Prospective harmonisation of quality standards: A model for pharmacopoeial convergence

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Outline

- Background - Ph. Eur. and USP harmonisation
- How this differs from PDG harmonisation
- Advantages of effective pharmacopoeial collaboration
- Advantages of prospective harmonisation
- Pilot phase and post-pilot activities of prospective harmonisation to date
- Monograph elaboration for the Ph. Eur. and USP
- How Ph. Eur. and USP monographs can differ
- Which products are eligible for prospective harmonisation?
- Ph. Eur. and USP contact information
- Useful links to harmonisation overviews for the Ph. Eur. and USP

Background – Ph. Eur. / USP harmonisation

- **Aim:** similar standards in Europe / US
  - ↳ Beneficial for manufacturers; cost and time savings
- **PDG** launched in 1989

First draft → Official inquiry → Consensus → Regional adoption/Implementation → Inter-regional acceptance

- **Prospective harmonisation**
  - **Pilot phase** launched in 2008
  - 4 official monographs (Celecoxib, Montelukast sodium, Rizatriptan benzoate, and Sildenafil citrate)
  - **Post-pilot phase**
  - 19 official monographs (10 active substances and 9 medicinal products)
  - 22 in various stages of development
- **Continue to increase awareness and manufacturer participation**

Comparison with PDG harmonisation

	PDG Harmonisation	Ph. Eur. and USP Prospective Harmonisation
Goal	Align test procedures and limits to a common quality standard Texts do not have to be identical	
Launched	1989	2008
Participating pharmacopoeias	Ph. Eur., USP, JP, WHO (joined as observer in 2001)	Ph. Eur. and USP
Focus	Revisions to existing excipient monographs and general chapters	New active substance and medicinal product monographs for products still under patent
Process	Official procedure	Respective internal processes for monograph elaboration
Work initiation	Determined by the PDG	Manufacturers' request (subject to the agreement of the Ph. Eur. and USP)

Advantages of effective pharmacopoeial collaboration

PROMOTE

Access to quality medicines, leveraging global expertise

INCREASE

Visibility

Importance of pharmacopoeias

Value of public quality standards

FACILITATE

Global access to state-of-the-art industry technology

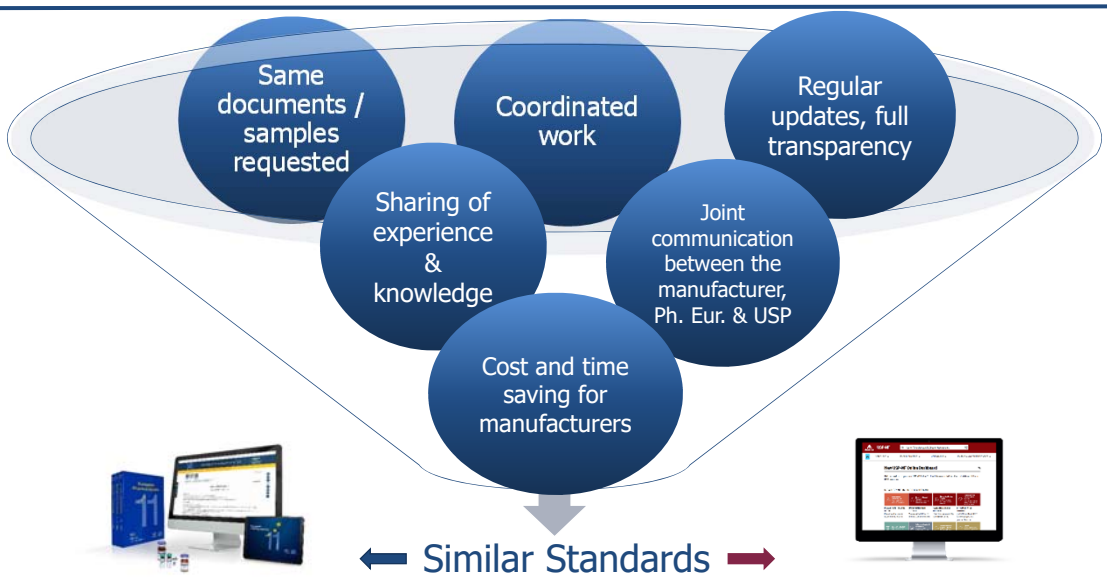
PRIORITIZE

Balance current paradigms and future trends

ENABLE

Global pharmaceutical trade

Advantages of prospective harmonisation



Monographs to date

Pilot phase
Celecoxib
Montelukast sodium
Rizatriptan benzoate
Sildenafil citrate

Post-pilot Active substance monographs
Aprepitant
Dronedarone HCl
Fingolimod HCl
Lacosamide
Prasugrel HCl
Raltegravir potassium
Regorafenib
Riociguat
Sitagliptin phosphate
Sorafenib tosilate

Post-pilot Medicinal product monographs
Dronedarone tablets
Lacosamide infusion
Lacosamide oral solution
Lacosamide tablets
Raltegravir chewable tablets
Raltegravir tablets
Riociguat tablets
Sitagliptin tablets
Sorafenib tablets

Ongoing projects
Brivaracetam – B. tablets –
B. injection or infusion – B. oral solution
Cabazitaxel acetone – C. concentrate for infusion
Dapagliflozin propanediol – D. tablets
Deferasirox
Etravirine – E. tablets
Fulvestrant injection
Mirabegron
Plerixafor – P. injection
Regorafenib tablets
Rivaroxaban – R. tablets
Teriflunomide – T. tablets
Ticagrelor – T. tablets

