Japan-US
Harmonization by Doing

Harmonization of clinical and regulatory approaches in the US and Japan

FDA U.S. FOOD & DRUG ADMINISTRATION

pmda 独立行政法人 医薬品医療機器総合機構 Pharmaceuticals and Medical Devices Agency

ひと、くらし、みらいのために
厚生労働省
Ministry of Health, Labour and Welfare

HBD Harmonization by Doing

What is Harmonization by Doing (HBD)?

Industry, regulators, and academia in Japan and the United States cooperate to harmonize regulatory and clinical best practices and develop new pathways for medical device development.

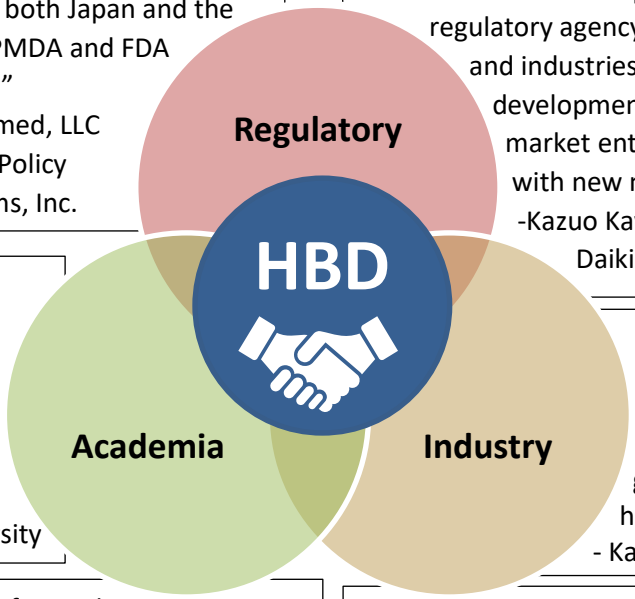
"There is regulatory harmonization to be achieved through the actual global development of individual products, and another strength of HBD activities is direct discussions between Japanese and U.S. regulatory authorities. We hope that many industries and academia will be interested in HBD activity and this activity will contribute to the global development of medical devices."
- PMDA/MHLW

"For almost 20 years, HBD members have continuously improved the clinical trial infrastructure through HBD activities. We could overcome any obstacles with strong enthusiasm hand in hand among HBD members."
- Shigeru Saito, Shonan Kamakura General Hospital

HBD has facilitated productive dialogue among Japanese and US stakeholders and shown that global trials can be successful.
- Kenneth Cavanaugh, U.S. Food and Drug Administration

"HBD has dispelled the misconception that it takes much longer to get products approved in Japan vs. the USA. When I was at CSI, we gained simultaneous approval of our technology in both Japan and the USA by working closely with PMDA and FDA and utilizing the HBD process."
- Robert Thatcher, CEO Diaxamed, LLC and Former Chief Healthcare Policy Officer, Cardiovascular Systems, Inc.

"Under different medical environments and treatment options, the HBD Program is considered to be useful and of value in establishing a global study to the regulatory bodies, industries, academia and even to patients. Also, the global regulatory agency cooperation with academia and industries can reduce the entire development time and accelerate market entry of alternative technology with new medical devices."
-Kazuo Kawahara, Boston Scientific & Daiki Yasuhara, Medtronic Japan



"HBD members help each other understand differences between Japan and the US and work together to find solutions. By helping each other we also help patients around the globe."
- Aaron Lottes, Purdue University

"Participation in HBD has made it possible to team up with experienced people. We have discussed common ground in patient-centered heart failure evaluations."
- Kate Stohlman, Corvia

"HBD has catalyzed better, safer cardiovascular devices reaching the bedsides of adults and children on both sides of the Pacific for two decades. HBD's tools of collaboration and trust across regulators, academics and manufacturers in Japan and the USA have shifted historical barriers into key synergies facilitating better, more efficient human subjects research programs and device approvals in both jurisdictions." - Mitchell W. Krucoff MD, Professor Medicine/Cardiology, Duke University Medical Center

"One big lesson learned in working with Japanese clinical sites was how efficient they were in enrolling patients and the high quality of the data collected and entered. While the per patient cost is generally higher, I am always willing to spend more budget dollars to enroll patients, with quality procedures and data collection, at a faster rate. Time is money."
- Robert Thatcher, CEO Diaxamed, LLC and Former Chief Healthcare Policy Officer, Cardiovascular Systems, Inc.

