

# What makes HBD so Unique and Significant?

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## Disclosure Statement of Financial Interest

I, Toshiyoshi TOMINAGA, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

# Regulatory Harmonization Harmony



# Harmony...

- is not unison or singing the same melody.
- A score is not enough; you have to sing!

**MARECHIARE**  
CANTO NAPOLETANO

N° 2

Finis di SALVATORE DI GIACOMO Musica di Francesco Paolo Tosti

Versione Pianoforte di BRUNO E. TRILLARA

*ALLEGRO* *oggetto e PP*

**CANTO**

I Quo - spo - tu la lu - na a Ma - re - chia - re pu -  
 I. Quon - do jao - ge in lu - na a Ma - re - chia - re, per -  
 - so il pi - ce - ce fann'a' am - ro - te  
 - so - so il pi - ce - ce fann'a' am - ro - te

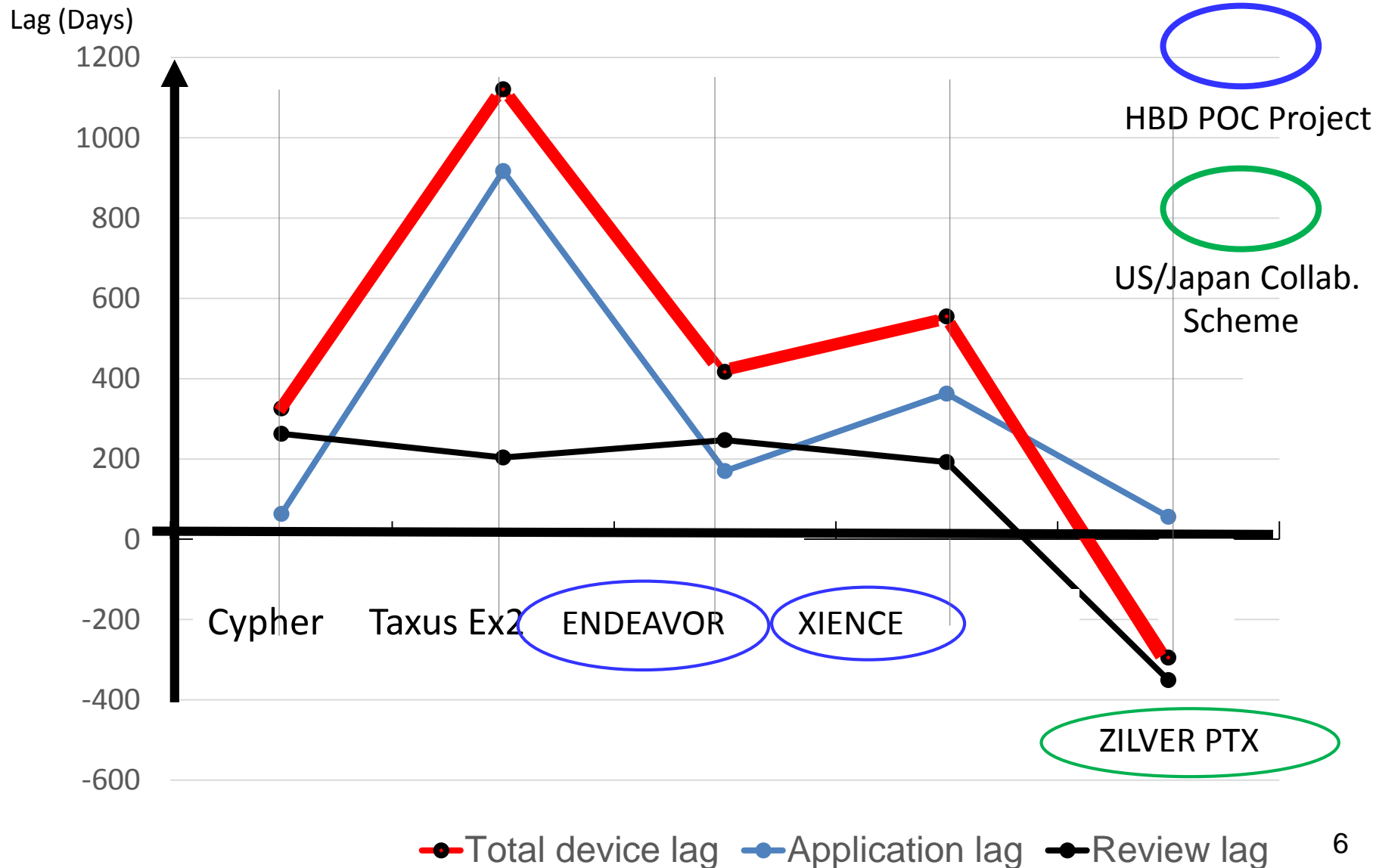
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Harmonized operations  
across countries

