HBD-for-Children
Progress and Challenges

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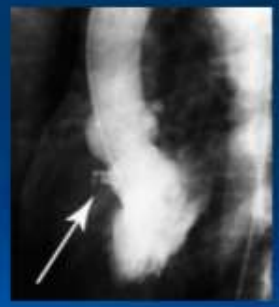
December 7th, 2017
National Center for Global Health and Medicine (NCGM)

Current Issues for Pediatric devices

- ✓ *Device Lag !*
- ✓ *Off-labeled Use*
- ✓ *Unmet device & indication*

History of Pediatric Interventional Cardiology in Japan (～1999)

- 1977, Kumade et al. PDA closure by Porstmann method
- 1979, Inoue et al. Balloon atrial septostomy using Inoue balloon
- 1985, Yokochi et al. PTPV
- 1990, Koike et al. Clinical trial for PDA closure using Rashkind PDA occluder (not approved)
- 1990, First Meeting of the Japanese Society of Pediatric Interventional Cardiology
- 1991, Fuse et al. First Report of PCI for Kawasaki disease
- 1992, Clinical trial for Clamshell ASD occluder(aborted)
- 1993, Nakanishi et al. Palmaz stent for PS (off-label)
- 1995, PDA closure using Gianturco coil
- 1996, Clinical trial for Angel Wings ASD occluder(aborted)
- 1996, Approval for Flipper coil
- 1998, Haneda et al. VSD closure using Flipper and "0.052 coils (off-label)
- 1998, Clinical trial for Amplatzer Septal Occluder



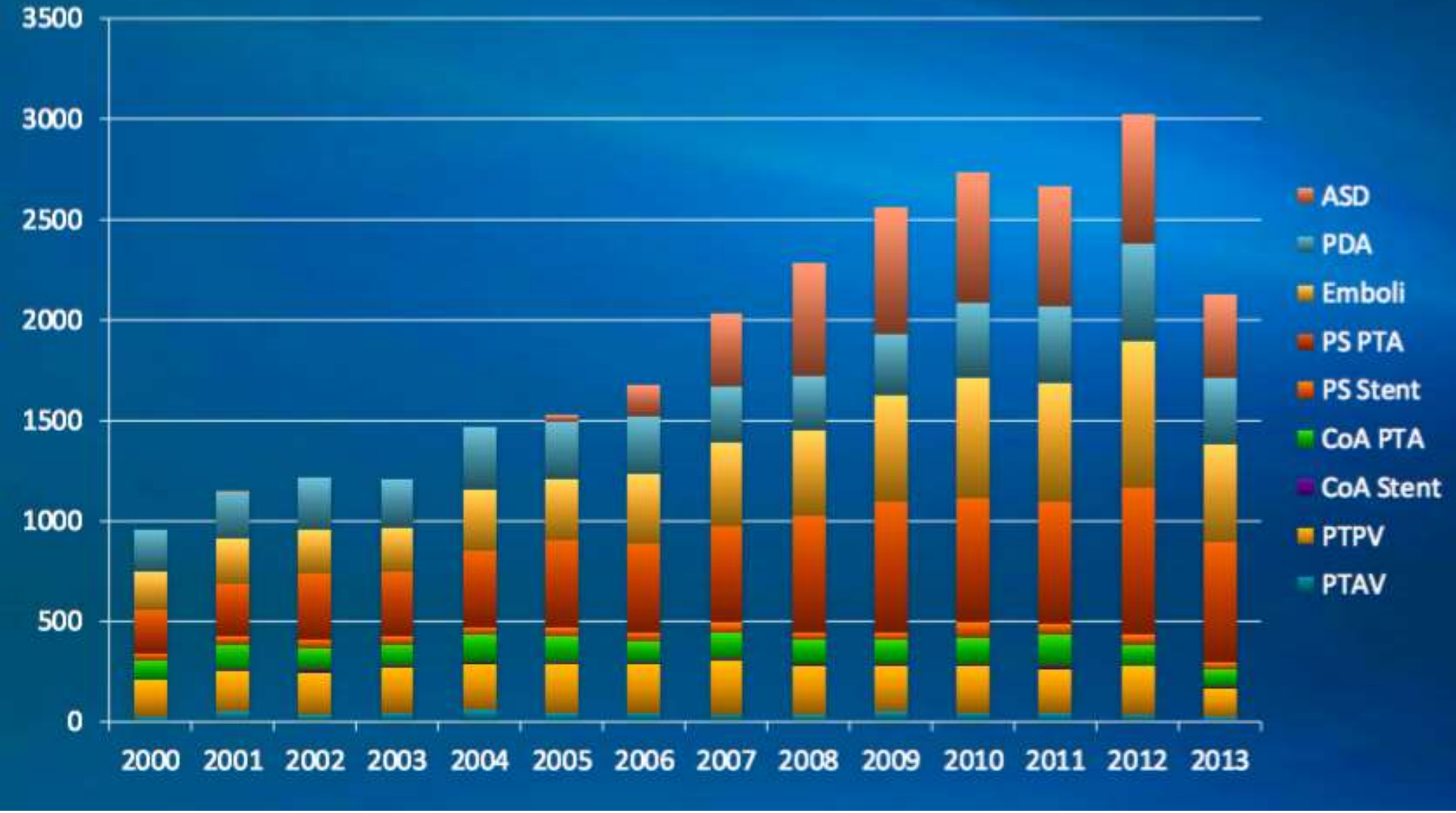
Courtesy of Dr.Tomita H.

