How to Participate in the Elaboration and Revision of Monographs

European Pharmacopoeia Training Session on Biologicals
4-5 February 2020

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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 **users** including regulatory authorities at Pharmeuropa stage
- Policy for monograph development is given in: 
  *Technical Guide for the Elaboration of Monographs* 
  (available on the EDQM website)

and specific Technical Guides:

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**Creation or Revision of a text**

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

- **Publication**
- **Request for creation / revision**
- **Approval by the Commission**
- **Allocation to a Working Procedure**
- **Assignment to a group of experts**
- **Creation / revision of the text by the Group**
- **Public enquiry in Pharmeuropa**
- **Text adopted by the Commission**

How to Request a Revision?

• Go the EDQM website:  https://www.edqm.eu/en/submitting-drafts-and-requests-revision

Proposing a New Monograph

⇒ Contact the EDQM [in Europe: National Pharmacopoeia Authority]

✓ Initial data: countries (in Europe) 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
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
And then?

- **Outside Ph. Eur. Member states:**
  - Contact EDQM which will refer the matter to a group of experts or to the Ph. Eur. Commission

- **Ph. Eur. Member states:**
  - Via National Pharmacopoeia Authority (address list on EDQM website and in Pharmeuropa)

Make clear what needs revising and, if possible, make a **concrete proposal**

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Revision: Why?

- **Developments in Regulatory Environment**
  - E.g., Guidelines, ICH Q3D-elemental impurities, ICH Q8/Q9/Q10/Q11, REACH

- **Scientific / technical evolutions**
  - E.g., Fast LC, PAT, new molecules, new therapies e.g. CT

- **Developments in Manufacture and Globalisation**
  - E.g., Continuous manufacturing, changed routes of synthesis

- **Increased demand for Generic and Biosimilar products**
  - E.g., New sources

- **New risks to Public Health**
  - E.g., Genotoxic impurities, TSE, contamination/falsification (heparins)

- **Need to regularly review and update Ph. Eur. texts**
  - Need to create new texts
Creation or Revision of a Text

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Revision Programme

✓ **Work programme** is announced via [EDQM 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 Pharmeuropa is seen for revision proposals
  - Provide samples, test draft proposal
How are Texts Elaborated / Revised?

- **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
**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 $\geq$ 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

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**Ph. Eur. Monograph Elaboration: P4 Examples**

**PROCEDURE 4 (single-source)**

- Teriparatide (2829)
- Insulin glargine (2571)
- Human coagulation factor VIIa (rDNA) concentrated solution (2534)
- Human coagulation factor VIIa (rDNA) concentrated solution (2522)
- Etanercept (2522)

*Currently under revision (P1)***
**Ph. Eur. Monograph Elaboration: P1 Examples**

**PROCEDURE 1 (multi-source)**

- Insulin, human (0838)
- Filgrastim concentrated solution (2206)
- Somatropin (0950, 0951, 0952, 2370)
- Follitropin concentrated solution (2206)
- Infliximab concentrated solution (2928)

**Creation or Revision of a Text**

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

1. Chair of the Ph. Eur. Commission
2. Delegation of a member state
3. Experts, EDQM
4. Publication
5. Request for creation / revision
6. Approval by the Commission
7. Allocation to a Working Procedure
8. Assignment to a Group of experts
9. Text adopted by the Commission
10. Public enquiry in Pharmeuropa
11. Creation / revision of the text by the Group

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By Whom?

✓ **Groups of experts and working parties** – appointed by the Ph. Eur. Commission
✓ 800 experts in pharmaceutical sciences 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
Creation or Revision of a Text

Chair of the Ph. Eur. Commission
Delegation of a member state
Experts, EDQM
How to Comment?!

NEW WEBSITE

How to comment

The Texts for comment database contains proposals for new and revised monographs and general texts that are intended for inclusion in the European Pharmacopoeia and are submitted for public comment. In the case of proposals for revision, text to be deleted is crossed out and replacements or additions are underlined.

