

PHARMACOPOEIAL DISCUSSION GROUP

SIGN-OFF DOCUMENT

WORKING PROCEDURES OF THE
PHARMACOPOEIAL DISCUSSION GROUP (PDG)

Revised version (October 2007)

European Pharmacopoeia

Signature

Name

Date



U. EITEL

30/10/2007

Japanese Pharmacopoeia

Signature

Name

Date

Wigzell for Toshiko Nakagaki
United States Pharmacopoeia

Oct 30, 2007

Signature

Name Date

29 Oct, 2007



DARREN R. ABERNETHY

1 WORKING PROCEDURES OF THE
2 PHARMACOPOEIAL DISCUSSION GROUP (PDG)

3 Revised version (October 2007)

4 **General**

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

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

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

12 Where necessary, meetings of experts are held to identify potential solutions to resolve difficult
13 problems.

14 The specific stages of the PDG Procedure (Process) involved in harmonisation are:

15 **Stage 1: Identification**

16 Based on inquiry among its users, the PDG identifies subjects to be harmonised among PDG
17 pharmacopoeias and nominates a coordinating pharmacopoeia for each subject.

18 The PDG distributes the work by consensus amongst the three pharmacopoeias. The PDG strives for a
19 balance in the distribution of coordinating pharmacopoeia assignments.

20 **Stage 2: Investigation**

21 The coordinating pharmacopoeia for a subject to be harmonised retrospectively collects the information
22 on the existing specifications in the three pharmacopoeias, on the grades of products marketed and on
23 the potential analytical methods.

24 The coordinating pharmacopoeia prepares a draft monograph or chapter, accompanied by a report
25 giving the rationale for the proposal with validation data.

26 Stage 2 ends with the proposal draft, which is mentioned in this procedure as "stage 3 draft". The Stage
27 3 draft, accompanied by supporting comments or data that explain the reasons for each test method or
28 limit proposed, is sent by the coordinating pharmacopoeia to the secretariats of the other two PDG
29 pharmacopoeias.

30 **Stage 3: Proposal for Expert Committee Review**

31 The three pharmacopoeias forward the Stage 3 draft to their expert committee (meeting or consultation
32 by correspondence).

33 Comments by the experts resulting from this preliminary survey are sent to their respective
34 pharmacopoeial secretariat, preferably within 2 months. The comment period should, however, not
35 exceed 4 months. Within 2 months of receipt of the comments, the Pharmacopoeial Secretariat should
36 consolidate them and forward them to the coordinating pharmacopoeia.

37 The coordinating pharmacopoeia reviews the comments received and prepares a harmonised
38 document (Stage 4 draft) accompanied by a commentary discussing comments received regarding the
39 previous text and providing reasons for action taken in response to those comments.

40 The Stage 4 draft, as far as possible in "global style," together with the commentary is sent to the
41 secretariats of the other pharmacopoeias (end of Stage 3).

42 **Stage 4: Official Inquiry**

1 The Stage 4 draft and the commentary are published in the forum of each pharmacopoeia in a section
2 entitled *International Harmonisation*. The draft is published in its entirety. The corresponding
3 secretariats may have to add information needed for the understanding of implementation of the texts,
4 e.g., the addition of the description of an analytical procedure or of reagents that do not exist in the
5 pharmacopoeia and a translation is added by the European and Japanese Pharmacopoeias. The style
6 may be adapted to that of the pharmacopoeia concerned or the "global style" may be used. The three
7 pharmacopoeias endeavour to publish the drafts simultaneously or as closely as possible.

8 Comments regarding this draft are sent by readers of the forum to their respective Pharmacopoeial
9 secretariat, preferably within 4 months and at most within 6 months of publication in the forum.

10 Each pharmacopoeia analyses the comments received and submits its consolidated comments to the
11 coordinating pharmacopoeia within 2 months of the end of the review/comment period.

12 The coordinating pharmacopoeia reviews the comments received and prepares a draft harmonised
13 document (Stage 5A draft) accompanied by a commentary discussing comments received regarding
14 the previous text and providing reasons for action taken in response to those comments.