History of Pediatric Interventional Cardiology in Japan (2000～)

- 2005, Approval for Amplatzer Septal Occluder
- 2008, Approval for Amplatzer Duct Occluder
- 2009, Clinical trial for AVP
- 2012, Approval for AVP
- 2013, Investigator-initiated clinical trial of CP stent for pulmonary stenosis (on going)
- 2014, Approval for RF wire
- 2015, Approval for Figulla Flex II

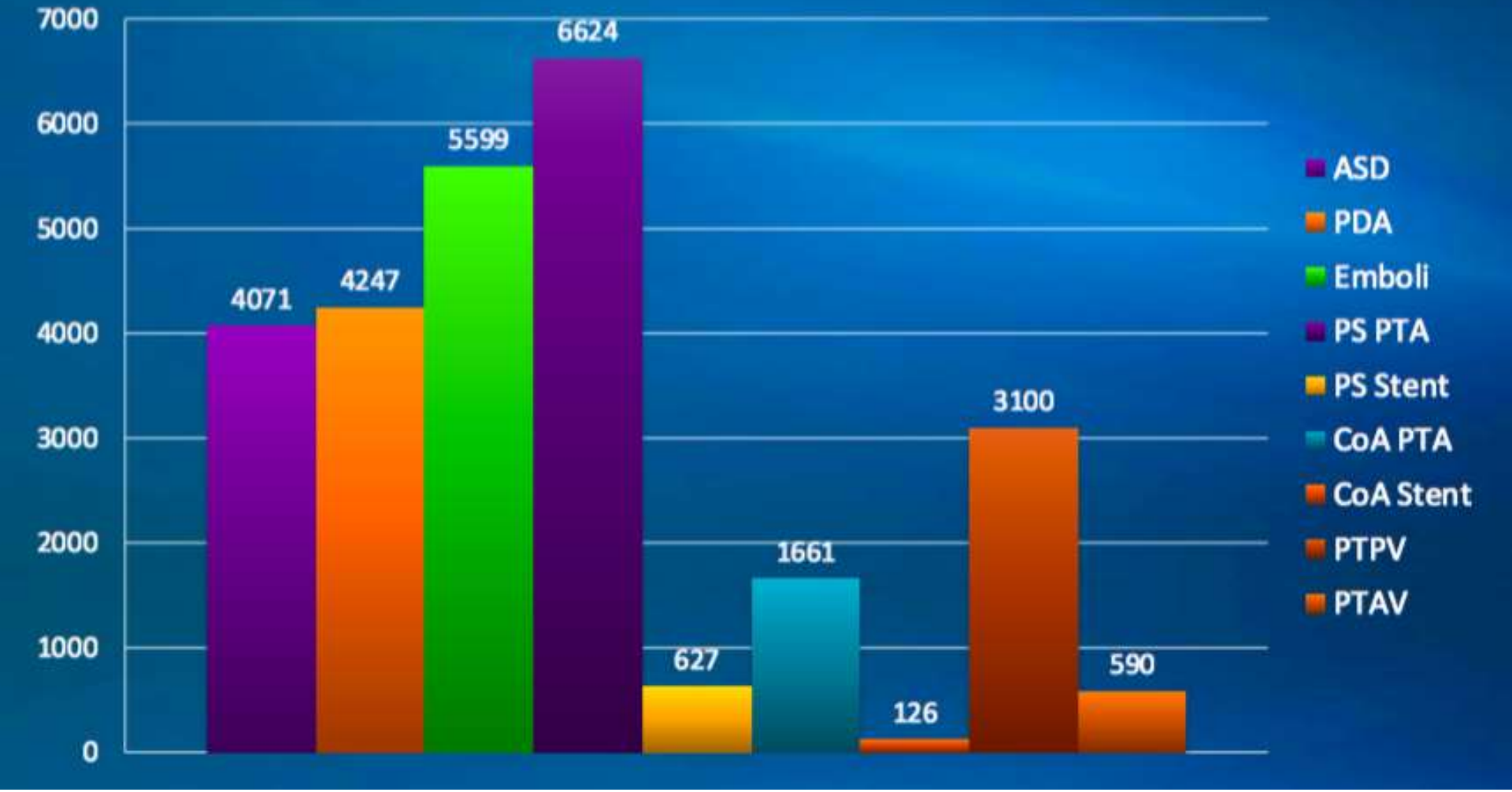
Courtesy of Dr.Tomita H.

