How to participate in the Elaboration and Revision of Monographs

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Basis for monographs

- Monographs must take account of all currently approved products
- Approved specification(s) are the main basis backed up by batch data
- Draft monographs are checked by regulatory authorities at Pharmeuropa stage
Creation or revision of a text

Chair of the Ph. Eur. Commission
Delegation of a member state
Experts, EDQM

Stages in elaboration or revision (1)

All procedures:

- Addition to work programme by the Ph. Eur. Commission: public announcement
- Interested parties can *(and should!)* express an interest
- Elaboration, experimental verification of the draft
- Publication in Pharmeuropa
- Study of comments by group of experts/working party
Stages in elaboration or revision (2)

- Submission to Commission for adoption
- Publication in the Ph. Eur.
- Implementation 1 year after adoption
  (see publication schedule available on website)

Overall timescale:
minimum 2 years
Including 5 months for public enquiry and at least 6 months between adoption and publication

Work programme (1)

Based on proposals from:
- National delegations
- Groups of experts
- EDQM

Manufacturers can submit proposals via one of the above
Work programme (2)

✓ Additions announced on:
  • Pharmeuropa-on-line (http://pharmeuropa.edqm.eu/home/) under “useful information”

✓ Status (steps 1-5) displayed on the website

Work status: see Knowledge database

Key to information on State of Work (SoW):

0 = on the work programme, no first draft
1 = first draft (new or revised monograph)
2 = published (or in press) in Pharmeuropa
3 = submitted to the Commission
4 = adopted by the Commission, ready for publication
5 = published in the Ph. Eur.
Creation or revision of a text

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Experts, EDQM

Monographs: how?

✓ **Procedure 1** (Group of experts):
  Multi-source products and monograph revisions
  On request, data are handled confidentially by EDQM

✓ **Procedure 4** (Group of regulators):
  Single-source products, direct co-operation with innovator
  Data are handled confidentially by EDQM
Groups of experts and working parties

- Approx. 800 experts from the Ph. Eur. members states and observers

- The Ph. Eur. Commission has revised its working procedures to open up to the nomination of experts from non-European Pharmacopoeia member states and non-observers states


59 active Groups of experts and working parties

- Antibiotics: 2%
- Biology incl. Blood derivatives and vaccines: 15%
- Chemically defined products: 22%
- Containers: 3%
- Dosage forms: 5%
- Gases: 4%
- Herbs and homoeopathy: 13%
- General chapters: 15%
- Microbiology: 3%
- Others: 17%
- Radiation products: 3%
- Antibiotics: 2%
- Biologics and Botox derivatives and vaccines: 15%
- Chemically defined products: 22%
- Containers: 3%
Monographs: how?

- **Procedure 1**
  - Multi-source products and monograph revisions
  - On request, data are handled confidentially by EDQM

- **Procedure 4**
  - Single-source products, direct co-operation with innovator
  - Data are handled confidentially by EDQM
  - Group of solely composed of regulators
P4 procedure: aim

- Create monographs for single-source substances/finished products (still under patent) with a potential for further generics
- Based on authorised products
- Monograph ready ≥ 2 years before patent expiry (ideally)
- Possibility of starting elaboration work 5 years after first MA approval
- Protection of proprietary information: expert group P4 solely composed of regulators, OMCLs and EDQM

P4 procedure: steps (1)

1. Ph. Eur. Commission: addition to work programme
2. Manufacturer: submits data package/samples
3. Rapporteur from expert group P4 and EDQM staff member prepare first draft
4. Discussion with manufacturer
5. Experimental verification (EDQM/OMCL(s))
6. Report and questions to manufacturer
7. Rapporteur/EDQM: draft for Pharmeuropa
**P4 procedure: steps (2)**

8. Group P4 approves draft for public consultation

9. Comments collected via National Pharmacopoeia Authorities

10. EDQM compiles comments

11. Rapporteur and EDQM examine comments, prepare revised draft, after approval by group P4

12. Presented for adoption (or republication)


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**New monographs**

Addition to programme depends on:

- Therapeutic importance
- Extent of use
- Number of countries in which product is approved
Proposing a new monograph

