“Show me the HBD-way”

(A Collaborative Scheme on Consultation and Review: FDA-MHLW/PMDA Views)

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"Getting Started with HBD Programs: How do we do it? *

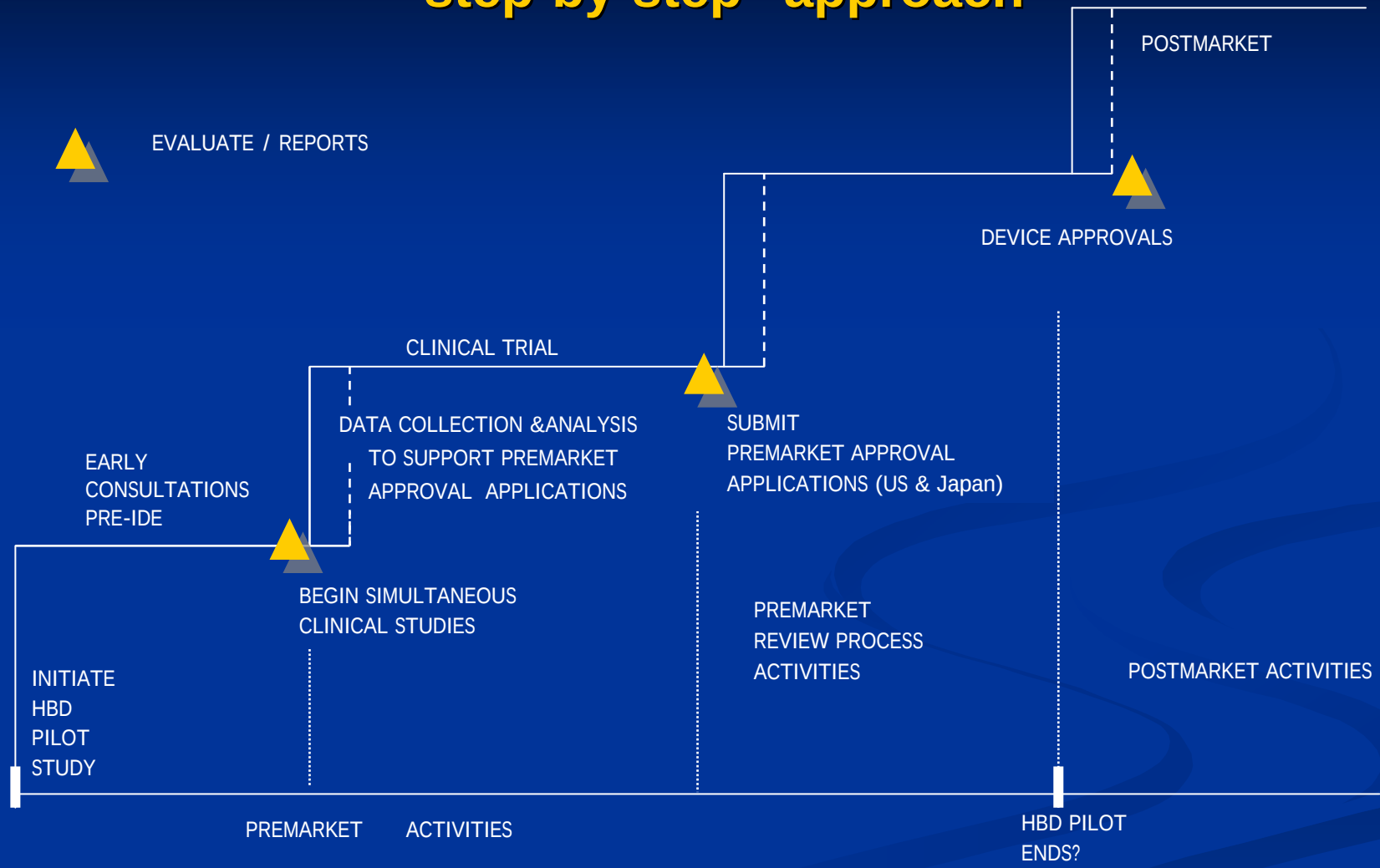
- **HBD market approval goal: conduct "simultaneous" clinical studies (common protocol) in Japan and US to obtain regulatory market approval at about the same time.**

- **The goal of an HBD Pilot: provide a model for a full HBD program.**
  - The Question/Challenge: given current regulations and practices, can we demonstrate that the goal of HBD can be achieved?