Trend in the Number of Procedures;
the JPIC questionnaire survey up-to 2013



Courtesy of Dr.Tomita H.

Total Number of Procedures;
the JPIC questionnaire survey up-to 2013



Courtesy of Dr.Tomita H.

Clinical trial & Device approval of Pediatric devices in Japan

- Clinical trial was completed, but not approved
  - Rashkind PDA occluder (1989)
- Clinical trial was aborted, and not approved
  - Clamshell ASD occluder (1992)
  - Angel Wings ASD occluder (1996)
- Clinical trial was completed, and approved
  - ASO, AVP
- Approved without clinical trial
  - ADO, RF wire, Figulla Flex II, Balloons, Coils

Investigator-oriented clinical trial of CP stent for PA & CoA
Completed and processing (Tomita H) in 2018

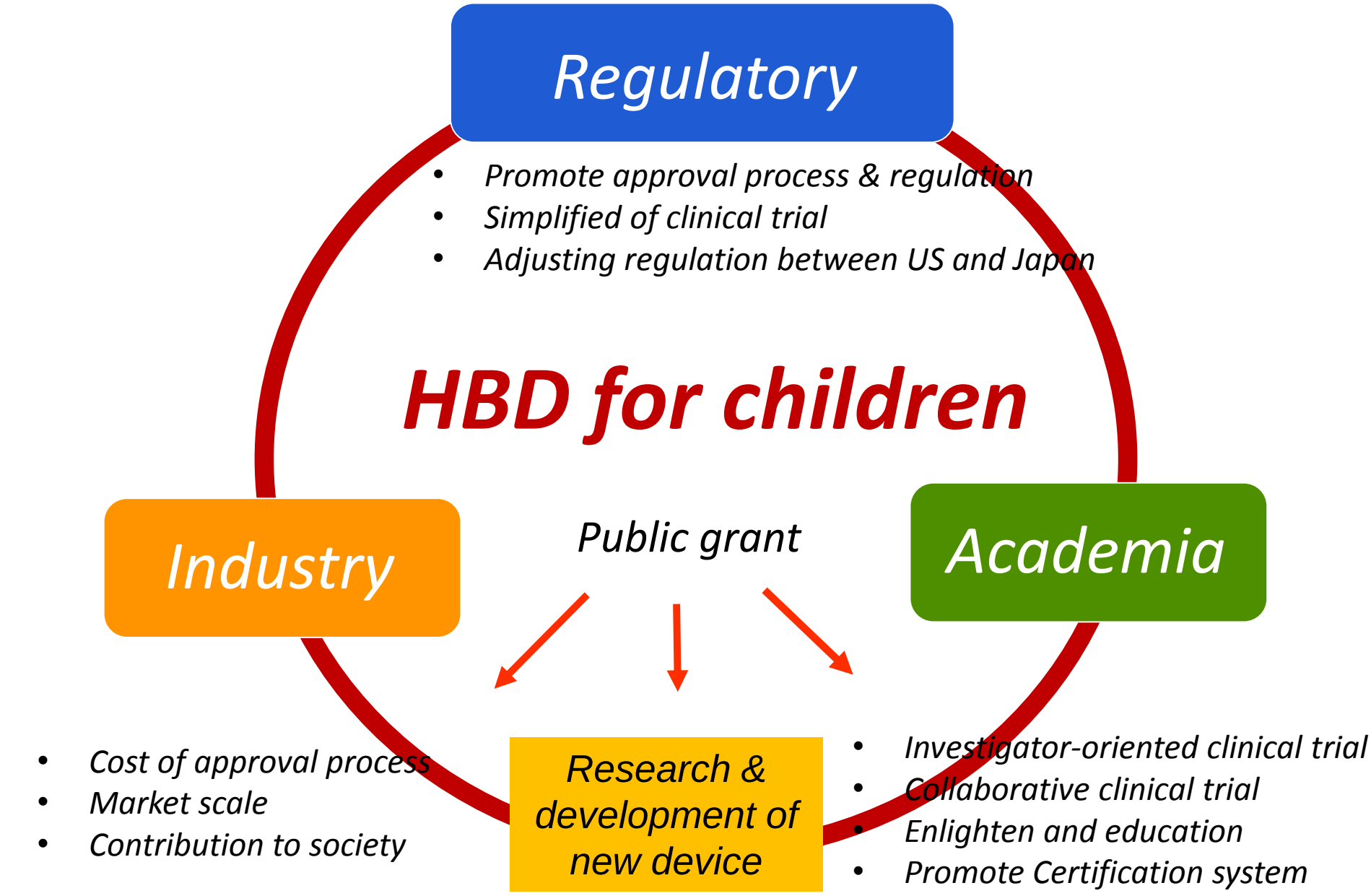
***Not*-approved devices in Japan**

Category	Availability	Device
1	Approved in US but not approved in Japan	- ADO II, PFO - Melody V - Sapien V（TPVI）
2	Not approved but used as Off-label in US and Japan for a long time	- Pulmonary stent (Genesis XD, etc.) - CP stent for PA &CoA* - Stent for RVOT
3	Not approved and not used in US & Japan , but used/approved in other countries (i.e. Europe:CE mark)	- ADO II-AS - PeriVSD occluder, - Venous P-valve - OptiMED PDA stent
4	Under development	- Harmony valve - BVS for children

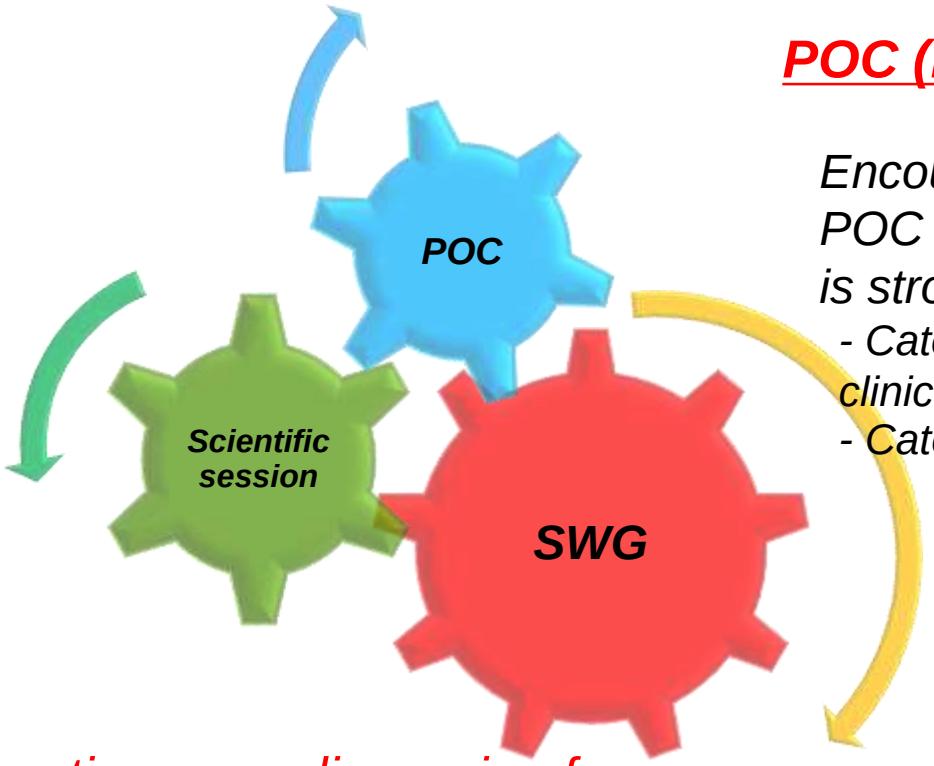
HBD-children
Harmonization-By Doing for Children

