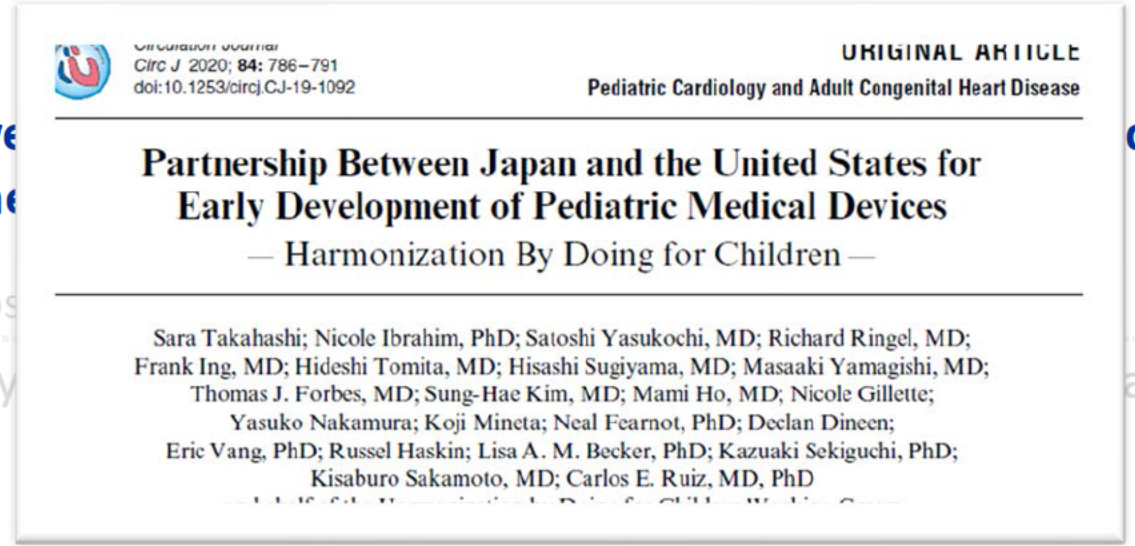

Circ J 2020; 84: 786–791
doi:10.1253/circj.CJ-19-1092

ORIGINAL ARTICLE
Pediatric Cardiology and Adult Congenital Heart Disease

Partnership Between Japan and the United States for Early Development of Pediatric Medical Devices

— Harmonization By Doing for Children —

Sara Takahashi; Nicole Ibrahim, PhD; Satoshi Yasukochi, MD; Richard Ringel, MD; Frank Ing, MD; Hideshi Tomita, MD; Hisashi Sugiyama, MD; Masaaki Yamagishi, MD; Thomas J. Forbes, MD; Sung-Hae Kim, MD; Mami Ho, MD; Nicole Gillette; Yasuko Nakamura; Koji Mineta; Neal Fearnot, PhD; Declan Dineen; Eric Vang, PhD; Russel Haskin; Lisa A. M. Becker, PhD; Kazuaki Sekiguchi, PhD; Kisaburo Sakamoto, MD; Carlos E. Ruiz, MD, PhD

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Regulatory pathway for clinical trials in the US and Japan

Consultation

- ✓ Device overview
- ✓ Outline of non-clinical data
- ✓ Outline of clinical trial protocol (including investigator's brochure and draft of informed consent document)

Clinical Trial Notification

Investigational Device Exemption

Meeting

- ✓ Device or product description
- ✓ Proposed indications for use or intended use
- ✓ Specific questions for FDA

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Consultation categories for clinical trials of medical device in the US and Japan

PMDA	FDA
General consultation ● Discuss device development process or appropriate consultation pathway	**Informational meeting** ● Share information on device development without expectation of specific feedback
Pre-meeting for formal consultation ● Discuss topics of future formal consultations	**Pre-submission** ● Obtain FDA feedback on various topics, including the clinical trial protocol
Pre-development formal consultation ● Discuss the outline of non-clinical data package and clinical trial protocol before the next formal consultation	
Clinical trial protocol formal consultation ● Discuss proposed clinical trial protocol	