* Presented at the 2005 Jan 28 Meeting in Tokyo, Japan

Process Milestone Chart

"step-by-step" approach



"Development Steps"

HBD Regulatory Paradigm (Background)

What?

- An international effort between U.S. and Japan
  - to seek ways to promote global development of medical devices (e.g. common clinical protocol)
  - and advance regulatory harmonization and/or convergence through concrete experiences "by doing."

How?

- Application of "proof of concept" principles – **POC project in HBD**
- Concrete experience gained in the development steps is crucial to identifying practical obstacles facing global development and finding workable solutions to better align the Regulatory Roadmaps in the U.S. and Japan.

** First HBD West Think Tank 2007 in North Carolina, USA*

"Aligning" the Regulatory Roadmaps

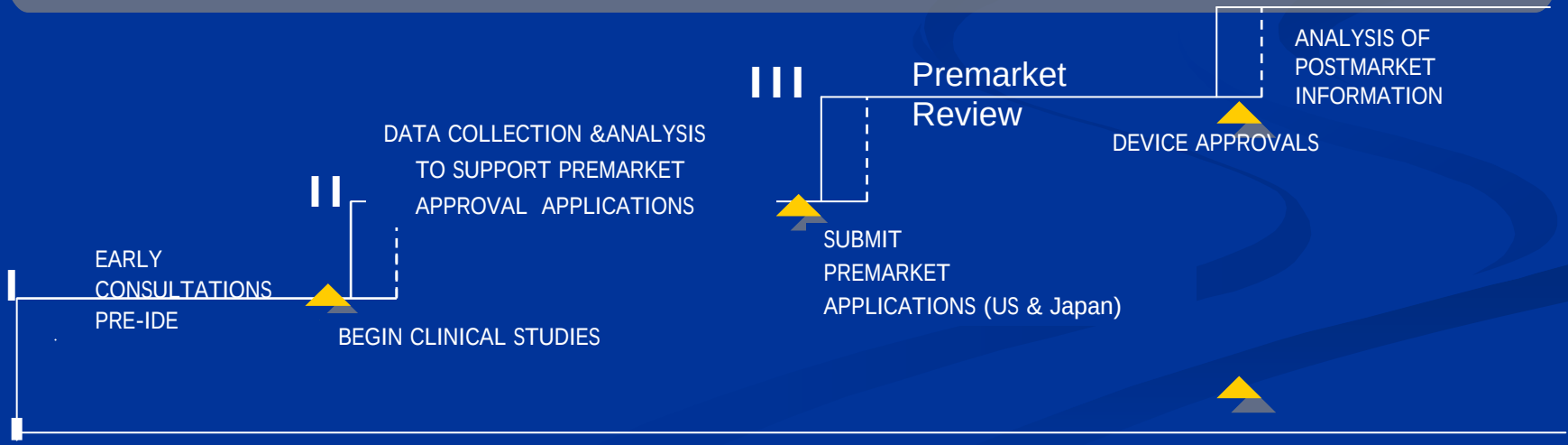
Tools already exist in both countries.

FDA

Pre-IDE	IDE & Clinical Trial	Pre-PMA	PMA Review	PMA Approval	Postmarket

MHLW/PMDA

Consultations	Clinical Trial Notification & Study	Pre-Application Consultation	Application Review	*Shonin*	"Postmarket"



