

**PHARMACOPOEIAL DISCUSSION GROUP**

**SIGN-OFF DOCUMENT**

**WORKING PROCEDURE OF THE  
PHARMACOPOEIAL DISCUSSION GROUP (PDG)**

Revised version 3 (October 2021)

**European Pharmacopoeia**

Signature

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*28/10/2021*

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*9-NOV-2021*

**WORKING PROCEDURES OF THE  
PHARMACOPOEIAL DISCUSSION GROUP (PDG)**  
Revised version 3, dated October 2021

4

**5 General**

6 Harmonisation may be carried out retrospectively for existing monographs or chapters or  
7 prospectively for new monographs or chapters.

8 The three pharmacopoeias have a commitment to respecting the agreed working procedures  
9 and the associated time deadlines as an essential part of the harmonisation procedure.

10 Harmonisation of pharmacopoeial documents in the PDG occur based on decisions of  
11 the expert bodies of each pharmacopoeia. The PDG works transparently in many ways,  
12 including, principally, the public notice and comment procedures of each pharmacopoeia.

13 Where necessary, meetings of experts including technical telecons/webex meetings are held  
14 to identify potential solutions to resolve difficult problems.

15 Sign-off can occur either electronically via email, by mail, or during the PDG meeting.  
16 The specific stages of the Pre-PDG and PDG Procedure (Process) involved in harmonisation  
17 are:

**18 Pre-PDG**

19 PDG identifies subjects to be harmonised among PDG pharmacopoeias and nominates a  
20 coordinating pharmacopoeia (CP) for each subject. The subject can include potential new  
21 topics, as well as revisions to existing topics to the PDG workplan. The Pre-PDG step provides  
22 a pipeline of potential topics/request for revisions to the PDG Work Plan.

23 • New topic: for a subject to be harmonised the CP develops a clear concept written  
24 document, scientific rationale, including Stakeholder input, impact and perspective.  
25 The CP will coordinate with the other PDG pharmacopoeias, determine impact of local  
26 requirements and barriers to harmonization and utilize technical teleconferences if  
27 needed (limited to 3 experts per pharmacopoeia). PDG decides on an  
28 approve/disapprove decision whether to add a new topic to the PDG workplan and  
29 on the agreed upon timeframe. Subject should be considered for removal after 12 months  
30 if no agreement is reached.

31 • Requests for revision: following coordination with the Experts from the three  
32 pharmacopoeias, PDG decides on an approve/disapprove decision whether to add a  
33 revision to the PDG workplan. Subject should be considered for removal after 12  
34 months if no agreement is reached.

**35 PDG approval**

36 Once a topic/request for revision is added to the PDG workplan, the three PDG  
37 pharmacopoeias strive not to revise their national (regional) text unilaterally, with the  
38 understanding that each pharmacopoeia would notify PDG of any required changes to local or  
39 regional text stemming from regulations and policy that will have impact on the harmonised  
40 text moving forward.

**1 Stage 1: Preparation of first draft**

2 Upon PDG approval to add the topic/request for revision to the workplan, the CP prepares and  
3 forwards the Stage 1 draft and supporting data to PDG for pharmacopoeial expert committee  
4 review/comment within the timeframe as proposed in the Concept Paper. The Stage 1 draft  
5 explains the reasons for each test method or limit proposed.

6 Each Pharmacopoeia shall provide feedback or rationale through consultation with experts or  
7 governing body within 3 months. The comment period should, however, not exceed 4 months.  
8 Each pharmacopoeia should consolidate their comments and forward to the CP.

9 The CP reviews the comments received and makes an initial go/no go decision on whether  
10 the proposed harmonised draft document can move on for public comment / inquiry (Stage 2  
11 draft). If the initial CP decision is "go", the Stage 2 draft is prepared as close as possible to  
12 "global style," together with the commentary and sent to the secretariats of the other  
13 pharmacopoeias.

14 The other pharmacopoeia's commit to providing a response within one month whether they  
15 can agree to publish the draft for public comment/inquiry. If all three pharmacopoeias agree  
16 the decision is a "go," the draft moves forward for public comment/inquiry.