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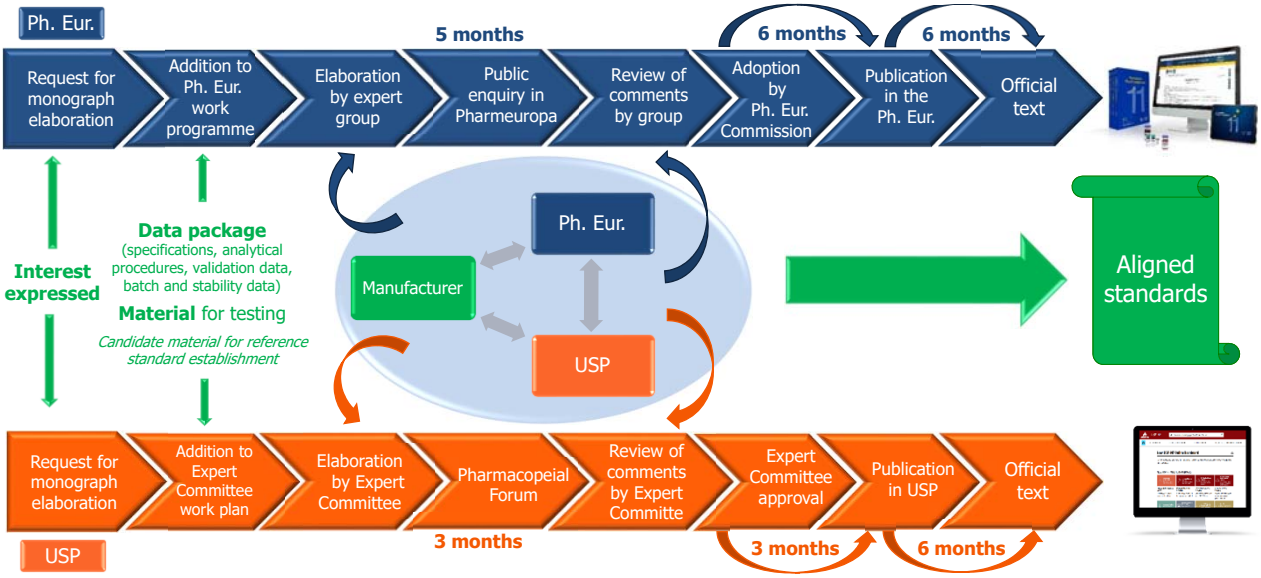
Ph. Eur. and USP monograph elaboration



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Some differences between Ph. Eur. and USP

Limits as approved by competent authorities (e.g. content, dissolution, impurities)	Limits as set in the individual pharmacopoeias	Dissolution test
Specific to the US market	Generally based on FDA approved limits	Several tests
Specific to the European market	Based on limits approved in Ph. Eur. member states (may be adapted based on batch/stability data)	One test

Solutions	System suitability tests (Tests for impurities / Assay)	Impurity identification
Concentrations and/or exact amounts to be used (masses, volumes)	Resolution, sensitivity, RSD in monographs	Relative retentions and/or reference standards for impurities
Generally exact amounts to be used (masses, volumes)	Resolution or p/v ratio in monographs Generally, sensitivity & RSD rely on *2.2.46*	Reference standards for specified impurities and those used for SST No relative retentions for unspecified impurities

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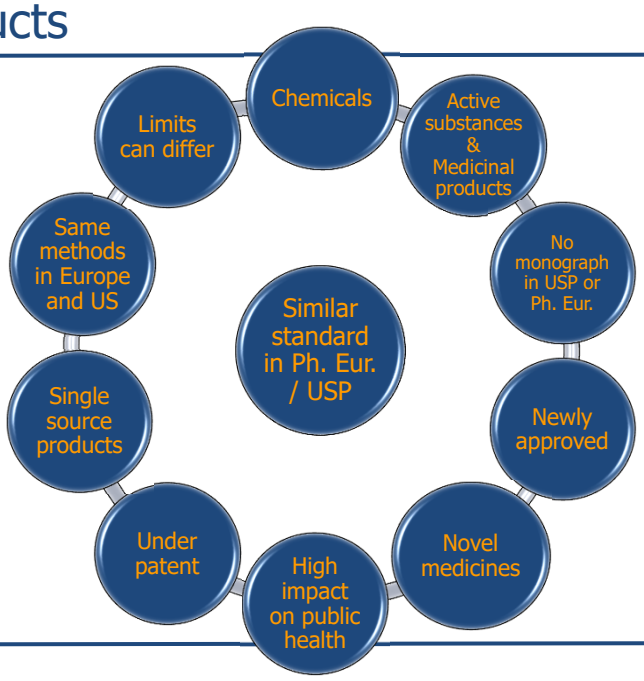
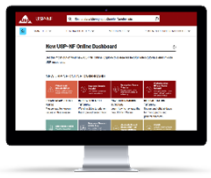
Eligible products





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Contact information

Ph. Eur. – epd@edqm.eu or via the HelpDesk

USP – Richard Lew (RLL@usp.org)

Useful links

Ph. Eur.

https://www.edqm.eu/en/pharmacopoeial-harmonisation

Elaboration of a monograph (Procedure 4) https://go.edqm.eu/ElaborationP4

News item *"All you ever wanted to know about procedure 4 but never dared ask!"*
https://www.edqm.eu/en/news/all-you-ever-wanted-know-about-ph-eur-procedure-4-never-dared-ask

USP

https://www.usp.org/harmonized-standards-overview

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Thank you for your attention

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