ICH Q4B
Expert Working Group

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

Presentation Outline

- Short History and Overview of ICH Q4B
- The Pharmacopoeias and the Regulators
- The Q4B Process and Annex
- Interaction: Q4B Expert Working Group (EWG) and PDG
- November 2008 Meeting Outcomes and Current Activities for the Q4B EWG

Background

- The harmonisation of specific compendial test chapters has been considered as critical by the ICH Steering Committee to attaining full utility of the ICH Q6A guideline (1998).
- Industry requested ICH SC to create an EWG to address how the regulatory authorities (3 regions) will recognise the interchangeability of harmonised pharmacopoeial chapters from Ph. Eur./JP/USP (PDG) – July 2003
- ICH SC established Q4 EWG with a scope to address 11 General Test Chapters discussed during development of ICH Q6A Guideline - November 2003
- SC approves Q4B Work Plan – April 2004

Background (Continued)

- SC approves development of an ICH Guideline with topic specific annexes – June 2004
- Q4B EWG begins evaluating PDG harmonised text – November 2004
- Step 2 ICH Q4B Core Guideline approved by SC – June 2006
- 1st Annex (Residue on Ignition/Sulphated Ash) approved (ICH Step 2) – June 2006
- Regulatory consultation (ICH Step 3) on Core Guideline completed by each regulatory region (60-day comment period) – October 2006

Background (Continued)

- Core Q4B Guideline reworked based on constituent comments; ICH Step 4 documents finalised for ICH signoff – November 2007
- Consist of “parent guideline” Step 4 Q4B – ERPTUIR (new title)
- “Evaluation and Recommendation Pharmacopoeial Texts for Use in the ICH regions”
- First Annex No. 1 approved at Step 4 – ROI/Sulphated Ash – November 2007
- SC approves limited expansion of scope – November 2008

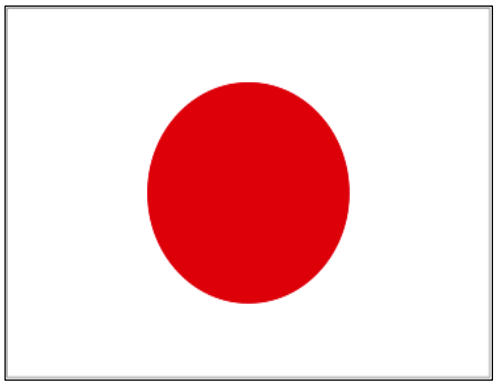
ICH Q6A-related General Chapters

Dissolution	Disintegration
*Uniformity of Content	*Uniformity of Mass
Extractable Volume	Particulate Matter
Sterility	Microbiological Quality
Bacterial Endotoxins	ROI/Sulphated Ash
Colour and Clarity (per ICH SC, work will just be on "Colour")	

Above chapters identified as the basis of Q4B activity

* Combined to Uniformity of Dosage Units

The Pharmacopoeias and the Regulators
Different Approaches for Moving Forward



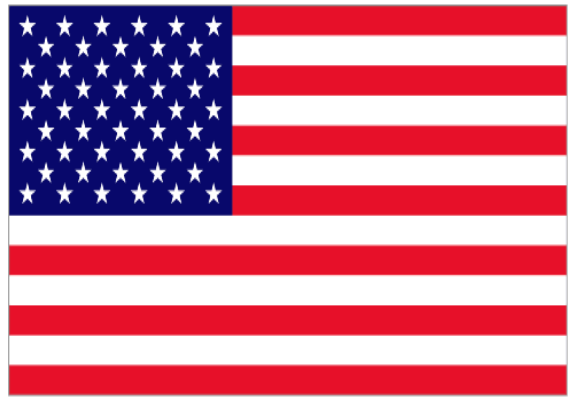
JP
(PMDA)

Governmental

Ph. Eur.
(EDQM)