17 If the decision by one or more pharmacopoeias is "no go", additional teleconferences may be  
18 held (limited to 3 experts per pharmacopoeia) to resolve "sticking points." Ideally, these  
19 teleconferences will be held within 1-2 months of the decision to "no go". The goal of these  
20 teleconferences will be to either successfully commit to publish a Stage 2 draft, determine  
21 necessary next steps to reach Stage 2 (e.g. obtaining sponsor data, development and  
22 validation of analytical methods, etc.), or remove the topic from the PDG workplan (see  
23 Suppression).

**24 Stage 2: Official Inquiry**

25 The Stage 2 draft and the commentary are published in the respective fora of each  
26 pharmacopoeia. The draft proposal is published in its entirety. The style may be adapted to  
27 that of the individual pharmacopoeia concerned or the "global style" may be used. The three  
28 pharmacopoeias commit to publish the drafts simultaneously or as closely as possible.

29 The corresponding secretariats may have to add information needed for the understanding of  
30 implementation of the texts, e.g., the addition of the description of an analytical procedure or  
31 of reagents that do not exist in the pharmacopoeia and a translation is added by the European  
32 and Japanese Pharmacopoeias.

33 Each pharmacopoeia analyses the comments received and submits its consolidated  
34 comments to the CP within 2 months of the end of the review/comment period.

35 The CP reviews the comments received. If the comments received during the public  
36 comment/inquiry stage are significant enough to preclude a reasonable chance to reach  
37 consensus at Stage 3, the CP will determine the appropriate course of action, with consultation  
38 of the other PDG pharmacopoeias. Otherwise, the CP prepares a draft harmonised document  
39 (Stage 3A draft) accompanied by a commentary discussing comments received regarding  
40 the previous text and providing reasons for action taken in response to those comments. When  
41 residual differences are anticipated for sign-off, the stage 3A draft includes a draft of the sign-  
42 off cover sheet (see below).

43 The Stage 3A draft together with the commentary is sent to the other two PDG  
44 pharmacopoeias.

**1 Stage 3: Consensus****2 A. Provisional**

3 The stage 3A draft is reviewed and commented on by the other two PDG pharmacopoeias  
4 within 2 months of receipt. The three pharmacopoeias shall do their utmost to reach full  
5 agreement already at this stage with a view to reaching a final consensus document.

6 If a consensus has not been reached, the CP prepares a pharmacopoeia teleconference within  
7 2 months to discuss remaining residual differences brought up through the public  
8 comment/inquiry period. The purpose of the pharmacopoeia teleconference is to make  
9 decisions on the remaining differences and whether they can be resolved, assigned as non-  
10 harmonised attributes or local requirements, if re-publication is necessary at Stage 2, or in  
11 extreme circumstances, remove from the workplan.

12 If harmonisation by attributes/provisions is applied, a special sign-off cover sheet (see  
13 Appendixes 1 and 2) indicating harmonisation is included with the draft. The text contains only  
14 harmonised attributes/provisions; non-harmonised attributes/provisions and local  
15 requirements are not included. The table is prepared as follows:

16 - 3 pharmacopoeias agree on the attribute/provision: '+' in all columns

17 - 2 pharmacopoeias agree that the attribute/provision should be included and have agreed  
18 on the method and limit: '+' in the column for those two pharmacopoeias, '-' in the column  
19 for the pharmacopoeia that will not stipulate the test

20 - 3 pharmacopoeias agree that the attribute/provision should be included but have not  
21 come to an agreement on the method and/or limit: state attribute/provision under 'Non-  
22 harmonised attributes/provisions'

23 - 1 pharmacopoeia only will include an attribute/provision: state under 'local attribute  
24 requirement'.

25 The CP collects information about needs for amendments (local requirements) corresponding  
26 to a general policy in the national or regional (European) area. Local requirements, if needed,  
27 will be listed on the sign-off cover sheet.

**28 B. Draft sign-off**

29 When full agreement is reached, the stage 3B draft is sent by the CP to the other  
30 pharmacopoeias no later than 4 weeks before a PDG meeting for final confirmation. Sign-off  
31 on stage 3B can occur either electronically via email, by mail, or during the PDG meeting.