Activities & Achievement

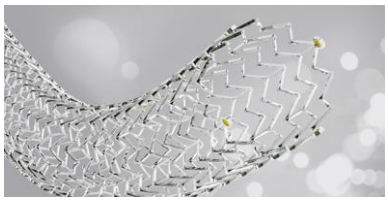
- HBD Think Tank Meetings alternating between Japan and the US
  - Identify and discuss barriers to device development and trials
  - Share working group activity updates
  - Discuss hot topic issues such as such as pediatrics devices, breakthrough, early feasibility studies, and real-world evidence

- Scientific Sessions at major US and Japan medical meetings, such as CRT, CVIT, JCS, PICS, TCT, VIVA
  - Discuss current topics relevant to the scientific community

- Publications to share lessons learned and highlight key information, e.g.
  - Global cardiovascular device innovation: Japan-USA synergies: Harmonization by Doing (HBD) program, a consortium of regulatory agencies, medical device industry, and academic institutions. doi: 10.1253/circj.cj-12-1431.
  - Design Strategies for Global Clinical Trials of Endovascular Devices for Critical Limb Ischemia (CLI) – A Joint USA-Japanese Perspective. doi: 10.1253/circj.CJ-18-0014.
  - Japan-USA Orbital Atherectomy for Calcific Coronary Lesions: COAST Study, HBD Proof-of-Concept. doi: 10.1016/j.carrev.2021.08.021.
  - Japan-USA Orbital Atherectomy for Calcific Coronary Lesions: COAST Study, a Harmonization by Doing Proof-of-Concept: The Japanese and US Regulatory Perspective. doi: 10.1016/j.carrev.2021.08.020.

- Proof of Concept (POC) Projects evaluate potential solutions
  - Completed projects demonstrated benefits of harmonization and led to shorter approval timelines:

Cook Medical Zilver® PTX®



* Global Harmonized Clinical Trial*

CSI Diamondback 360® Coronary Orbital Atherectomy System

* Simultaneous US – Japan Approval *

  - Corvia® Atrial Shunt – global trial
  - 4C Medical Mitral Valve – early feasibility
  - Orbus Neich TricValve®
  - Diaxamed Sealed Synthetic Graft

Corvia Atrial Shunt

Diaxamed Graft

HBD Harmonization by Doing

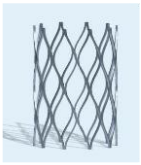
HBD for Children

Goal: Better understand the barriers to pediatric device development in the US and Japan to enable "The right devices for the right patients at the right time"

"Launched in 2016, the HBD for Children members have successfully harmonized new pediatric devices by upgrading review systems, leveraging RWD, and refining PMA. We will make further progress!!"
- Japanese Society of Pediatric Cardiology and Cardiac Surgery (JSPCCS) HBD for Children committee

- Standardizing definitions and endpoints for pulmonary artery stenosis and mechanical circulatory support
- Publication: Partnership Between Japan and the United States for Early Development of Pediatric Medical Devices – HBD for Children. doi: 10.1253/circj.CJ-19-1092.
- Completed POC: Medtronic Harmony Transcatheter Pulmonary Valve
  - First US-Japan global clinical trial of pediatric medical device
    Approved in US March 2021 and Japan August 2021

- Current POC: Renata Medical
  - Adjustable stent purposefully designed for pediatrics to last a lifetime



How to join HBD

If you are an academic researcher or clinician, work in the medical device industry, or are involved with medical device regulation, contact us to join HBD! by emailing: hbd.contact@pmda.go.jp

There is no obligation on participation. You could learn many things about medical device development, regulations, etc. If you provide any input to HBD, that would be very welcome.

If you want to propose a new 'Proof Of Concept' project for a device you are developing:

1. Present your project during monthly HBD virtual meeting
2. Discuss how HBD may be able to help
3. Join future meetings to ask questions, share updates and best practices, and learn along with other HBD members

HBD

Contact us
Email: hbd.contact@pmda.go.jp

Websites: https://www.pmda.go.jp/int-activities/int-harmony/hbd/0015.html
https://www.fda.gov/MedicalDevices/InternationalPrograms/USJapanRegulatoryCollaboration/default.htm

If you are interested in HBD, join us!

February 2023