International Harmonisation of pharmacopoeial monographs

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- Need for pharmacopoeial harmonisation ?
- Who is PDG ?
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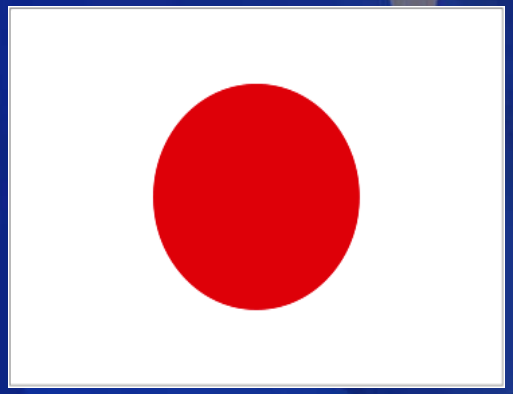
Pharmacopoeial Harmonisation

- Starting point: Industry is more and more developing products intended for submission worldwide
- Aim: “single set of global specifications” (see ICH Q6A Guideline objective)
- Avoid redundant testing by suppliers and pharmaceutical industry to meet differing standards

PDG: Different regulatory environments



JP

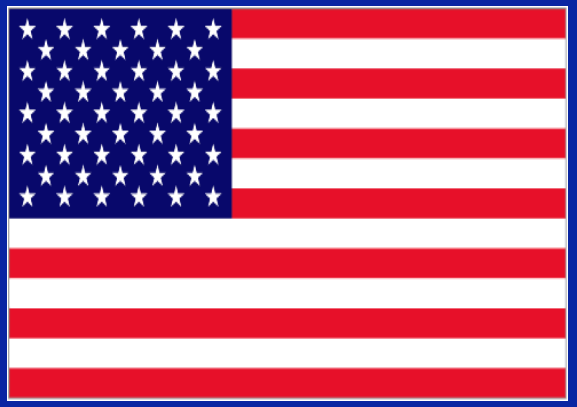
PMDA/ MHLW

Governmental

Ph.Eur.

EDQM,Council of Europe

Inter-governmental



USP

Independent of Government

The PDG: its mission

Drives International Harmonisation of requirements in parallel and in co-ordination with the ICH activity

Has focused on:

- Excipients
- General Chapters

PDG process

- Stage 1: identification
- Stage 2: investigation
- Stage 3: expert committee review of first draft
- Stage 4: forum publication
- Stage 5: consensus
- Stage 6: regional adoption, implementation and indication of harmonisation
- Stage 7: inter-regional acceptance (by Q4B)

PDG procedure stage 6

- Stage 6: Regional adoption and implementation
- 6A: Adoption and publication
- 6B: Implementation
- 6C: Indication of harmonisation
  - but highlight residual differences
  - (Ph.Eur. chapter 5.8)

Achievements: excipients

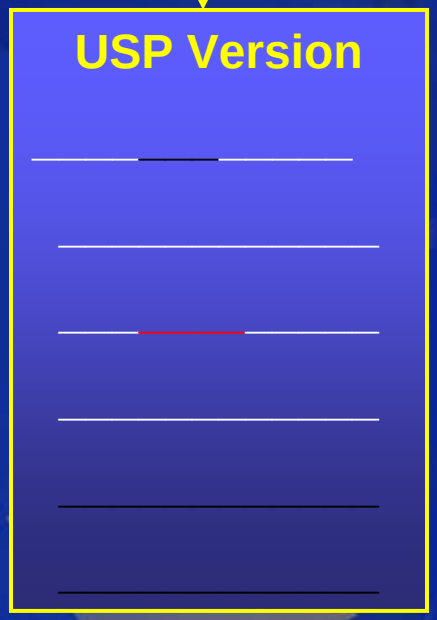
- 40/62 Excipients monographs
- Harmonisation by attribute:
  - Recognise sticking points (Non-harmonised-attributes)
  - Publish “core” harmonisation result
- Co-operation with Tri-PEC