## 1 **Stage 4: Regional adoption and implementation**

2 Stage 4 takes place individually according to the procedures established by each  
3 pharmacopoeial organisation.

### 4 A. Adoption and publication

5 The document is submitted for adoption to the organisation responsible for each  
6 pharmacopoeia. Each pharmacopoeia incorporates the harmonised draft according to its own  
7 procedure.

8 If a pharmacopoeia needs to include a local requirement after the sign-off of a text, it will submit  
9 a proposed revision of the sign-off cover sheet to PDG. This can be done electronically or at  
10 the PDG meeting.

### 11 B. Implementation

12 The pharmacopoeias will inform each other of the date of implementation in the particular  
13 region.

14 The date of implementation of a harmonised document varies in the three PDG regions  
15 depending on their legal requirements, need of translation, and publication schedules. Each  
16 pharmacopoeia generally allows some period of time after publication for implementation, to  
17 allow manufacturers and other users to achieve conformity.

### 18 C. Indication of harmonisation

19 Each pharmacopoeia will introduce a statement indicating the harmonisation status according  
20 to the policy of the pharmacopoeia. In case of residual differences, these are indicated by  
21 specific symbols (black diamonds indicate non-harmonised attributes/provisions, white  
22 diamonds indicate local requirements). The residual differences all correspond to differences  
23 that have been agreed upon by PDG, via the sign-off cover sheet.

## 24 **Stage 5: Inter-regional acceptance (for chapters previously evaluated by ICH Q4B for 25 Regulatory Interchangeability)**

26 16 chapters were evaluated by the ICH Q4B Expert Working Group. Following the Q4B  
27 evaluation process, a formal notification of regulatory acceptance was posted on the ICH  
28 website.

29 A topic-specific annex to Q4B guideline for each monograph or chapter concerned is  
30 processed for publishing and implementation by each regional authority.

## 31 **Revision**

32 Procedure for the revision of harmonised monographs and chapters

33 The pharmacopoeias participating in the PDG have agreed not to unilaterally revise any  
34 harmonised document (monograph or chapter) after it has been signed-off or published.

35 A pharmacopoeia requesting the revision of a monograph or chapter must provide the PDG  
36 with a formal request including a rationale for revision and appropriate supportive data.  
37 The PDG as a whole – instead of an individual pharmacopoeia – may also request a revision.

1 Criteria for justification of revision may include but are not limited to:

- 2 - public health and safety reasons;
- 3 - insufficient supply of pharmacopoeial quality product on the market;
- 4 - specified analytical reagents or equipment are not available;
- 5 - new methods of preparation of product/reagent are not covered by the current  
6 monograph;
- 7 - analytical methods can be replaced by more appropriate/accurate/precise methods;
- 8 - new technologies that are suitable to be included in the pharmacopoeias.

9 The process for revisions follows the Working Procedure of the PDG as described above under  
10 "Pre-PDG". Revisions of a sign-off document are indicated as revision 1, 2, 3, etc., for the sake  
11 of consistency.

12 Whenever agreed by the PDG, an expedited procedure may be followed. In certain  
13 circumstances, where appropriately justified, the expedited procedure would result in a revision  
14 reverting to Stage 3A as opposed to Stage 1. In these instances, the pharmacopoeia  
15 requesting the revision of a monograph or chapter using the expedited procedure submits a  
16 formal request for revision, including, in addition to the information supplied in the normal  
17 revision process, a justification for recommending the expedited procedure. Agreement by  
18 the PDG to the expedited procedure is handled on a case-by-case basis. After the PDG gives  
19 the green light for the revision, the CP may proceed directly with the elaboration of a Stage 3A  
20 draft.

21 If, for public health reasons, there is an urgent need to rapidly update a harmonised PDG  
22 standard, a PDG pharmacopeia may, with the agreement of the other PDG pharmacopoeias,  
23 unilaterally introduce local requirements to address that need, while simultaneously proposing  
24 a revision through the PDG working procedure as described.

25 Revisions to texts that have already been harmonised can further be introduced as local  
26 requirement if, after consultation with all the parties, there is no consensus for the proposed  
27 revision.