Contact your National Pharmacopoeia Authority (in Europe)
or EDQM (outside Europe)

✓ Initial data: countries where the product is approved

✓ Data package:
  • Current specifications
  • Analytical procedures (SOPs)
  • Method validation reports
  • Batch and stability data
  • Samples of the finished product, substance and impurities
  • Full description of data package is available
Revision: why? (2)

- **New sources** have new impurity profiles
- **New quality** issues arise
- **Analytical methods** change / development: more convenient methods, more powerful/sensitive methods, more reliable methods become available
- **International harmonisation** (PDG, ICH, VICH)

How can manufacturers request revision?

- **Europe**: via National Pharmacopoeia Authority (address list on EDQM website and in Pharmeuropa)
- **Outside Europe**: contact EDQM which will refer the matter to a group of experts or to the Commission

Make clear what needs revising and if possible make a **concrete proposal**
Data for revision

- Revision can only be undertaken if the request is backed up by sufficient data
- Provide batch data, sample chromatograms, etc. to enable a decision on the need for revision
- Supply validated methods (if possible, cross-validated against official Ph. Eur. method) and samples notably for all impurities controlled by the new method

Revision programme

- Work programme is announced via EDOM website and to industry associations and pharmacopoeia liaison contacts (http://www.edqm.eu/en/european-pharmacopoeia-work-programme-607.html)
- Stakeholders to:
  - Declare an interest for relevant items
  - Make sure you see Pharmeuropa for revision proposals
  - Provide samples, test draft proposal
After revision: why?

FAQ: “Why did you revise the monograph on...?”

The answer can be found out via:

- Briefing notes in Pharmeuropa
- Collected briefing notes posted on the website for each new edition/supplement ([http://pharmeuropa.edqm.eu/home/menupage/English/Useful%20Information/Supplementcomments82.pdf](http://pharmeuropa.edqm.eu/home/menupage/English/Useful%20Information/Supplementcomments82.pdf))
- Knowledge database (monograph history)

Knowledge database

History: contains information concerning certain technical modifications to some revised/corrected texts published since Ph. Eur. 5.0. This information complements the modifications indicated by lines in the margin in the supplements and is not necessarily exhaustive.
### Monograph under elaboration

<table>
<thead>
<tr>
<th>Status</th>
<th>Monograph Title</th>
<th>Substance Name</th>
<th>Information Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work in progress</td>
<td>Deltifron oral solution</td>
<td>Deltifron (solution bouvable de)</td>
<td>Available</td>
</tr>
<tr>
<td>Work in progress</td>
<td>Deltifron oral solution</td>
<td>Deltifron solutio per osicula</td>
<td>Available</td>
</tr>
<tr>
<td>Work in progress</td>
<td>3 - CON</td>
<td>29.3</td>
<td>Available</td>
</tr>
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</tbody>
</table>

The section reflects the status of the text with regard to the work of:
- the Pharmacopoeia Discussion Group (PDG), a joint collaboration between the United States Pharmacopeia, the Japanese Pharmacopoeia and the European Pharmacopoeia.
- the International Conference on Harmonisation (ICH) Quality Guideline on Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH (Q4B).

Further information can be found in chapter 5.8 (Pharmacopoeial Harmonisation) of the European Pharmacopoeia.

### Monograph under revision

#### On-going revision

If certificate(s) of suitability have been granted for the substance in question, their list is shown. This is an excerpt from the online List of CEP.

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</tbody>
</table>

- **Aim of the revision**
- **State of work**
- **The number of the last issue of Pharmeuropa into which a draft of the monograph was published**
How to participate?

- Participation depends on the procedure used
- For all procedures ⇒ provide samples for testing and participate as early as possible (i.e. before the text is published in Pharmeuropa)
- Only information on APIs and excipients used in already approved products licensed in Europe is considered

Pharmacopoeia liaison

- EDQM wishes to have a pharmacopoeia liaison contact for each major manufacturer/user
- Channel information and requests from manufacturer to EDQM
- Reception point for contact by EDQM
- Benefits for both sides
Thank you for your attention!