15 The Stage 5A draft together with the commentary is sent to the secretariats of the other two PDG
16 pharmacopoeias.

17 **Stage 5. Consensus**

18 A. Provisional

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

22 If a consensus has not been reached, the coordinating pharmacopoeia prepares a revised version
23 (Stage 5A/2), taking relevant substantiated comments on the Stage 5A document from the two other
24 pharmacopoeias into consideration. The revised document (Stage 5A/2) together with the commentary
25 is sent to the secretariats of the other two PDG pharmacopoeias. The revised document is reviewed
26 and commented by the other two PDG pharmacopoeias preferably within 2 months of receipt. This
27 review/comment and revision process of the 5A document is repeated (Stage 5A/n) until the three PDG
28 pharmacopoeias reach a consensus or until the co-ordinating pharmacopoeia considers that
29 harmonisation by attribute should be applied.

30 If the co-ordinating pharmacopoeia considers that certain attributes in the monograph or certain
31 provisions in a general chapter (especially for retroactive harmonisation) are such that it will not be
32 possible to harmonise within a reasonable time period, then harmonisation by attributes/provisions will
33 be applied. If harmonization by attributes/provisions is applied, a special cover page (see Appendixes 1
34 and 2) indicating harmonization is included with the draft. The text contains only harmonised
35 attributes/provisions; non-harmonised and local attributes/provisions are not included. The table for
36 monographs is prepared as follows:

37 - 3 pharmacopoeias agree on the attribute: '+' in all columns

38 - 2 pharmacopoeias agree that the attribute should be included and have agreed on the method
39 and limit: '+' in the column for those two pharmacopoeias, '-' in the column for the
40 pharmacopoeia that will not stipulate the test

41 - 3 pharmacopoeias agree that the attribute should be included but have not come to an
42 agreement on the method and/or limit: state attribute under 'Non-harmonised attributes'

43 - 1 pharmacopoeia only will include an attribute: state under 'local attributes'.

44 If the stage 5A draft is substantially different from the stage 4 draft, the PDG may decide that it should
45 be published again in the forums; the draft then reverts technically to stage 4 revised.

46 B. Draft sign-off

1 When full agreement is reached, the 5B draft is sent by the coordinating pharmacopoeia to the other
2 pharmacopoeias not later than 4 weeks before a PDG meeting for final confirmation. The document is
3 then presented for sign-off at the PDG meeting.

4 **Stage 6: Regional adoption and implementation**

5 *Stage 6 takes place individually according to the procedures established by each pharmacopoeial*
6 *organisation.*

7

8 A. Adoption and publication

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

11 Adopted texts are published by the three pharmacopoeias in the Supplements or, where applicable, in
12 a new edition.

13 If necessary, the Stage 5B draft may be adopted with some amendments (local requirements)
14 corresponding to a general policy in the national or regional (European) area. If a pharmacopoeia
15 includes a local attribute after the sign-off of a text, it will inform the PDG.

16 B. Implementation

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

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

22 C. Indication of harmonisation

23 Each pharmacopoeia will introduce a statement indicating the harmonisation status. EP and USP
24 reference the corresponding text of the other PDG pharmacopoeias. JP references the harmonised
25 text. In case of residual differences, these are indicated by a specific symbol (black diamond).

26 Harmonisation is achieved when all pharmacopoeias have highlighted harmonisation and any residual
27 differences, based on a general policy in the national or regional area.

28 Concurrent to Stages 6A, B and C, a dialogue is opened between PDG and ICH Q4B Expert Working
29 Group for the purpose of obtaining regulatory acceptance of the harmonised text. The co-ordinating
30 pharmacopoeia provides documents to ICH Q4B EWG as defined in the ICH Q4B Guideline.

