PHARMACOPOEIAL DISCUSSION GROUP

SIGN-OFF DOCUMENT

WORKING PROCEDURE OF THE

PHARMACOPOEIAL DISCUSSION GROUP (PDG)

Revised version 4 (October 2023)

European Pharmacopoeia

Signature	Name	Date
	C. Vialle	03 Oct. 2023

Indian Pharmacopoeia Commission

Signature	Name	Date
	DR. GAURAU PRATAP SINGH	03 Oct, 2023

Japanese Pharmacopoeia

Signature	Name	Date
H. Maegama for K. Nakai	Hikoichiro Maegama	03. Oct. 2023

United States Pharmacopeia

Signature	Name	Date
	JAAP VENEMA	03 OCT 2023

WORKING PROCEDURES OF THE PHARMACOPOEIAL DISCUSSION GROUP (PDG)

Revised version 4, dated October 2023

General

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

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

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

Where necessary, meetings of experts including technical teleconference/videoconference meetings are held to identify potential solutions to resolve difficult problems.

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

Pre-PDG

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

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

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

PDG approval

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

Stage 1: Preparation of first draft

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

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

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

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

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

Stage 2: Official Inquiry

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

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

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

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

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

Stage 3: Consen

B. A. Provisional

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

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

A sign-off cover sheet (see Appendixes 1 and 2) indicating harmonisation is included with the draft. The text contains only harmonised attributes/provisions; non-harmonised attributes/provisions and local requirements are not included. The table is prepared as follows:

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

- at least 2 pharmacopoeias agree that the attribute/provision should be included and have agreed on the method and limit: '+' in the column for those pharmacopoeias, '–' in the column for the pharmacopoeia(s) that will not stipulate the test

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

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

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

B. Draft sign-off

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

Stage 4: Regional adoption and implementation

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

A. Adoption and publication

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

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

B. Implementation

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

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

C. Indication of harmonisation

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

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

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

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

Revision

Procedure for the revision of harmonised monographs and chapters

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

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

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

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

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

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

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

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

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

Suppression

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

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

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

The other pharmacopoeias may continue working bilaterally on any topic outside PDG.

Correction of a sign-off text

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

Correction of a sign-off cover sheet

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

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.

Harmonised provisions:

Provision	EP	IP	JP	USP
Introduction	+		+	+
...	+		+	+
...	+		+	+
...	+		-	+

Non-harmonised provisions:

1)

2)

Local requirements

EP	IP	JP	USP

European Pharmacopoeia

Signature Name Date

Indian Pharmacopoeia Commission

Signature Name Date

Japanese Pharmacopoeia

Signature	Name	Date

United States Pharmacopeia

Signature	Name	Date

Appendix 2

PHARMACOPOEIAL DISCUSSION GROUP

SIGN-OFF DOCUMENT
CODE: ... (Monograph)
NAME: ... (Monograph)

Harmonised attributes:

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

Legend
+: will adopt and implement
–: will not stipulate

Non-harmonised attributes:
...

Local requirements

EP	IP	JP	USP

Reagents and reference materials

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

European Pharmacopoeia

Signature Name Date

Indian Pharmacopoeia Commission

Signature Name Date

Japanese Pharmacopoeia

Signature Name Date

1 **United States Pharmacopeia**

2 Signature Name Date

3

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

Indian Pharmacopoeia Commission

Signature	Name	Date

Japanese Pharmacopoeia

Signature	Name	Date

United States Pharmacopeia

Signature	Name	Date

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

Indian Pharmacopoeia Commission

Signature	Name	Date

Japanese Pharmacopoeia

Signature	Name	Date

United States Pharmacopeia

Signature	Name	Date