HBD for Children

- Achievements and future directions

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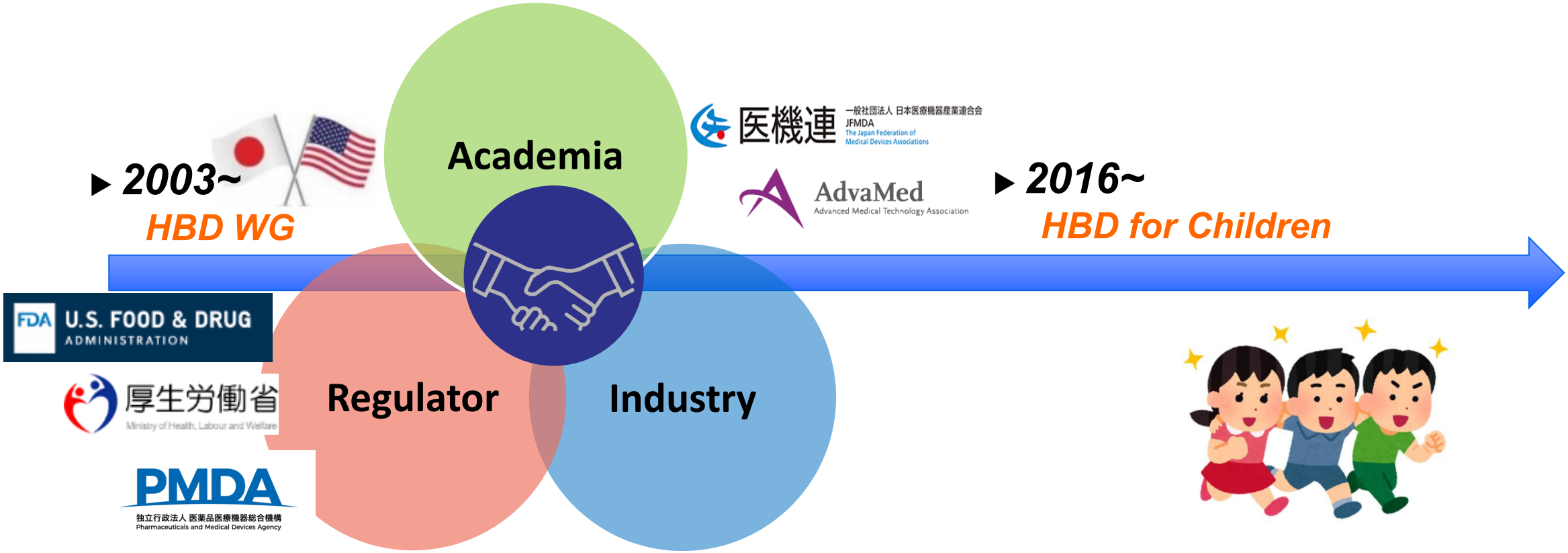
Agenda

1. Overview of HBD for Children activities
2. POC project
3. Key consideration in the development of pediatric medical devices
4. Examples of regulatory framework in Japan
5. Future directions for HBD-for-Children

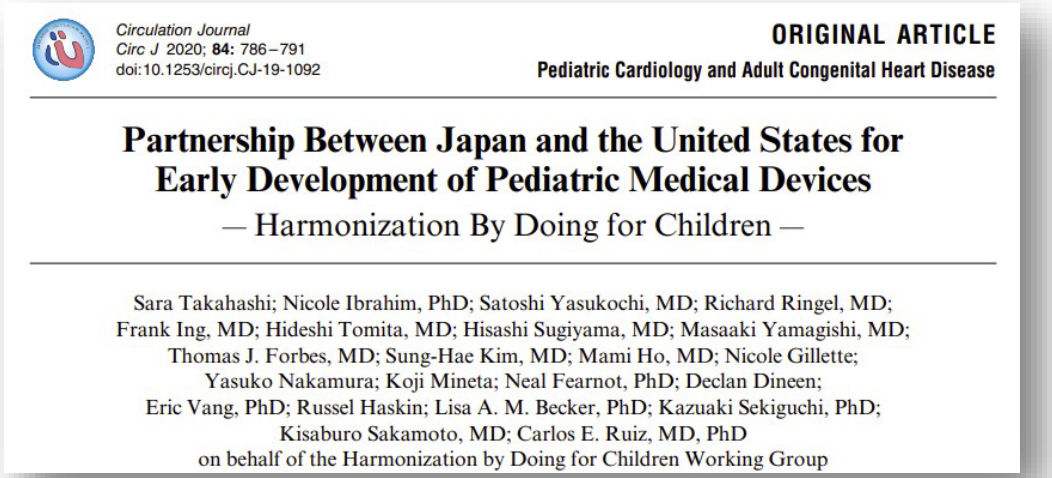
Purpose of HBD for Children Activities

To promote pediatric medical device development, *we discuss* ***the challenges and solutions*** between academia, industry and regulators in Japan and the US.