Governmental

Partnership



USP

Independent of Government

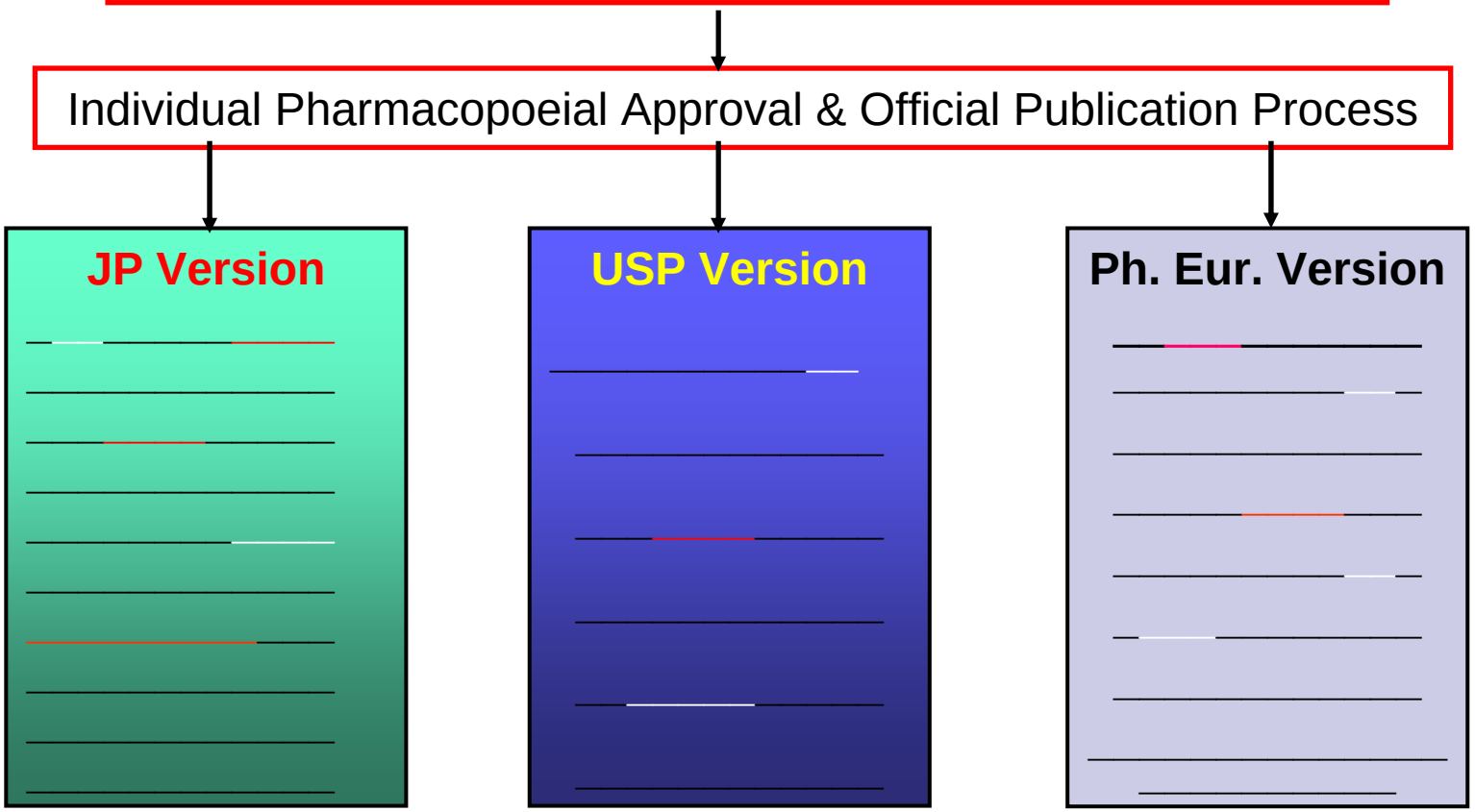
Not for profit organisation

ICH

The Q4B Process
Value of the Q4B Activity

- A component of international harmonisation efforts to assist in common specifications
- A savings in time, effort and cost
  - Industry: to globally unify testing strategies [for applications and other regulatory (compliance) needs] – one test rather than three
  - Regulators: to reduce or eliminate the need to go through a justification procedure as to the use of other compendial methods (done one time to eliminate repetitive justifications)

PDG Process Results in Harmonised Text



Challenge to regulators: Do differences impact on the ability to achieve a result with the same accept and reject capability? Are they interchangeable?

