Harmonization, Convergence, and ICH Reform

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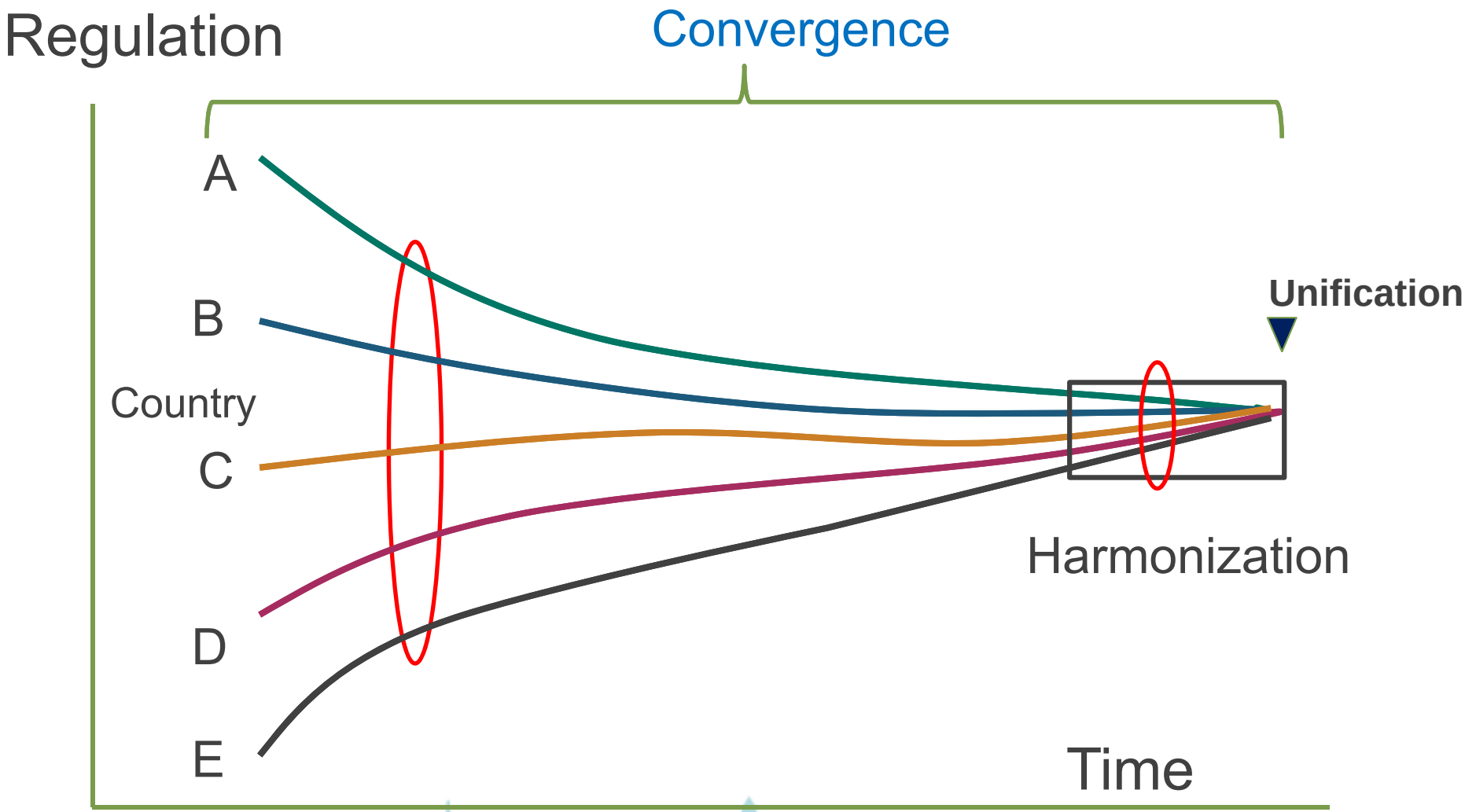
Harmonization and Convergence

- 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”



