



# Harmonization, Convergence, and ICH Reform

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# Harmonization and Convergence

## ▶ Regulatory Harmonization

- The process by which the interpretation and/or application of technical guidelines can be made **uniform or mutually compatible**. (FDA CBER)
- Harmonization of technical requirements for medicines regulations, i.e. legislation, guidelines, procedures, etc. (WHO)

## ▶ Regulatory Convergence (APEC)

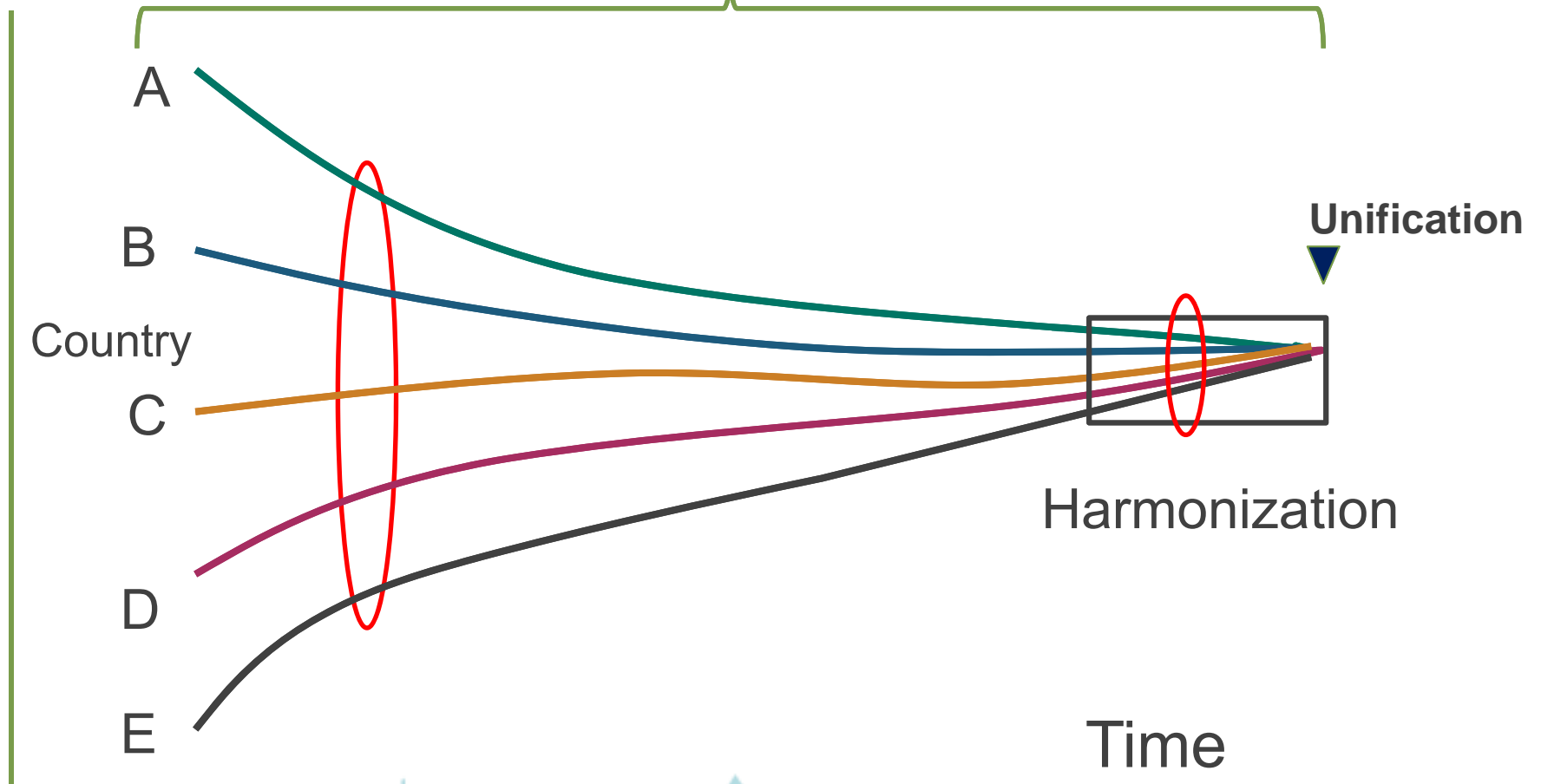
- Represents a **process** whereby regulatory requirements across economies **become more similar or aligned over time** as a result of the gradual adoption of internationally recognized technical guidance documents and standards.
- Does not represent harmonization of laws and regulations, which is not necessary to allow for the alignment of technical requirements and greater regulatory cooperation.