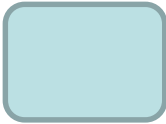
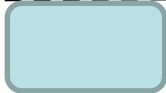

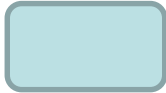

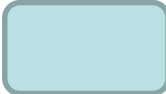



Harmonized Guidelines/regulations are  
not at all sufficient for harmonized  
operations (of clinical development),  
which ultimately help deliver safe and  
effective MDs quickly to patients.

Regulations and guidelines

# USA-Japan Device Lags for new Drug Eluting Stents approved in Japan between 2002-2012



# Progress of Alignment in USA/Japan developments

Product	The U.S./ Others Countries	Japan	Notes
Cypher			No clinical trial in Japan on safety and efficacy.
Taxus Ex2			A small Japanese study to confirm safety after the US development with RCT.
ENDEAVOR			An open study to confirm safety and efficacy in Japanese with aligned protocol.
XIENCE V	 		One RCT (US) and two registries (US and Japan) conducted per one protocol simultaneously.
ZILVER PTX			MRCT in US, Japan, and Germany on the equal footing

Time ↓

Time ↓

# Real and false (as it turned out) disharmony

## 1. Real disharmony

1. Experience in coated drugs (Cypher's sirolimus: novel in Japan )
2. Concomitant anti-platelet therapy (US: clopidogrel, Japan: ticlopidine)
3. Size and location of the target vessels
4. Lifestyle (SEIZA for Japanese, chair for westerners?)
5. Standard Therapy (for ZILVER PTX, US: Bare Metal Stent, Japan: Balloon)

## 2. Feared disharmony proven to be false

1. US/Japan GCP difference
2. Costs to conduct clinical trial too high in Japan



# HBD...

1. tried US/Japan simultaneous clinical trials
  1. and creatively overcame real disharmony/difficulty step-by-step
  2. and found some fears were bogus.
2. performed desk-top researches
  1. so cumbersome that nobody dared.
  2. and dispelled some myths (GCP, STED)
3. negated stereotyped notion and lethargy that
  1. Japan is different.
  2. Japan cannot do it.
4. proved that  
Everything is difficult before it becomes easy.



# HBD POC (Proof of Concept) project

By doing!!

## Examples of concept:

1. US-Japan clinical trials with single protocols are possible. (2003-)
2. Japan Device GCP and US Device GCP are virtually the same (2009-2010, 2012-2013, GCP comparison)
3. A start-up can conduct global clinical trials and win approval (2013-2017, Orbital atherectomy device)

## Process

- Any HBD members can propose a project (clinical or desk-top research)
- Project leaders share perceived challenges and all HBD members collaborate to actualize the project.
- No need to share confidential information.
- The insights gained are shared with the stakeholders.
- No preferential treatment by regulatory authorities for participating companies.

# Expectation on HBD

- Continued POC projects, especially Japan-origin encouraged.
- Preempt disharmonies by early capture of “hot” topics
- Publication of HBD achievements

Why don't you join HBD!