Addressing Challenges with POC Projects ("doing") through Working Groups

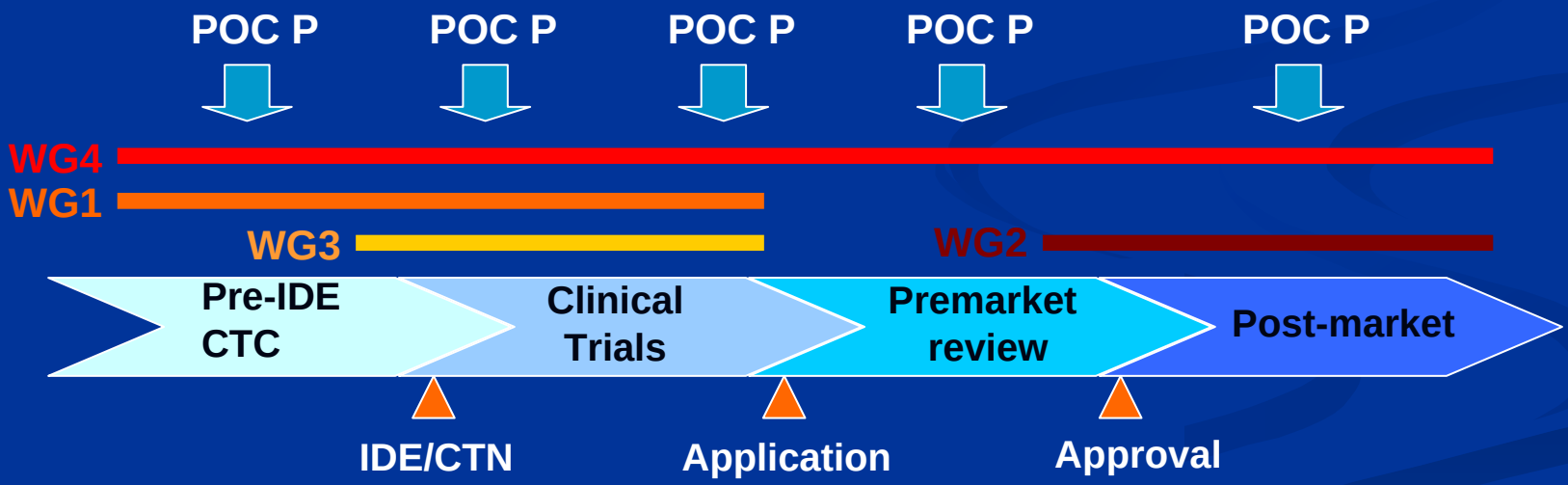
Who? *http://www.fda.gov/cdrh/international/hbdpilot.html#7*

- *Each WG can propose its own "POC project" to improve the situation and prove whether it works in actual practice.*
- **WG1: the convergence from parallel clinical trials in Japan and the U.S. toward single clinical trial protocols.**
- **WG2: leverage postmarket data (registry) to reduce requirements of market entry of new model.**
- **WG3: improvements in clinical trial infrastructure**
- **WG4: regulatory convergence, effective communications**

Regulatory Roadmap and Coverage by WGs

- The whole process of developing a medical device can be covered by a series of POC projects. In other words, it is possible that a product at any stage along the Regulatory Roadmap can "enter" the POC Project scheme.

- The development step studied can span from pre-trial stage to post market stage covering the whole range of the Regulatory Roadmap.



Getting started: POC projects

- In general, the WG jointly with the collaborator/sponsor from industry will propose and develop a plan for a POC project (the actual experience by the collaborator and make the information available for examination).
- Each WG will develop its inclusion/exclusion criteria to select adequate cases/products for its POC project according to its objectives and concept. The criteria will be shown to industry.
- Submit proposal to HBD SC for approval

Note: Some projects may require regulators' consent.

FDA-MHLW/PMDA Collaborative Scheme on Consultation and Review

AIM

- By effectively communicating during consultation and review on specific cases, the regulators will:
  - Have a better understanding of how the U.S. and Japanese experience can complement each other.
  - Improve the consultation and review process by exchanging scientific and regulatory views.

Note: The HBD FDA-MHLW/PMDA joint effort is a collaborative project and does not affect each Authority's ability to make its decision independently.