Main activities of HBD for Children

- Think Tank Meeting (once a year)
- Scientific Sessions
- Publications of Activity Results :
- POC (Proof of Concept) Project
- Teleconference (once every two months)



Circulation Journal
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 —

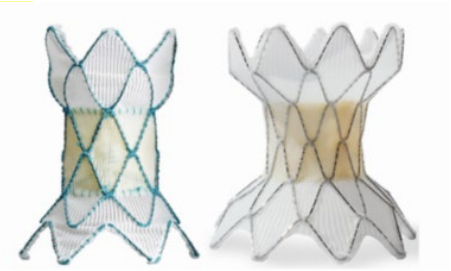
Sara Takahashi; Nicole Ibrahim, PhD; Satoshi Yasukochi, MD; Richard Ringel, MD; Frank Ing, MD; Hideshi Tomita, MD; Hisashi Sugiyama, MD; Masaaki Yamagishi, MD; Thomas J. Forbes, MD; Sung-Hae Kim, MD; Mami Ho, MD; Nicole Gillette; Yasuko Nakamura; Koji Mineta; Neal Fearnot, PhD; Declan Dineen; Eric Vang,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

Circ J 2020; 84: 786 – 791

- ARC: Pulmonary Artery Stenosis, Mechanical Circulatory Support
- New project: Key consideration in the development of pediatric medical devices

POC (Proof of Concept) Project

In the early stage of innovative medical device development,
the similarities and differences between Japan and the US are grasped
and the problem is clarified for the simultaneous application/approval of Japan and the US.



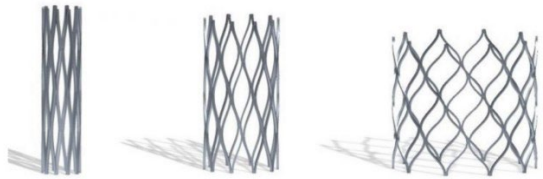
https://www.fda.gov/medical-devices/recently-approved-devices/medtronic-harmony-transcatheter-pulmonary-valve-tpv-system-p200046

■ “Harmony TPV System” Medtronic

Self-expanding transcatheter pulmonary valve.

It was approved for the first time using HBD for Children framework.

(A global clinical study was conducted, and approval was obtained in Japan and the US ***at approximately the same time***.)



https://www.seattlechildrens.org/healthy-tides/adjustable-heart-stent/

■ “Renata Minima Stent” Renata Medical

Balloon expandable stent.

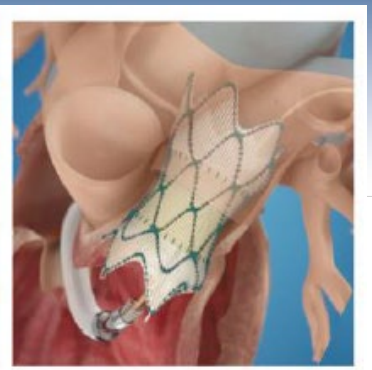
Treatment of native or acquired pulmonary artery stenoses or coarctation of the aorta in neonates, infants, and children.Approved in the US.

■ “Synfolium” Teijin Limited

Surgical patches for congenital heart disease. Approved in Japan.

https://www.omp.ac.jp/public/press/u5lpoq00000045c2.html

Case Studies-1: Harmony TPV Systems (Medtronic)



- First transcatheter prosthetic valve in Japan for patients with pulmonary valve regurgitation.
  ※POC selection items of HBD for Children
- Intended use: Patients with a history of surgical repair to the right ventricular outflow tract or transcatheter intervention (balloon valvuloplasty) and severe pulmonary regurgitation.

- Background of development :

  ➢ **Designated as an orphan medical device**

  ⇒Approved in a review period of **9 months** (priority review).

  Approved in the US and Japan at about the same time (2021).

