

The European Pharmacopoeia & International Harmonisation

Dr. Claude Coune

Head of the Publications & Multimedia Department
EDQM, Council of Europe



International Harmonisation

- Increasing exchanges on worldwide market
- 1989/1990:
 - 25th anniversary of the EP in Strasbourg
 - International conference in Tokyo
 - Excipient International conference in Orlando
- 1990: Creation of PDG (PhEur/JP/USP)

The PDG: its members ⁽¹⁾

Pharmacopoeias have different status:

- **USP** -Independent, legal status by FD&C Act
- **Ph Eur** - **Intergovernmental** legal status conferred by International European Convention under aegis of Council of Europe
 - **relationship to licensing process**
- **JP** - Part of Ministry of Health, Labour & Welfare (Status by Pharmaceutical Affairs Law)

The PDG: Ph. Eur. particularity ⁽²⁾

- Liaison with competent authorities is maintained by Ph. Eur. throughout the process
- Having to reaching consensus is part of daily work

The PDG: its mission ⁽³⁾

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

Has focused on:

- Excipients
- General Chapters

Achievements: excipients

- 36/62 Excipients monographs
- Harmonisation by attribute:
 - Recognise sticking points
 - Publish “core” harmonisation result
- Co-operation with Tri-PEC

Achievements: General Chapters

- 25/35 General Chapters
 - 11 of 12 Q6A general chapters
 - 6 biotech general chapters
 - 8 powder characterisation general chapters

The PDG procedure

- PDG is an informal group
- PDG Procedure is well defined but informal
- Formal procedure for each pharmacopoeia has to be maintained
- To ensure **rapid** publication of signed-off texts PDG procedure has been woven in to the Ph Eur procedure

PDG stages

- Stage 1: identification
- Stage 2: investigation
- Stage 3: expert committee committee review of first draft
- Stage 4: forum publication
- Stage 5: consensus \Rightarrow sign off text
- Stage 6: regional adoption and implementation in the 3 Pharmacopoeias
- Stage 7: inter-regional implementation by regulators of 3 regions (ICH-Q4B)

PDG procedure Stage 6

- Stage 6C Indication of harmonisation
 - Each pharmacopoeia will introduce a statement indicating the harmonisation status. Ph Eur and USP reference the corresponding text of the other PDG pharmacopoeias. JP references the harmonised text. In case of residual differences, these are indicated by a specific symbol (black diamond).

PDG procedure Stage 6

- Stage 6C Indication of harmonisation
 - Harmonisation is achieved when all pharmacopoeias have highlighted harmonisation and any residual differences, based on a general policy in the national or regional area.

The PDG procedure at regional levels

- Declaration of inter-changeability
 - Ph Eur: General Notices – General Chapter 5.8 Footnote and symbol ◆
 - USP: General Chapter <1096>, symbol ◆ + footnote symbol ◆
 - JP: MHW declaration + table in the information note, in JP declaration of harmonisation with the sign-off text, symbol ◆
- Maintenance Procedure
 - No unilateral revision

Status of chapter 5.8 ⁽¹⁾

- Pharmacopoeias are **slow** in publishing sign-off texts
 - Ph Eur: Implementation of sign-off text maximum 1 year + 4 months after sign-off
 - JP needs time for translation of sign-off text to Japanese and back into English
 - USP sometimes continues to publish USP local text after sign-off

Ph Eur will not indicate harmonisation before the 3 pharmacopoeias have published the sign-off text.

Status of chapter 5.8 ⁽²⁾

- Some of the Chapters are being evaluated by ICH Q4B

Ph Eur will not indicate harmonisation before ICH Q4B has evaluated interchangeability.

Relationship PDG / ICH

- PDG has participated in aspects of interest in Q1, Q2, Q3A, Q3C, Q5, Q6A and Q6B.
- PDG to meet in parallel to ICH
- PDG Work Programme brought in line with ICH objectives
- **Q4B** created for regulatory acceptance of harmonised texts

ICH Q6A guideline requested harmonisation of:

Uniformity of Mass

Disintegration

Particulate Matter

Extractable Volume

Microbial Contamination

Residue on Ignition/ Sulfated Ash

Uniformity of Content

Dissolution

Colour/Clarity

Sterility

Bacterial Endotoxins

Achievements: items Q6A

OK Q4B	Particulate Contamination (sub-visible particles) rev.1 Sulphated ash/ Residue on Ignition rev. 2 Extractable volume of parenteral preparation
Study Q4B	Microbial examination of non-sterile preparations Dissolution test Disintegration test Uniformity of mass/content
Sign-off	Sterility test
PDG	Bacterial endotoxins (to be revised) Colour (stage 3)

PDG stages

- Stage 1: identification
- Stage 2: investigation
- Stage 3: expert committee committee review of first draft
- Stage 4: forum publication
- Stage 5: consensus \Rightarrow sign off text
- Stage 6: regional adoption and implementation in the 3 Pharmacopoeias
- **Stage 7: inter-regional implementation by regulators of 3 regions (ICH-Q4B)**

Impact of harmonisation ⁽¹⁾

- Excipients: impact similar to the normal pharmacopoeia revision
- General chapters can have significant impact for users

Impact of harmonisation (2)

- Users often under-estimate the potential until late in the process
- Comments on Pharmeuropa/PF/JPF rarely give data on the impact of harmonisation
- Transition period may be necessary:
 - Uniformity of dosage units
 - Microbiological quality test methods

Impact of harmonisation ⁽³⁾

- Industry is supportive of the activities of the PDG and Q4B **but** finds the work much slower than expected
- PDG considers the achievements (59 signed off) over the last few years, **but** sign-off is only half way through the efforts...

What we need to do?

- Wherever possible, move faster
- Respect deadlines
- Increase transparency and impact awareness for users
- Pursue the work in the spirit of the ICH process

Thank you