28 Any proposal for introduction of local attributes, together with an assessment of the impact on  
29 the harmonisation status of the text, will be communicated to the other pharmacopoeias. If any  
30 of the other pharmacopoeias disagrees with such a deviation from the PDG's Working  
31 Procedure or the assessment shows that the harmonisation status is largely affected, this may  
32 result in suppression of the text from the work plan (see Suppression).

**1 Suppression**

2 An item can be proposed for suppression from the work programme when one or more  
3 pharmacopoeia(s) wishes to withdraw from harmonisation of a topic. Reasons for withdrawal  
4 include the intention to revise when there is no possibility of agreement being reached by  
5 the PDG or when no progress has been made on a topic by the PDG for more than 3 years,  
6 and no path forward could be agreed.

7 Proposals for suppression are submitted no later than 4 weeks before a PDG meeting together  
8 with the reasons justifying the request. Following a decision by the PDG, each pharmacopoeia  
9 provides the information on suppression of the topic to its stakeholders. If a pharmacopoeia  
10 unilaterally decides to revise a previously harmonised text, its stakeholders are informed via  
11 the pharmacopoeia's forum or website during the official inquiry and the decision of this  
12 pharmacopoeia to move forward with the revision is based on the feedback received.

13 Any of the pharmacopoeias unilaterally introducing a subsequent revision of a text that was  
14 previously harmonised through PDG would clearly inform their respective stakeholders about  
15 the status change.

16 Any two pharmacopoeias may continue working together bilaterally on any topic outside PDG.

**17 Correction of a sign-off text**

18 Any pharmacopoeia which has identified an error in a sign-off text may submit a request for  
19 correction to PDG together with appropriate justification. A cover sheet (see Appendix 3) is  
20 prepared by the pharmacopoeia requesting the correction, together with appropriate  
21 justification. The cover sheet includes the name and code of the general chapter or  
22 monograph, the date of the sign-off and the description of the correction. After confirmation by  
23 PDG, the cover sheet is signed-off at the PDG meeting. When needed for clarity purposes, a  
24 full text including the correction is to be signed-off together with the cover sheet.

**25 Correction of a sign-off cover sheet**

26 Any pharmacopoeia which has identified a need for addition of a new local requirement or a  
27 correction of a local requirement/non-harmonised attribute already included in a previously  
28 signed-off cover sheet will inform PDG accordingly, together with appropriate justification.  
29 When needed for clarity purposes, the pharmacopoeia provides PDG with a full text including  
30 the new/corrected local requirement/non-harmonised attribute or with the published local text,  
31 if available. A corrected cover sheet (see Appendix 4) is prepared by the pharmacopoeia  
32 requesting the correction. The cover sheet includes the name and code of the general chapter  
33 or monograph, the date of the sign-off and the description of the new/corrected local  
34 requirement/non-harmonised attribute with tracked changes. After agreement by PDG that this  
35 is a local requirement/non-harmonised attribute, only the corrected cover sheet is signed-off  
36 at the PDG meeting.

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**Appendix 3**

**PHARMACOPOEIAL DISCUSSION GROUP**

**CORRECTION**

**CODE: ... (General Chapter or Monograph)**  
**NAME: ... (General Chapter or Monograph)**  
**(Correction of the sign-off document ... signed on ...)**

Item to be corrected: ...

[reproduce complete sign-off cover sheet]

**European Pharmacopoeia**

Signature	Name	Date
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**Japanese Pharmacopoeia**

Signature	Name	Date
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**United States Pharmacopoeia**

Signature	Name	Date
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**Appendix 4**

**PHARMACOPOEIAL DISCUSSION GROUP**

**CORRECTION OF SIGN-OFF COVER SHEET**

**CODE: ... (General Chapter or Monograph)**  
**NAME: ... (General Chapter or Monograph)**  
**(Correction of the sign-off cover sheet ... signed on ...)**

[include complete corrected sign-off cover sheet]

**European Pharmacopoeia**

Signature	Name	Date
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**Japanese Pharmacopoeia**

Signature	Name	Date
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**United States Pharmacopeia**

Signature	Name	Date
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*Yg*  
*Km PD*