Harmonization By Doing (HBD) is the cooperative effort, jointly promoted ***by the academia, industry and regulators of the US and Japan*** since 2003, to discuss the issues and solutions in implementing global clinical trials and in promoting harmonization between the medical device regulations of both countries, putting emphasis on practice (by doing). So far, HBD has made significant contributions in promoting global device development and in resolving "device lag" issue through collaboration, such as conducting global clinical trials, mainly in the field of cardiovascular medical devices. ***HBD-Children*** are now aiming at expanding the scope of this unique effort to the field of cardiovascular medical devices for ***pediatric use,*** to make further contribution in promoting the development of pediatric medical devices, which sometimes lags behind.

Since 2016


Regulatory
Promote approval process & regulation
Simplified of clinical trial
Adjusting regulation between US and Japan
HBD for children
Industry
Public grant
Academia
Cost of approval process
Market scale
Contribution to society
Research & development of new device
Investigator-oriented clinical trial
Collaborative clinical trial
Enlighten and education
Promote Certification system

How we proceed ?



POC (Proof of Concept) project

Encourage industries to present a POC project with their products which is strongly needed in clinical practice

- *Category 2-3 : how to use the existing clinical data?*
- *Category 3-4* : *start international trial*

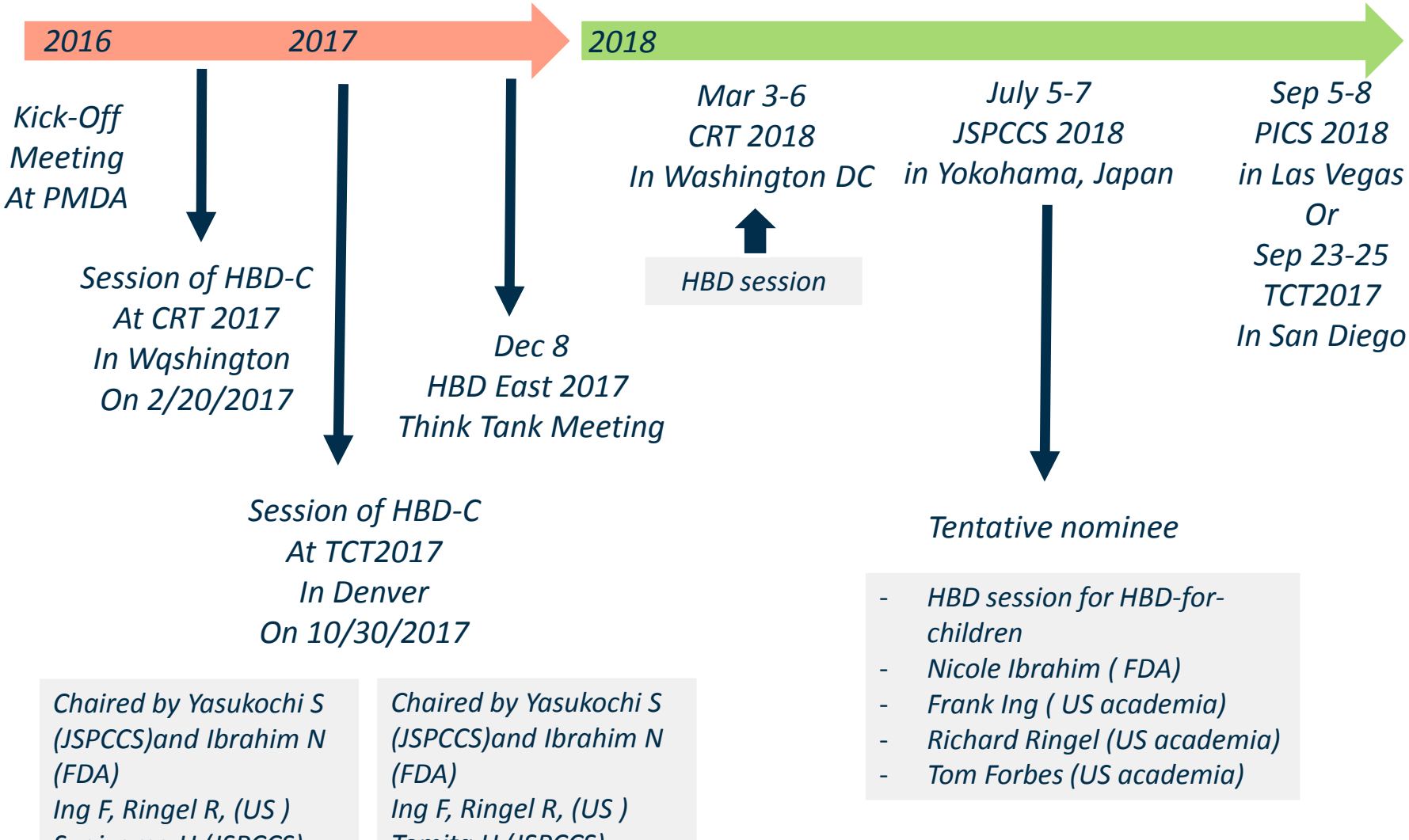
Collaborative open discussion for promoting approval process