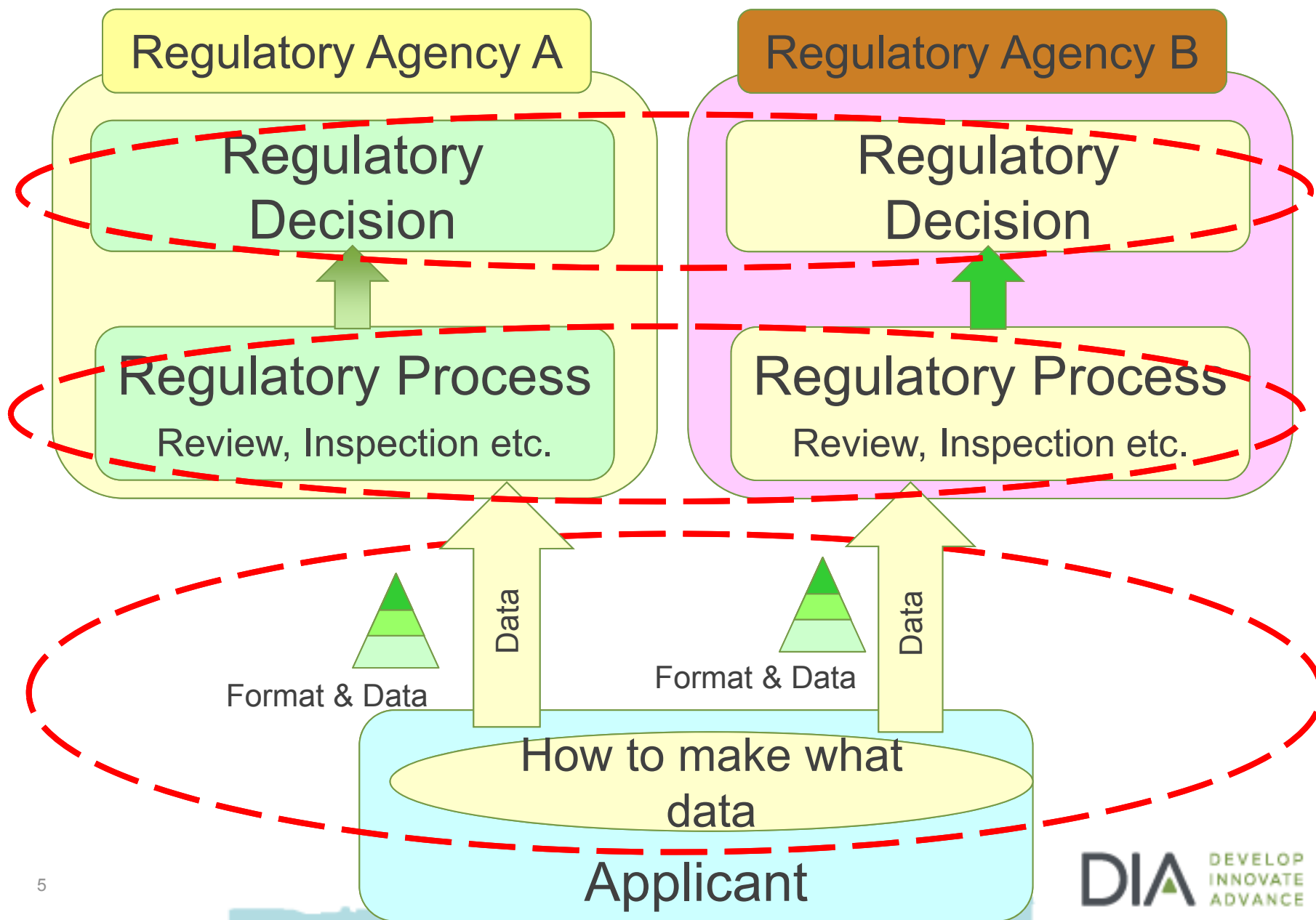
# “Convergence” and “Harmonization”

Regulation

Convergence



# What to harmonize?



# Different Level of Convergence/Harmonization and Guidelines

## ICH:

- Q1A: Stability Testing of New Drug Substances and Products
- Q2: Validation of Analytical Procedures: Text and Methodology

## GHTF

- SG1 Definition of the Term 'Medical Device'

## IMDRF:

- IMDRF/MDSAP WG/N3FINAL:2013: Requirements for Medical Device Auditing Organizations for Regulatory Authority Recognition
- IMDRF/MDSAP WG/N4FINAL:2013: Regulatory Authority Assessor Competence and Training Requirements



# Confusion

1. “Convergence” does not necessarily mean “similar,” can even mean “quite different.”
2. What is being converged/harmonized?
  - “After 20 years of ICH, why doesn’t PMDA rubberstamp FDA’s approval?”
  - “Because it’s CONVERGENCE, all the authorities should make the same decision; “Approved once, marketable everywhere!””



# Challenges for ICH and Its Reform





# Challenges

(ICH has been highly successful, but...)

## 1. Changing Environment

Globalization of venues/stakeholders involved in R&D, Manufacture, Distribution, consumption, etc.

## 2. Regulators' role and transparency

- “huddled up with industry behind the closed door?”
- Regulatory documents (guidance) should be made by regulators.

## 3. Outsiders' frustration

Poor “global implementation” of basic ICH Guidelines, e.g. Q7 (API GMP), E6 (GCP).