According to the Guide for the work of the European Pharmacopoeia:

- for manufacturers and other interested parties from member states of the Ph. Eur. Convention, comments on Pharmacopoeia texts should be submitted via the national pharmacopoae authority,
- for manufacturers and other interested parties from non-member states of the Ph. Eur. Convention, and for multinational interested parties:
  - comments on Pharmacopoeia texts should be submitted preferably via the national pharmacopoae authority of the member state where the product is authorized;
  - in cases where comments are submitted to the EDQM, they should be addressed to the secretariat (EDQM), indicated at the end of each text;
- for industry associations or other associations:
  - communications should be made via the EDQM secretariat.

The addresses of the national pharmacopoae authorities and of the EDQM are published on the Pharmeuropa website under the tab "Useful Information." In order to facilitate the processing of comments received by the secretaries of the national authorities and the EDQM, please mention in any correspondence the FA.No reference number indicated at the beginning of each text. If the comment refers to a specific part of the text, please also mention the corresponding number. This number can be found in the HTML version of the text on Pharmeuropa's online, in the Tabs for comment database.

Comments that propose modifications of texts should be supported by analytical data obtained on a significant number of batches. Proposed changes of methodology should be supported by experimental results if a comparison that the method published in Pharmeuropa for comment and the proposed alternation.

Only comments sent before the deadline indicated at the top of each text will be considered for the preparation of the final version. It is stressed that these proposals have not been adopted by the European Pharmacopoeia Commission and shall not be regarded as official.

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Publication

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Public enquiry in Pharmeuropa

Creation / revision of the text by the Group
Adoption of the Text (New or Revised)

- Submission to Ph. Eur. 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

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)
  - Knowledge database (monograph history)

No briefing notes for corrections
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.

Text under Elaboration

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<tr>
<th>Status</th>
<th>Elaboration</th>
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<tr>
<td>Number</td>
<td>20632</td>
</tr>
<tr>
<td>English Name</td>
<td>Test for bacterial endotoxins using recombinant factor C (2.6.32.)</td>
</tr>
<tr>
<td>French Name</td>
<td>Essai des endotoxines bactériennes par la méthode de facteur C recombinant (2.6.32.)</td>
</tr>
</tbody>
</table>

The monograph has been authorised but work has not started yet.

1. Work has started (first draft).
2. The monograph has been authorised for publication in Pharmeuropa (see Pharmeuropa number).
3. The monograph has been submitted for adoption to the European Pharmacopoeia Commission.
4. The monograph has been adopted.
5. The monograph is about to be published, or has been published (see the supplement number indicated and the calendar of the editions below).

Text under Revision

- Aim of the revision
- State of work
- The number of the last issue of Pharmeuropa into which a draft of the monograph was published.

For guidance purposes: provides additional information to users e.g. column / trade names. 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.
Ph. Eur. Monograph Elaboration/Revision: to Summarise

Monographs are based on quality described for registered products

Call for interest

1. Request for monograph elaboration/revision
2. Endorsement by the Ph. Eur. Commission
3. Assignment to a Group of Experts
4. Creation/revision of the text by the Group
5. Public enquiry by the Ph. Eur. Commission

- Data package
  (current specifications, analytical procedures; validation data; batch and stability data)
- Material for testing
- Candidate material for RS establishment
- Review of data package
- Draft monograph development
- Laboratory study/collaborative testing – all preparations (protocol preparation; method verification; data analysis)
- Draft published for comments
  (testing of draft monograph) – 3 months commenting period
- Evaluation of stakeholder feedback
  (technical comments, data)

Once a monograph is published and implemented, MAH’s of registered products have to assure their product meets the requirements of the monograph

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

Stay connected with the EDQM

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LinkedIn: https://www.linkedin.com/company/edqm/
Twitter: @edqm_news
Facebook: @EDQM_CouncilofEurope