…Clinical trial, Application

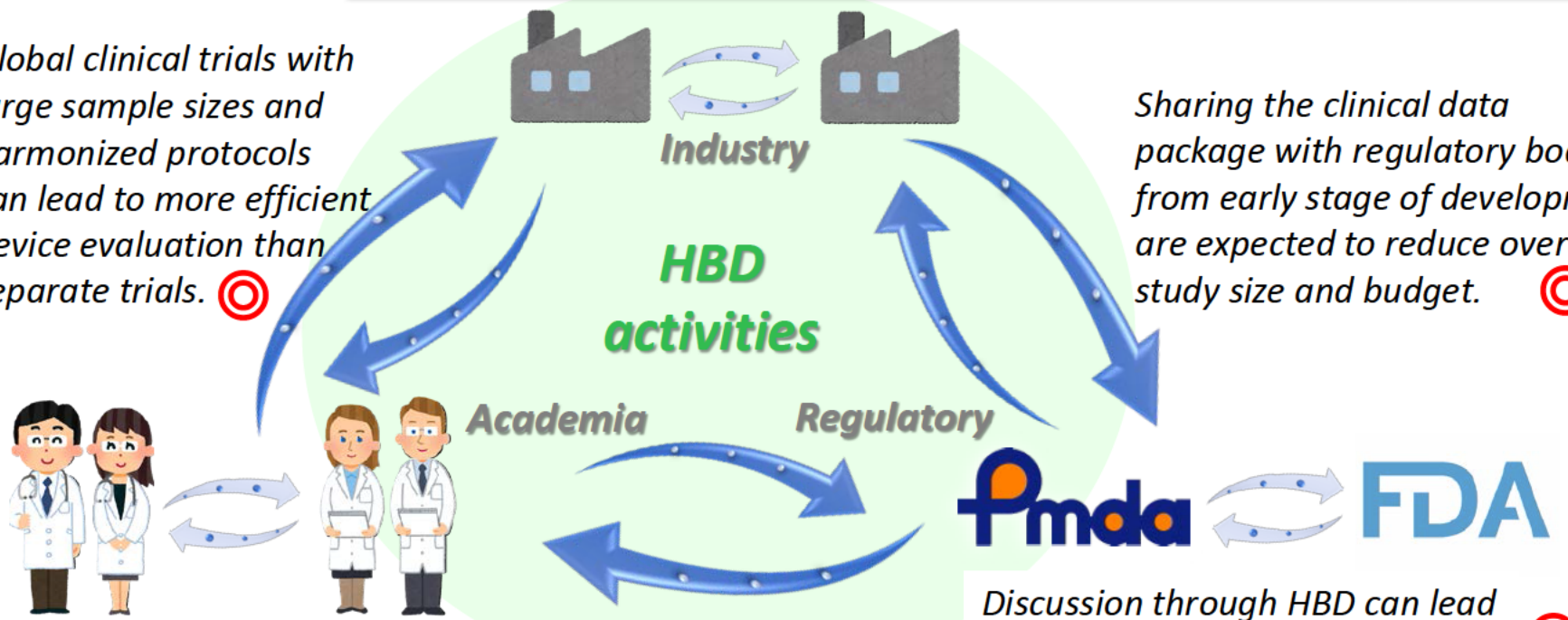
The Pros and Cons of Global Clinical Studies

<Advantages>

Global clinical study contributes early introduction of medical devices!!

Global clinical trials with large sample sizes and harmonized protocols can lead to more efficient device evaluation than separate trials. ◎

Sharing the clinical data package with regulatory bodies from early stage of development are expected to reduce overall study size and budget. ◎



Communication using HBD's relationship is expected to accelerate patient recruitment. ◎

Discussion through HBD can lead to facilitate the efficient review. ◎

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＜Disadvantages＞

Minor Differences in the following points between the US and Japan

- ✓ Medical practices and technical terms (including the definition of device relatedness)
- ✓ GCP inspection procedure
- ✓ Review/consultation options for the non-clinical data package

Comparing GCP Requirements for Medical Device Clinical Trials in the US and Japan

By Harmonization-by-Doing Working Group 4

Introduction

The convergence of US and Japanese medical device regulations and practices provides an opportunity to accelerate delivery of innovative medical devices to patients in need of medical treatment. Reciprocal acceptance of Good Clinical Practices (GCPs) would facilitate multinational studies and promote the use of clinical data to support regulatory submissions in multiple countries. The process of regulatory

to the complexity. By understanding the nature of these differences, it may be possible to more accurately determine whether data from an alternate GCP provide similar assurances of valid scientific information and patient protection.

GCP, as described in standards and regulations, governs the quality of clinical trials for medical products, including medical devices, but the differences between GCP requirements have not been well studied. Further study of these differences is needed to enhance the meaning of compliance with one set of GCP requirements versus another.

Regulatory Focus 2010; April: 40–44

It showed substantial similarities.

Expectation for future global development

- We all recognize not only the advantages but also the disadvantages, based on the practical experience such as Misago® and Zilver®.

- Cooperation among academia, industry, and regulatory agency in both the US and Japan is essential for proper evaluation of the device and promotion of global development.

- The global development efforts are expected to become more active, based on the practical experience.

CRT23 HBD Ongoing activities

1. Proof of Concept (POC) project

Purpose

- To encourage global development by finding solutions for identified issues.

- ✓ 4C medical's mitral valve
- ✓ OrbusNeich Medical Trading's Tric Valve
- ✓ Diaxamed's Sealded Synthetic Graft
- ✓ Lim Flow's device for CLI treatment
- ✓ CORVIA MEDICAL's IASD System II
- ✓ Mitre Medical Corp.'s Mitral Touch System
- ✓ (HBD-for-children) Medtronic's Harmony TPV system, Renata Medical's Minima stent etc.

2. Preparation for publication of papers

3. (HBD-for-children) Standardization of definitions and endpoints

- ✓ Pulmonary artery stenosis
- ✓ Mechanical circulatory support

Thank you for your kind attention.

If you have any questions, please contact us.

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