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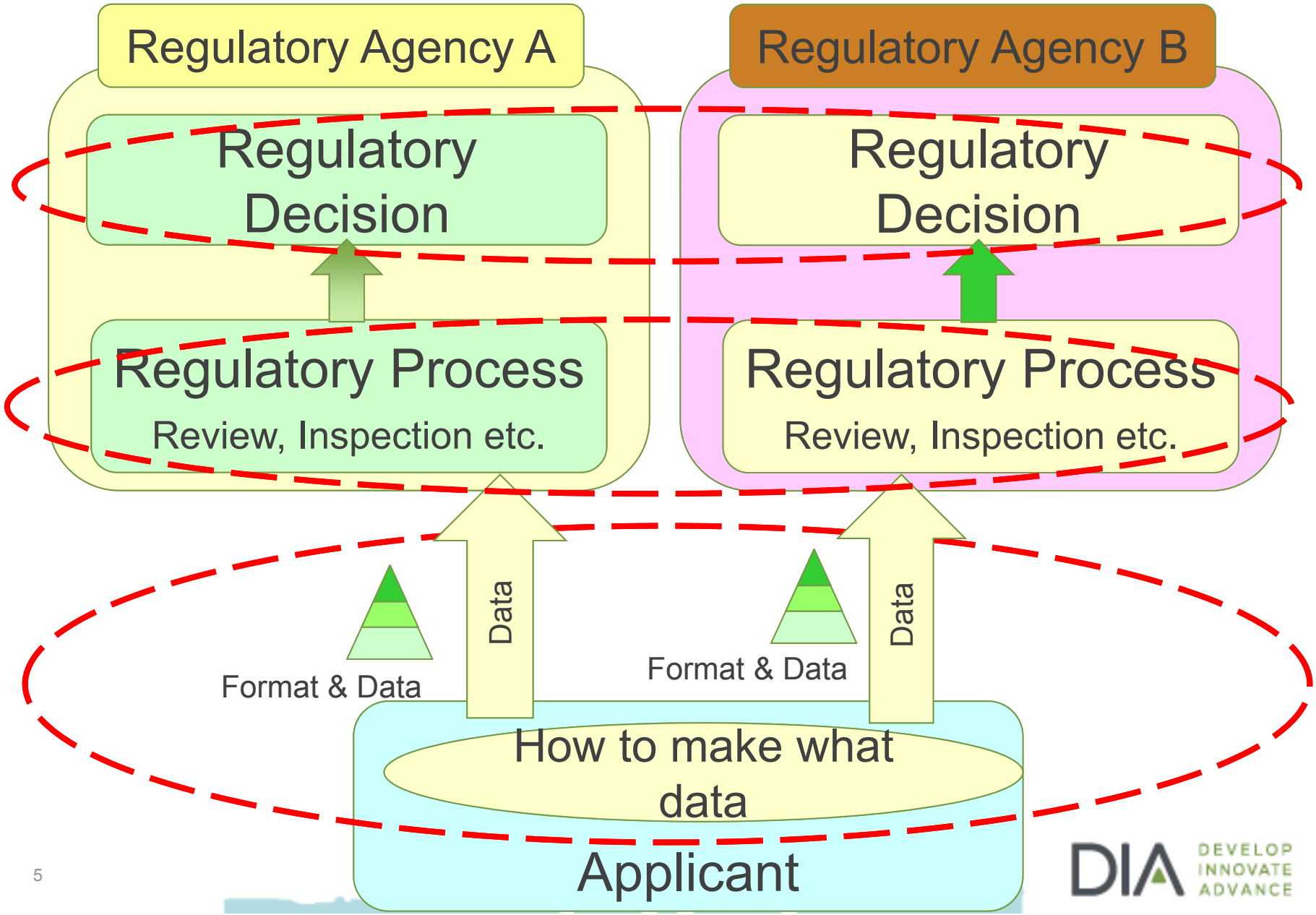
What to harmonize?