Envisioned Procedure for Collaborative Scheme on Consultation & Review:

1. POC project is proposed
2. FDA and MHLW/PMDA agree that the project is eligible to enter the Scheme.
3. The relevant WG confirms that the project meets the inclusion/exclusion criteria for POC project.
4. The Sponsor and the relevant WG draft the details of the proposed POC project and submit it to the HBD SC for approval.
5. Pre-IDE meetings/Clinical Trial Consultations or pre-market reviews are conducted under direct/indirect contact of regulators.
6. Stakeholders gain insight on how to improve the activities and advance the HBD process.

Inclusion/Exclusion Criteria: *Basic Regulatory Requirements*

(1) Sharing non-public information between government officials. (Confidentiality Agreements in place).

(2) Sharing of trade secret information with a foreign government requires a signed consent from Sponsor/Person who submitted the information to the regulatory authorities.

(3) Sponsor must be willing to disclose the existence of a consultation/a submission that qualifies for the collaborative scheme to the HBD Steering Committee and accordingly to the public.

Inclusion/Exclusion Criteria: *Specific Regulatory Requirements*

(1) Clinical trial format is Parallel or Single Protocol

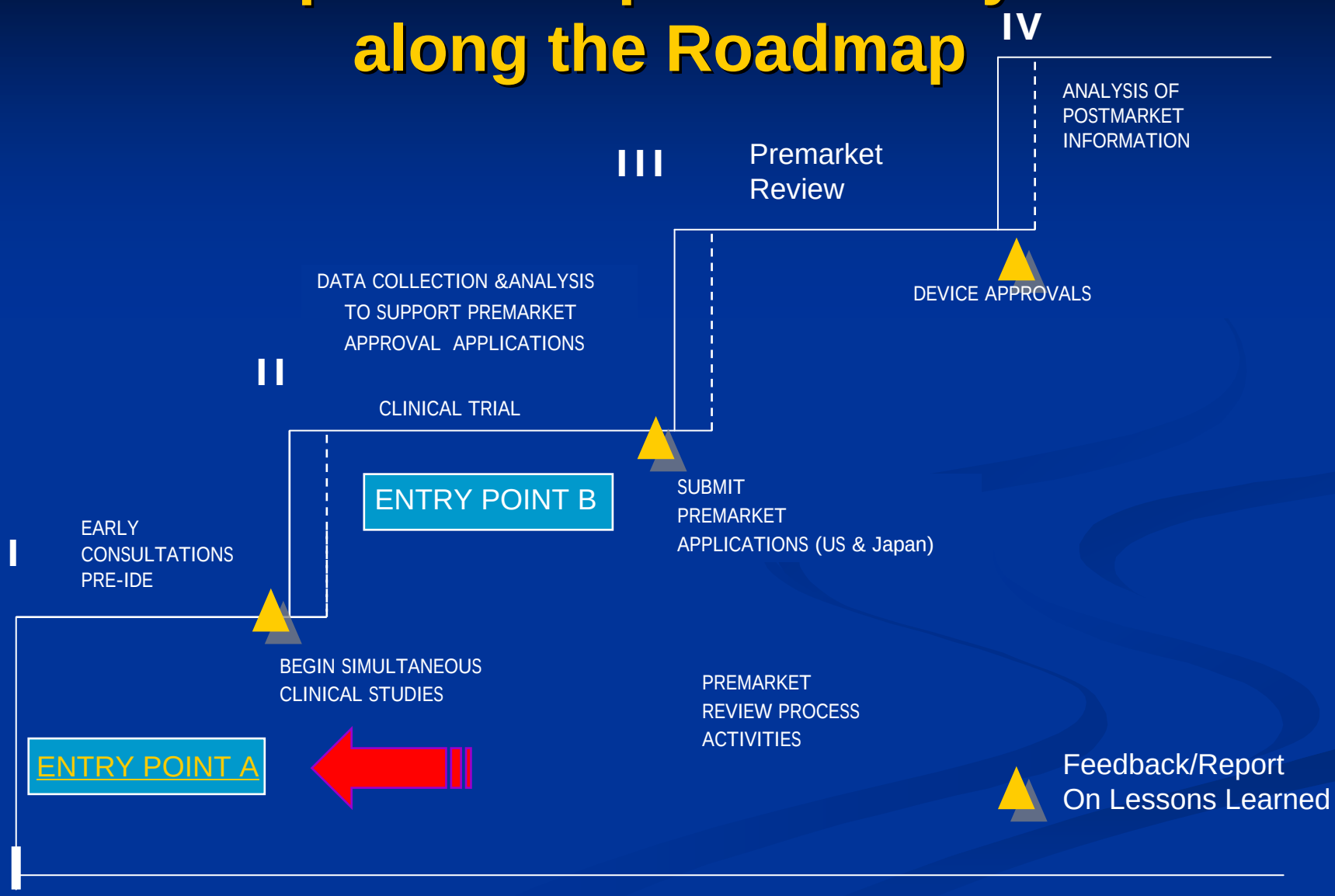
(2) There should be a Public Health Benefit
- Sponsor to provide justification for how their product will have a significant public health benefit (*example*: unmet medical need)
- FDA and MHLW/PMDA must both agree on benefit