- What is an appropriate clinical evaluation based on existing evidence?
  - *Single protocol of clinical trial (primary endpoint, number of cases, patient population)etc.*

WG discussion

Understand the problem at each category and find the resolution
  - *Promotion & facilitation of product development for industries*
  - *Guidelines, papers*

HBD-Children Work Report & schedule



HBD for Children Session at CRT 2017 in Washington DC

9:45 – 12:00 ***2017.2.19-21***

Moderators: Nicole Ibrahim (FDA), Satoshi Yasukouchi (JSPCCS)

- *Endovascular treatment devices developed worldwide in the field of pediatric cardiology –US academia (Frank Ing) 15 min*
- *Clinical needs and current situations of endovascular treatment devices for pediatric cardiology– JP academia- Hisashi Sugiyama 15 min*
- *Issues and current situations in the development of endovascular treatment devices for pediatric cardiology in the US – US industry - Dan Gutfinger (St Jude Medical) 15 min*
- *Support for the development of pediatric medical devices in the US – FDA/CMS: - Nicole Milligan (FDA) 15 min*
- *Support for the development of pediatric medical devices in Japan – PMDA/MHLW- Sara Takahashi (PMDA) 15 min*
- *Discussion: What should we do from now on? 60 min*

  Discussants: All presenters, Haruki Shirato (PMDA), Jen Piselli (FDA), Rich Ringel (Joseph M. Sanzari Children's Hospital), Carlos Ruiz (Hackensack University Medical Center)

HBD Children session at TCT2017 in Denver

2017.10.31

14:00-15:20
Special Session V: HBD For Children: Meeting the Challenge Together
Chairs: Satoshi Yasukochi, Nicole Ibrahim

- *Introduction and Achievement of HBD-for-Children: (Yasuko Nakamura) 5 min*
- *Current CV Device Use and Unmet Needs in Children: US Academic View (Frank Ing) 10 min*
- *Current CV Device Use and Unmet Needs in Children: Japanese Academic View (Hideshi Tomita) 10 min*
- *The Landscape of CV Device Innovation for Children: Industry View (Declan Dineen) 10 min*
- *The Landscape of CV Device Innovation for Children: Industry View (Lisa Becker) 10 min*
- *The Landscape of CV Device Innovation for Children: Regulatory View (Nicole Milligan) 10 min*
- *The Landscape of CV Device Innovation for Children: Regulatory View (Sara Takahashi) 10 min*
- *Discussion: (All speakers and Carlos Ruiz) 15 min)*

Categorize the candidate product for POC

Category	Availability	Device
1	Approved in US but not approved in Japan	- ADO II - Melody V - Sapien V（TPVI）
2	Not approved but used as Off-label in US and Japan for a long time	- Pulmonary stent (Genesis XD, etc.) - CP stent for PA &CoA*
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4	Under development	- Harmony valve

On going projects

1. *Clinical trial for POC*

   - *Harmony valve (Medtronics) in Japan & US will start December 2017.*

2. *Exchange the clinical data information to promote the process for approval either by FDA or by PMDA*

   - *PA stent in US (CCISC registry)*

     CCISC (Congenital Cardiovascular Interventional Study Consortium)

   - *ADO-II-AS in US (ongoing)*

   - *CP stent for PA& CoA in Japan (JPIC) (will final submiccion in 2018)*

More to come ?