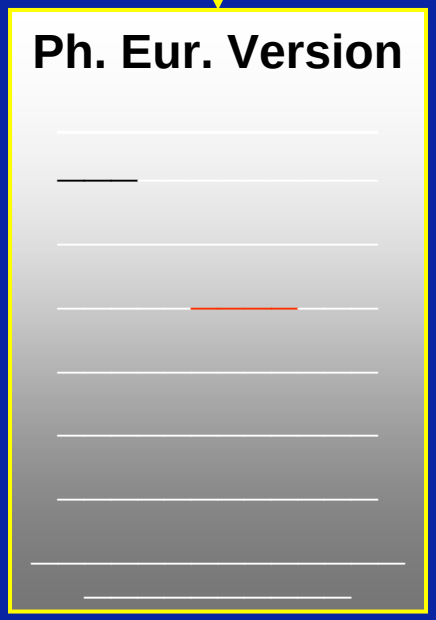
Achievements: General Chapters

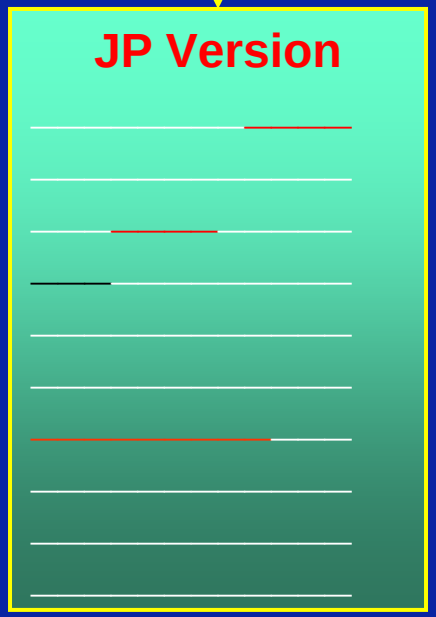
- 27/35 General Chapters
  - 10 of 11 Q6A general chapters
  - 6 biotech general chapters
  - 11 powder characterisation general chapters

PDG Process Results in Harmonised Text

Individual Pharmacopoeial Approval & Official Printing Process







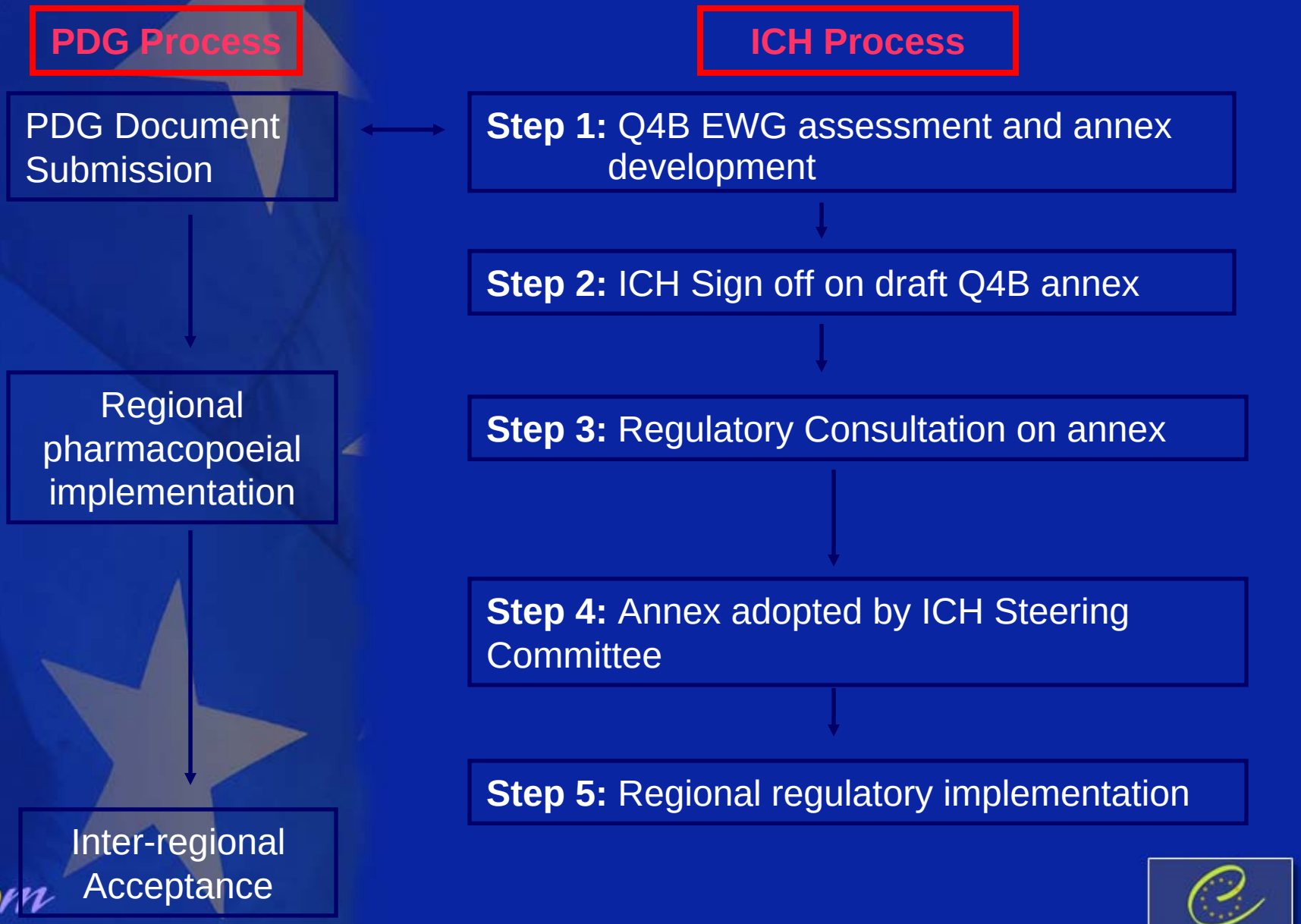
Challenges for the regulators:

Do differences impact on the ability to achieve same result with same accept/reject capability? Are they interchangeable?

Why evaluation by ICH EWG Q4B ?

- Despite PDG efforts general chapters remained effectively unharmonised
- Implementation of sign-off texts as agreed ?
- Need for formal declaration of regulatory acceptance to be expedited, to facilitate achieving true harmonisation in practice
- Considered critical to attain full utility of ICH Q6A GL
- Industry and regulators promoted such greater cooperation to ICH SC 2003

Q4B Topic Specific Annex Process



PDG Achievements in Brussels

Sign Off Topics – GeneralChapters/Excipients

- Laser diffraction measurements of particle size (new)
- Carmellose (new)

- Dissolution Testing: Rev. 2
- Bacterial Endotoxin: Rev. 1

- Additional minor revisions

PDG Achievements in Brussels

- Process improvements since Portland:
  - Small working group to monitor and communicate PDG topics on a regular basis beneficial for progress
  - Development of online repository of PDG documents ongoing
  - Continuous Process Improvement as standing agenda item

Current Status of Q4B evaluation

Residue on Ignition (Annex 1) step 5

Extractable Volume (Annex 2)

Particulate Matter (Annex 3) step 4

Microbial Contamination
(Annexes 4A, 4B, 4C)

Disintegration (Annex 6)

Uniformity of Dosage Units (Annex 5)

Dissolution (Annex 7) step 2

Sterility (Annex 8)

Current Status of Q6A General Chapters

- Bacterial Endotoxins signed-off in PDG, to be submitted to Q4B in July 2009
- Colour: Request for more information from JP in order to evaluate impact on Japanese industry

Indication of Harmonisation Status

PDG agreement to review previously published harmonised excipient monographs to

- indicate harmonisation status
- highlight residual differences
- achieve harmonisation at a higher level

Interaction PDG/Q4B

- SC approved future Q4B activities:
  - Tablet friability (PDG Stage 6)
  - Analytical Sieving (PDG Stage 6)
  - Bulk Density and Tapped Density (PDG Stage 6)
  - Capillary electrophoresis (PDG Stage 6)
  - Polyacrylamide gel electrophoresis (PDG Stage 6)

Interaction PDG/Q4B

- Possible future PDG activities under discussion:
  - Chromatography
  - pH
  - Spectrophotometry (including NIR)
  - Water determination

Summary

- PDG harmonisation process improved
- Regulatory scrutiny of sign-off and published texts (ICH Q4B) has "sharpened" the process
- First texts "can be used as interchangeable" in the ICH regions
- Scope of Q4B widened
- Work on dosage-form general chapters and excipients is the priority
- Currently EP/USP bilateral pilot project on prospective API harmonisation

Thank you