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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

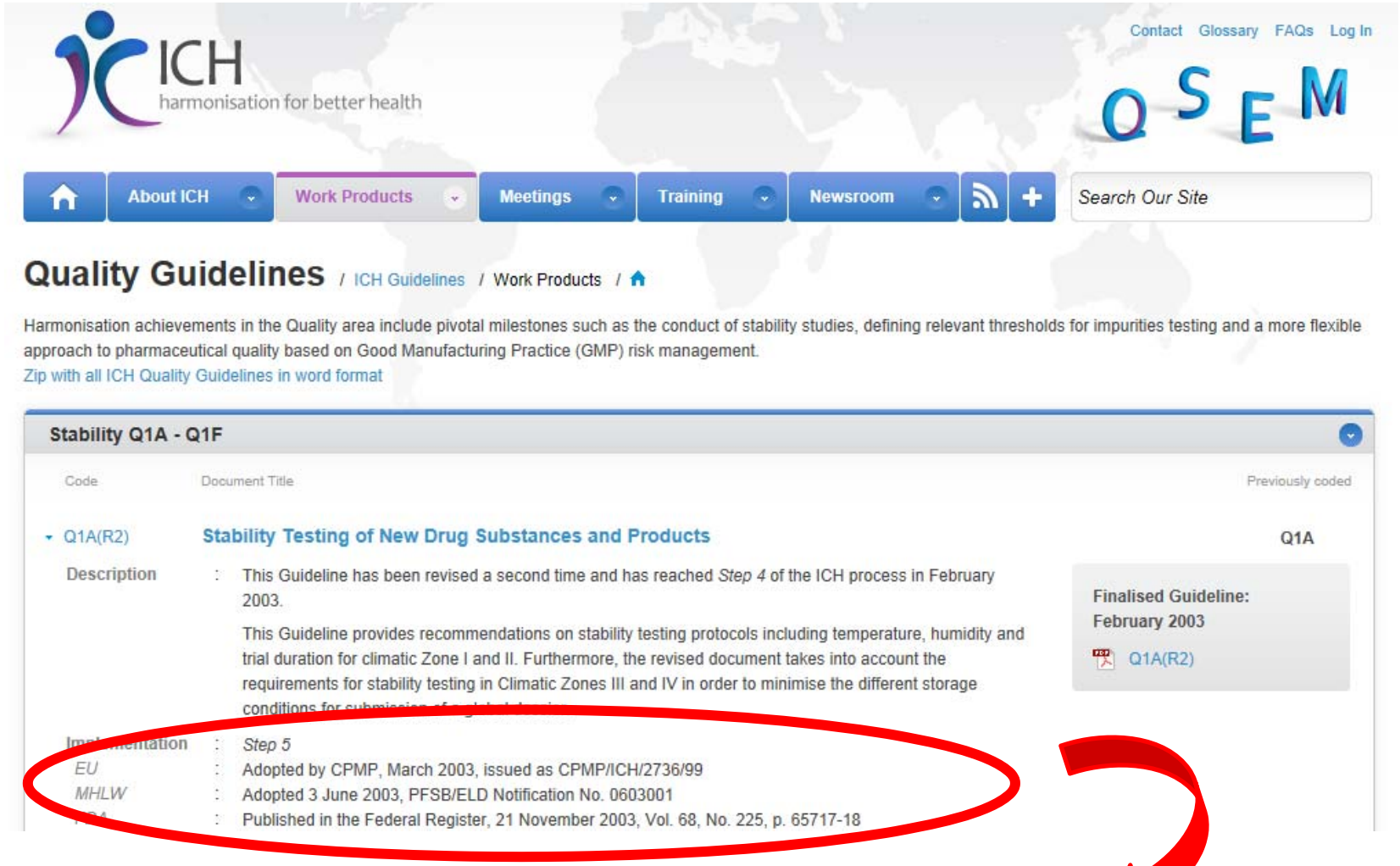
   Globalization of venues/stakeholders involved in R&D, Manufacture, Distribution, consumption, etc.

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



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

FDA : Published in the Federal Register, 21 November 2003, Vol. 68, No. 225, p. 65717-18

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
   - Partcipation in decision making (consensus (prefereed)/ 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 complicance 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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