  ➢ **Global clinical trials**

  (Efficacy) Percentage of subjects with favorable hemodynamic function at 6 months

  (Safety) Death related to procedure or device at 30 days after implantation

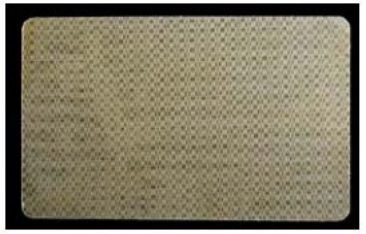
  ➢ **Post-marketing surveillance (PMS)** was conducted to evaluate long-term results.

▼ SSED（FDA） ▼ PMDA Report

Case Studies-2:Synfolium (Teijin Medical Technology Co., Ltd.)

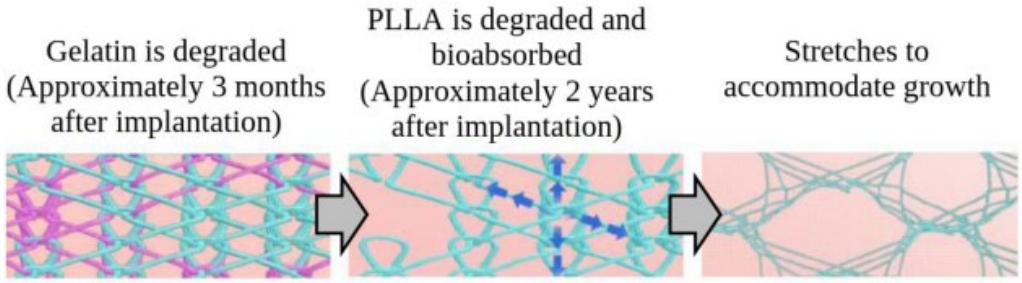
<Synfolium (Teijin Medical Technology Co., Ltd.)>

- Intended use: To be used for blood flow, securing blood flow paths, and generation/reconstruction of surrounding tissues in congenital cardiac surgery.



- A product consisting of a biodegradable poly-L-lactic acid (PLLA) yarn and a non-bidegradable polyethylene terephthalate (PET) yarn coated with a cross-linked gelatine meombrane.

- Background of development :
  - ➢ **SAKIGAKE** designation device):
- Approved **6 months** after application for approval.
  - ➢ **Domestic clinical trial**



- (Primary endpoint) Percentage of surgical success at 1 year after surgery.
  - ➢ Post-marketing surveillance (PMS) assessed the use for aorta, long-term results and so on that were not registered in the clinical trial.

▼ PMDA Report

Publication in Progress: Key Considerations in Pediatric Medical Device Development

Based on the successful cases of pediatric medical device development in Japan and the US, a concept paper of pediatric MD development are making with the stakeholders between both countries.

Particular considerations for pediatric medical devices

- ✓ Clarification of the target patient.
  Age, body size, disease state, existing treatment status, potential for reintervention with growth, etc.
- ✓ Organization of treatment strategies for existing treatments according to age, body size, etc.
- ✓ Efficacy and safety assessments taking into account growth (including long-term results) .
- ✓ Balance between pre-marketing (clinical trial) and post-marketing (PMS, etc.) considering the sample size, etc.

Japanese Regulatory Initiatives to Advance Pediatric MD Development

Type	Grant for costs	Review period	Features
Program for requesting medical devices with high clinical needs	-	○	• High clinical needs • To discuss the prompt introduction of medical equipment into the medical field
Support program for medical device used for treatment of orphan disease	◎	○	• Support of fees for development and consultation to PMDA • Priority review. • Max 90% support for approval application fees
SAKIGAKE designation system (Forerunner designation)	-	◎	• Priority scientific advice • Pre-review in consultation • Priority review（Min：6month）
Conditional approval	-	○	• Balancing the pre- and post-market requirements
Subsidization program for application of pediatric medical device	◎	○	• Max 90% support for approval application fees

Early consultation is highly recommended if you have any ideas to utilize above regulatory framework in Japan!

Future directions for HBD for Children

For promoting pediatric medical device development in Japan and the US…

- **Accumulate experiences in the development of individual products**
- **Promote to conduct global clinical trials**
- **Facilitate the use of registry data in clinical evaluation and postmarket surveillance**
- **Clarify and visualize pathways to successful pediatric MD development.**

It is important to identify issues and find solutions through constructive discussion and mutual understanding between the stakeholders.

Thank you for your kind attention.

If you have any questions, please contact us.

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