# How ICH Guidelines are implemented

The screenshot shows the ICH website header with the logo and tagline 'ICH harmonisation for better health'. Navigation links include 'Contact', 'Glossary', 'FAQs', and 'Log In'. A menu bar contains 'Home', 'About ICH', 'Work Products', 'Meetings', 'Training', and 'Newsroom'. A search bar is labeled 'Search Our Site'. The main content area is titled 'Quality Guidelines' and includes a breadcrumb trail: 'ICH Guidelines / Work Products / Home'. A paragraph describes harmonisation achievements in the Quality area, mentioning pivotal milestones like stability studies and GMP risk management. A link is provided to 'Zip with all ICH Quality Guidelines in word format'.

The screenshot shows a table titled 'Stability Q1A - Q1F'. The table has columns for 'Code', 'Document Title', and 'Previously coded'. The entry for 'Q1A(R2)' is expanded to show 'Stability Testing of New Drug Substances and Products'. The 'Description' field contains text about the guideline's revision and its application to climatic zones. The 'Implementation' field is circled in red and lists the adoption dates for EU, MHLW, and FDA. A callout box on the right indicates the guideline was finalized in February 2003 and provides a PDF icon and the code 'Q1A(R2)'.

Code	Document Title	Previously coded
Q1A(R2)	<b>Stability Testing of New Drug Substances and Products</b>	Q1A
Description	This Guideline has been revised a second time and has reached <i>Step 4</i> of the ICH process in February 2003. This Guideline provides recommendations on stability testing protocols including temperature, humidity and trial duration for climatic Zone I and II. Furthermore, the revised document takes into account the requirements for stability testing in Climatic Zones III and IV in order to minimise the different storage conditions for submission of applications.	
Implementation	<i>Step 5</i>	
EU	Adopted by CPMP, March 2003, issued as CPMP/ICH/2736/99	
MHLW	Adopted 3 June 2003, PFSB/ELD Notification No. 0603001	
FDA	Published in the Federal Register, 21 November 2003, Vol. 68, No. 225, p. 65717-18	

- Implementation : *Step 5*
- EU : Adopted by CPMP, March 2003, issued as CPMP/ICH/2736/99
- MHLW : Adopted 3 June 2003, PFSB/ELD Notification No. 0603001
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# Focus of Reform

1. Governance and transparency
  - regulators' role
  - transparency and openness of ICH and its processes
2. International outreach:
  - involvement of other regulators and global industry sectors that are affected by ICH guidelines
3. Funding:
  - ICH less dependent on industry funding
4. Legal entity:
  - the current informal setting becomes difficult



# First Step of The Reform

1. New Procedures of adopting guidelines (2012)
  - Role of Regulators enhanced
  - Regulators decision to take topics, Regulatory Chair, etc.
2. Transparency
  - Agendas and minutes of the Steering Committee meetings, Work plans of EWGs, etc. published on ICH Website
3. Health Canada and Swissmedic becoming regular Steering Committee member (2014)



# New Working Groups

Based on its 5-year plan to revitalize and further develop a set of guidelines, the following new WGs were established in 2014:

- Q12 EWG – new guideline on life cycle management
- E 17 EWG- new guideline on Multi Regional Clinical Trials
- E18 EWG- new guideline on Genomic sampling
- S11 EWG- new guideline on nonclinical safety testing



# Reform currently being discussed



# Governance under New Legal Entity

## 1. Structure

- Assembly --- decision making
- Management Committee --- administrative matters.

## 2. Membership

- Assembly
  - Members : drug regulatory authorities and international pharmaceutical industry associations
  - Observers : authorities and organizations
- Management Committee
  - initially Permanent Members (current SC members) and subsequently also Elected Members.

# Assembly Members (Qualification, etc.)

## 1. Regulators

- Engagement in the ICH Process
  - regular attendance, past appointment of experts
- Application of ICH Guidelines
  - *Q1: Stability Testing guidelines*
  - *Q7: GMP for Active Pharmaceutical Ingredients*
  - *E6: Good Clinical Practice guideline*

## 2. Industry associations

- An international pharmaceutical industry association representing members from more than 3 continents
- Engagement in the ICH Process
- Impact of ICH Guidelines

## 3. Observers



# Assembly Members (Rights and Duties)

## 1. Regulators

- Participation in decision making (consensus (preferred)/ vote)
- Appoint experts in Working Groups
- **Commit to implement ICH guidelines**

## 2. Industry associations

- Attend the ICH Assembly meetings
- Appoint experts in Working Groups developing ICH Guidelines which will affect that Member
- Participation in decision making with some exceptions, e.g. adoption of ICH guidelines
- **Support compliance with ICH guidelines**



# Next Steps

1. Reform to be completed in January, 2016
2. As soon as the legal entity has been established, any party eligible as member can apply for membership. Decisions on admission by the Assembly.
3. Funding
  - initially by the Permanent Members of the Management Committee (the current SC members)
  - then by all the Assembly members (membership fee).



# Discussion

1. More sophisticated guidelines will be made, whereas the membership will expand to not-so-sophisticated authorities.
2. ICH responsible for the past basic guidelines' implementation by new members?
  - Expectation from outside
  - To stay relevant, ICH cannot be ivory-towerish (?)
  - More emphasis on Training (?)



# Thank You

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Question?