31

32 **Stage 7: Inter-regional acceptance**

33 Following Q4B evaluation process, a formal notification of regulatory acceptance is posted by ICH.

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

36 **Revision**

37 Procedure for the revision of harmonised monographs and chapters

38 The Pharmacopoeias participating in PDG have agreed not to revise unilaterally any harmonised
39 document (monograph or chapter) after sign-off or after publication.

40 A pharmacopoeia requesting the revision of a monograph or chapter shall apply the following criteria
41 for justification of revision:

- 42 • Public health and safety reasons.
- 43 • Insufficient supply of pharmacopoeial quality product on the market.

ORA

- 1 • Specified analytical reagents or equipment are not available
2 • New methods of preparation of product/reagent are not covered by the current monograph
3 • Analytical methods can be replaced by more appropriate/accurate/precise methods.
- 4 A pharmacopoeia requesting the revision of a monograph or chapter shall provide PDG with a formal
5 request including a rationale for revision and appropriate supportive data.
- 6 The PDG as a whole has to agree to initiate the revision. A coordinating pharmacopoeia will be
7 nominated.
- 8 The coordinating pharmacopoeia, on the basis of data provided by the pharmacopoeia requesting the
9 revision, will prepare a Stage 3 draft (tracked-changed and clean versions).
- 10 The Working Procedure of the PDG will then be followed. The revisions of a sign-off document
11 prepared for this or other reasons are indicated as revision 1, 2, 3, etc.
- 12 Whenever agreed by the PDG, an expedited procedure may be applied. In certain circumstances
13 where appropriately justified, the expedited procedure would result in a revision reverting to Stage 5A
14 as opposed to Stage 3. In these instances, a pharmacopoeia requesting the revision of a monograph or
15 chapter using the expedited procedure will submit a formal request for revision, including, in addition to
16 the information supplied in the normal revision process, a justification for recommending the expedited
17 procedure. Agreement by PDG to the expedited procedure will be handled on a case-by-case basis.
18 After agreement by PDG to proceed with the revision, the coordinating pharmacopoeia may proceed
19 directly with the elaboration of a stage 5A draft.
- 20 The PDG as a whole instead of a pharmacopoeia may also request a revision.
- 21 **Correction**
- 22 Any pharmacopoeia which has identified an error in a sign-off text may submit a request for correction
23 to PDG together with appropriate justification. A cover sheet (see Appendix 3) is prepared by the
24 pharmacopoeia requesting the correction. The cover sheet includes the name and code of the general
25 chapter or monograph, the date of the sign-off and the description of the correction. After confirmation
26 by PDG, the cover sheet is signed-off at the PDG meeting.

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Q/A

Appendix 1

PHARMACOPOEIAL DISCUSSION GROUP

SIGN-OFF DOCUMENT

CODE: ...(General chapter)

NAME: ... (General chapter)

It is understood that sign-off covers the technical content of the draft and each party will adapt it as necessary to conform to the usual presentation of the pharmacopoeia in question; such adaptation includes stipulation of the particular pharmacopoeia's reference materials and general chapters.

Non-harmonized provisions:

- 1)
- 2)

European Pharmacopoeia

Signature

Name

Date

Japanese Pharmacopoeia

Signature

Name

Date

United States Pharmacopoeia

Signature

Name

Date

W. K.

Appendix 2

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**PHARMACOPOEIAL DISCUSSION GROUP
SIGN-OFF DOCUMENT
CODE: ... (Monograph)
NAME: ...(Monograph)**

- Harmonised Attributes

Attribute	EP	JP	USP
Definition	+	+	+
Identification	+	+	+
...	+	+	+
...	+	+	+
...	+	+	+
...	+	+	+
...	+	-	+
...	+	+	+
...	+	+	+
...	+	-	+
...	+	+	+

Legend

- + : will adopt and implement
- : will not stipulate

- Non-harmonised attributes

...

- Local attributes

Reagents and reference materials

Each pharmacopoeia will adapt the text to take account of local reference materials and reagent specifications.

Date:

Signatures:

European Pharmacopoeia Japanese Pharmacopoeia United States Pharmacopoeia



Appendix 3

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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: ...

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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