Q4B Process Steps

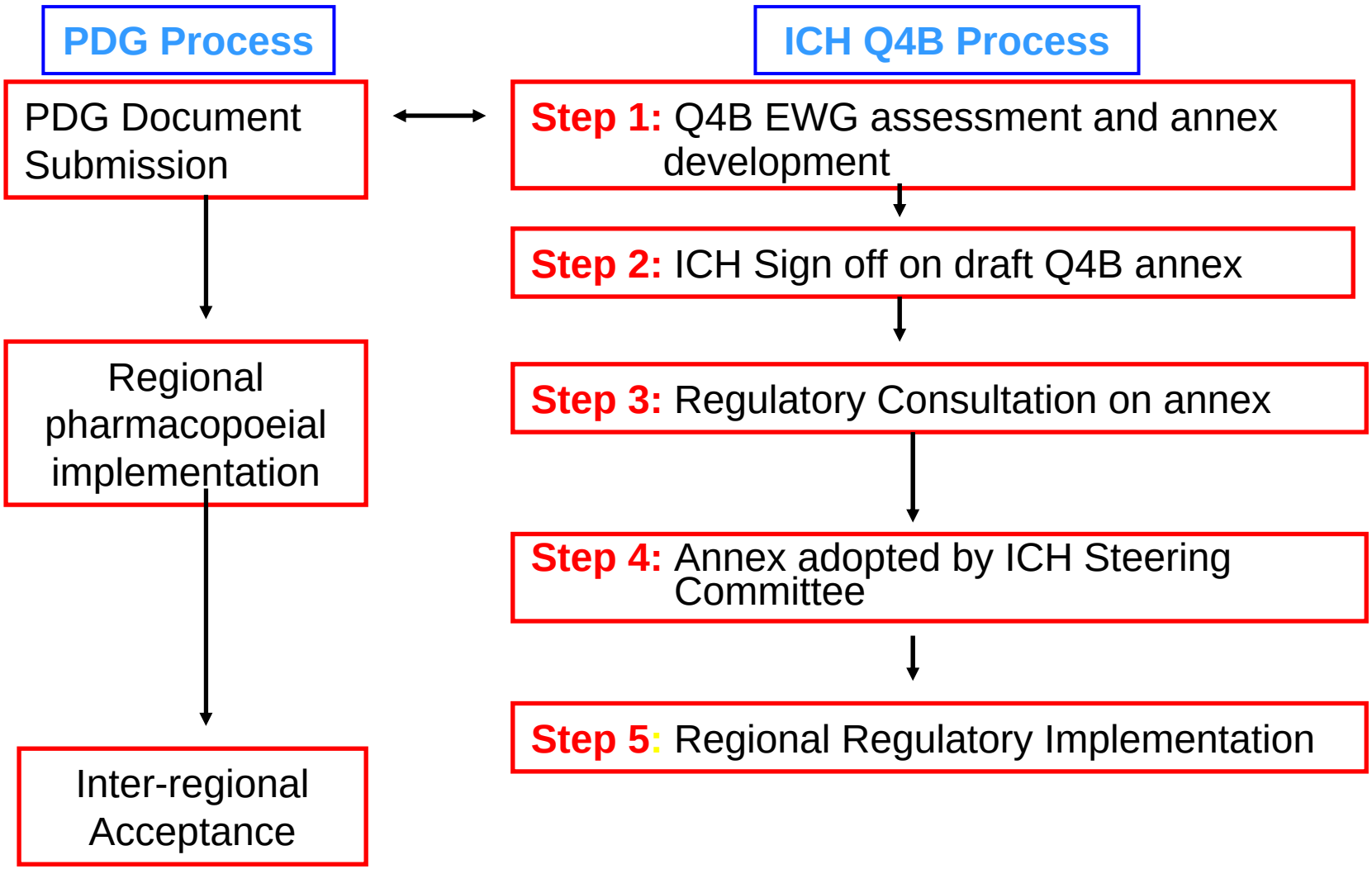
FOR EACH TOPIC:

- PDG provides to Q4B Expert Working Group:
  - PDG-harmonised text
  - JP/Ph. Eur./USP draft versions of how harmonised text will be implemented in their compendia
  - Briefing note to delineate any local differences or potential issues
  - Printing timelines to move approved pharmacopoeial text to official status
- Q4B member parties bring the documents back to their constituents for independent evaluation

Q4B Process (continued)

- Q4B EWG reviews the evaluations
- Issues discussed within Q4B EWG for possible resolution
- Evaluation results and possible resolution mechanisms conveyed back to and/or discussed with PDG
- Once issues are resolved, Q4B EWG recommends approval (ICH Step 2) to the ICH SC
- Start of Annex process – Moving the Q4B evaluation outcome into the regulatory mechanisms for each region

Topic Specific Annex Process



Q4B EWG and PDG Interaction

- Dedicated time (set aside) at each formal ICH EWG meeting venue to discuss issues
- Stakeholder partnering – all parties focused to achieve interchangeability
- Direct feedback mechanisms to resolve issues
- Clear delineation of what steps are necessary for problem resolution
- Success more likely versus single, independent efforts

Q4B Successes -- November 2007 Yokohama

Primary objectives achieved:

- Core Q4B Guideline (establishing Q4B Process)

  Completed and signed off at ICH Step 4 -- Step 5 Regional Implementation

- Title for the Q4B Core Q4B Guideline

The Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions

- First Annex No.1 – ROI/Sulphated Ash completed at Step 4

Current Status – Q4B EWG ICH November 2008, Brussels

- Step 2 documents moved to Step 4 sign-off and Step 5 Regional Implementation:

  (Annexes 4A, 4B, 4C)

  (Annex 5 – completed but hold for sign-off)
- Additional annexes moved to Step 2 sign-off:
  - Annex 6 UDU
  - Annex 7 Dissolution Test
  - Annex 8 Sterility Test

Limited Scope Expansion ICH November 2008, Brussels

Steering Committee approved addition of 5 new PDG-harmonised general chapters to the Q4B process:

1. Tablet Friability
2. Bulk and tapped density
3. Analytical Sieving
4. Capillary Electrophoresis
5. PAGE

Current Status – Q4B EWG

ICH November 2008 Meeting, Brussels, Belgium

Completed Annexes to the Core Q4B Guideline

- #1 Residue on Ignition/Sulphated Ash — **Step 5 Regional Implementation**
- #2 Extractable Volume — **Step 5 Regional Implementation**
- #3 Particulate Matter — **Step 5 Regional Implementation**
- #4A, 4B, 4C Microbiological Tests — **Step 5 Regional Implementation**

Current Status 2009 (continued)

Work in Progress

- #5 Disintegration Test **.....Draft Step 4, waiting to be signed [Spring 2009]**
- #6 Dissolution Test
- #7 Uniformity of Dosage Units

Signed at Step 2 – Regulatory Consultation (ICH Step 3)

- #8 Sterility Test
- Bacterial Endotoxins
- Colour

Submissions awaited from PDG

Acknowledgements

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