(3) Pre-clinical testing should be complete enough to allow clinical trial initiation at the time of IDE submission / Clinical Trial Notification.

(4) Compliance, GMP/QMS issues etc., should have similar progress on both the US and Japanese regulatory fronts at the time of market application

(5) Development status of the product is similar in the US and Japan.

Development Steps and Entry Points along the Roadmap



Collaborative Consultation and Review Scheme

ENTRY POINT A

I

- Sponsor expresses interest?
  - Contact FDA and PMDA/MHLW (pre-IDE Meeting or Early Consultations)
- **Is There a Public Health Benefit?**
  - Sponsor to provide a justification for how their product will have a public health benefit
  - FDA and PMDA/MHLW must both agree on benefit
- Teleconference between FDA and MHLW/PMDA (without Industry)
  - Email MHLW/PMDA or FDA to share information or opinions
  - Email Agenda Prior to Teleconference
  - Ask for a Go / No Go decision via email after teleconference
- Discussion of pre-clinical testing such that adequate testing will be conducted to allow clinical trial initiation
- Sponsor should start thinking about any differences in compliance and manufacturing issues between US and Japan
- If FDA and PMDA/MHLW both agree the product can be eligible for the Scheme, sponsor provides POC proposal to WG, who will bring it to the SC for approval

Collaborative Consultation and Review Scheme

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II

- Sponsor to sign letters to permit trade secret information sharing between FDA-MHLW/PMDA
- Sponsor to submit proposal on clinical trial time frame and details of clinical plan to FDA-MHLW/PMDA
- Pre-clinical testing must be adequate enough to support clinical trial initiation in both countries
- Sponsor commits to provide the same core information to FDA-MHLW/PMDA
  - ➢Flag any differences in the information provided
- Schedule teleconference to discuss proposal.
- Collaborative interactions between FDA-MHLW/PMDA and/or sponsor (via teleconference, email, fax, etc.)
- Submit IDE to FDA or Clinical Trial Notification to MHLW/PMDA for review and appropriate regulatory decisions
- Initiation of US-Japan Clinical Trials (if approved in both countries)
- Compliance, GMP issues etc., should have similar progress on both the US and Japanese regulatory fronts
- Pre-clinical testing must be adequate enough to support a Market Application for both countries.

III

- "Parallel" submission of Market Application
  - ➢Sponsor commits to provide the same core information to FDA-MHLW/PMDA
  - ➢FDA-MHLW/PMDA conducts review of marketing application and exchange views