VSD occluder

Helix

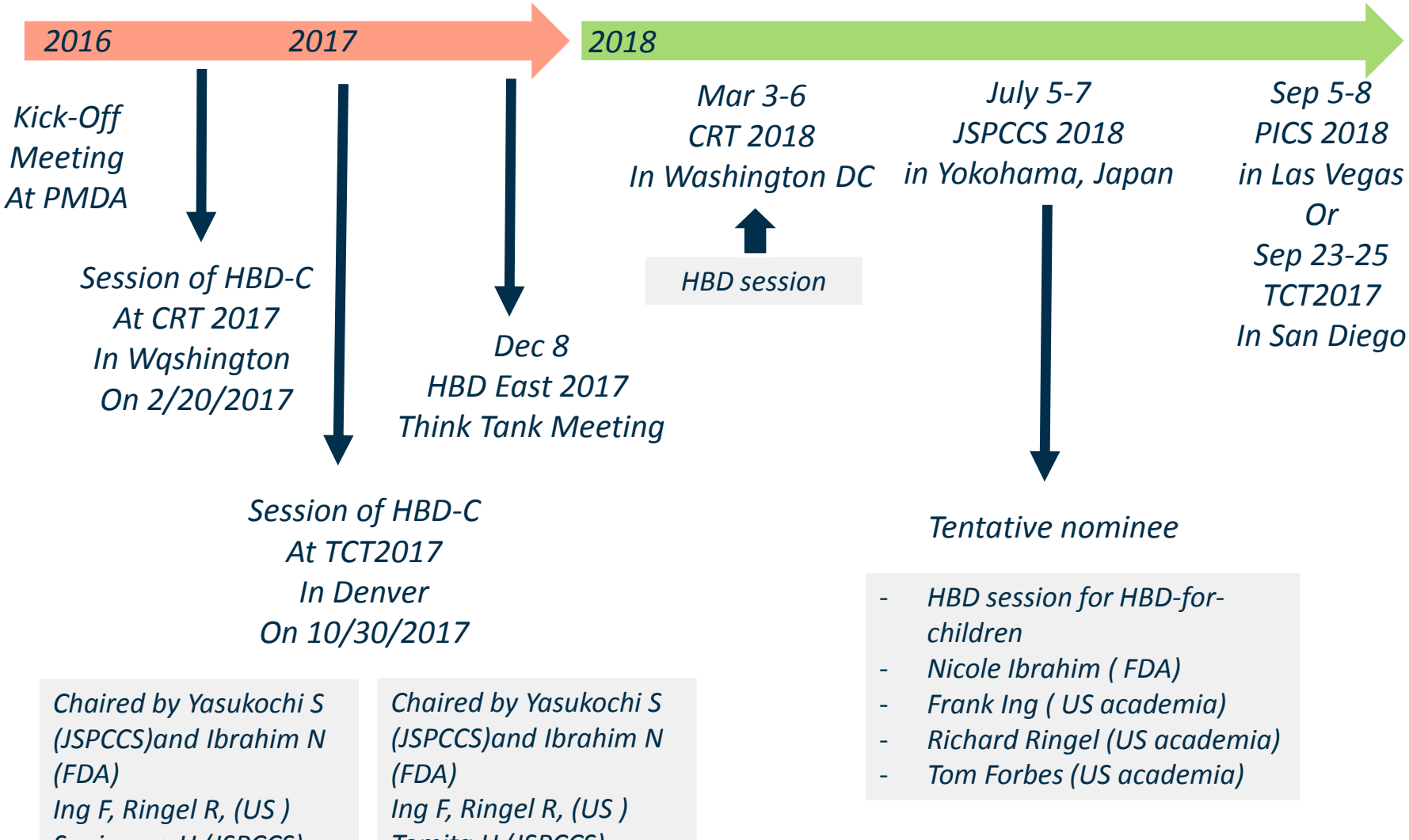
Melody valve

Sapien valve

Baleo Stent

Venous P- valve

HBD-Children Work Report & schedule



What do we expect HBD-children?

1. *Promotion of a collaborative clinical trials for unmet pediatric devices.*

   By international collaboration to overcome the small market volume of patient numbers with wide diversity of the disease, pathophyiology, age distribution, and its application criteria.

2. *Promotion of a approval processing for off-labeled or unmet pediatric device use at regulatory bodies*

   Exchange or accumulation of previously collected appropriate clinical date or other measures enough to be approved by regulatory bodies at both sides

Harmonization → Globalisation

Optimization for Pediatric Care

” right device for right patient on right time”

Join our crusades