IV

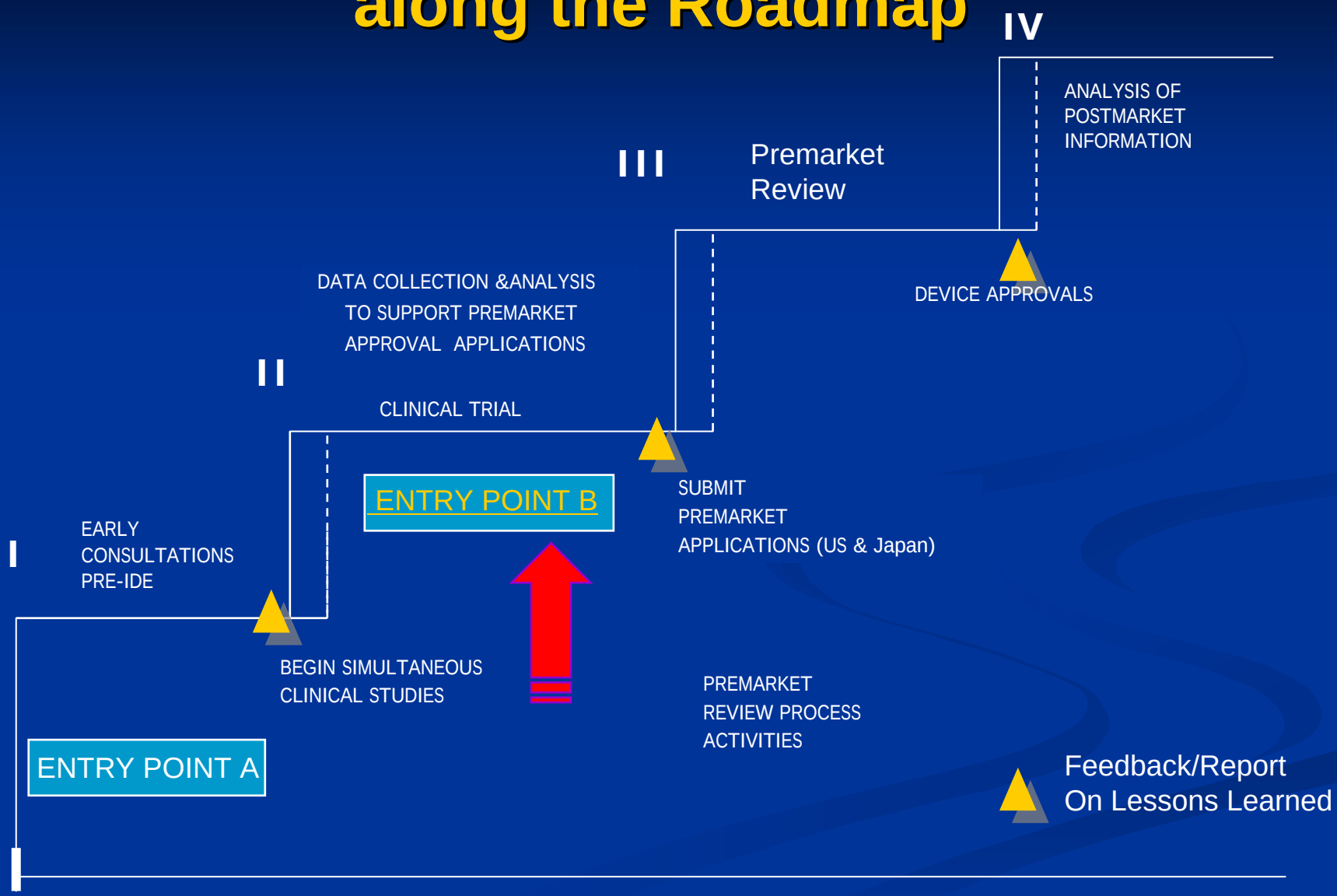
- **GOALS:**
  - ➢Appropriate regulatory decisions made by FDA and MHLW/PMDA , ensuring each Authority's independence.
  - ➢More robust review and decision making after due consideration to diverse scientific and regulatory views of regulators on actual submission.

V

- Sharing of Post Market Information

15

Development Steps and Entry Points along the Roadmap



ENTRY POINT B

II

Collaborative Consultation and Review Scheme

All criteria for HBD induction at Entry point A must be met prior to induction at Entry Point B

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- Sponsor to sign letters to permit trade secret information sharing between FDA-MHLW/PMDA
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V

- Sharing of Post Market Information

HBD Think Tanks and shared meetings provide ideas and recommendations pertinent to aspects of future planning and strategy