

1 **GUIDE FOR THE WORK OF THE EUROPEAN PHARMACOPOEIA**

2
3 The Commission has prepared this Guide in order to build an efficient network for the activities of
4 the European Pharmacopoeia Commission and those who participate in its work: delegates, experts,
5 *ad hoc* specialists, national secretariats, EDQM as the secretariat, European organisations, industry,
6 universities and others.

7 The Guide describes the desired working methods that should be followed unless in exceptional and
8 justified cases, there are good reasons for not doing so. It explicits and complements the *Rules of*
9 *Procedure of the European Pharmacopoeia Commission*. It shall also be read in conjunction with the
10 *Code of Practice for the work of the European Pharmacopoeia*.

11 The work of the Commission and its Groups of Experts and Working Parties requires a certain
12 commitment from the participants and a willingness to respect established procedures so that public
13 health authorities and the public have an assurance that the human and scientific resources have
14 been used in a timely and efficient manner.

15 In the context of this document, "*expert from Ph. Eur. Member State*" means a person nominated by
16 a Contracting Party wherever he/she is working and irrespective of his/her nationality, and "*expert*
17 *from non-Ph. Eur. Member State*" means any other expert showing interest in participating in the
18 work of the Ph. Eur.

19 *All references in this Guide for work to functions, titles or positions shall be construed as applying*
20 *equally to men and women.*

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1 1. EUROPEAN PHARMACOPOEIA COMMISSION

2 1.1 Activities

3 1.1.1 The legal framework for the use, elaboration and updating of the European Pharmacopoeia
4 in close collaboration with its stakeholders is summarized in Annex 1.

5 1.1.2 A notification for suspected deficiencies in European Pharmacopoeia monographs to be used
6 by the licensing authorities is given as Annex 2.

7 1.1.3 The Commission defines its Code of Practice.

8 1.1.4 The Commission elaborates detailed working procedures for the elaboration of monographs
9 (See Annex 3)

10 1.1.5 The Commission establishes a list of basic documents that are to be provided to each
11 appointed expert and if deemed appropriate to *ad hoc* specialists (see Annex 4).

12 1.2 Delegations

13 1.2.1 If a delegation intends to raise technical matters relating to an item on the agenda for a
14 forthcoming session of the Commission, it should notify in written in advance the Chair of
15 the Commission, the Chair of the Group of Experts or Working Party concerned and the
16 Secretariat. Appropriate steps should then be taken to resolve the points at issue before the
17 item is discussed in session.

18 1.2.2 Delegations should submit in writing editorial comments on documents for adoption to the
19 Chair of the Commission, the Chair of the Group of Experts or Working Party concerned and
20 the Secretariat.

21 1.2.3 Delegations should ensure that nominations of Chairs, experts and/or *ad hoc* specialists for
22 appointment to the Groups of Experts or Working Parties are sent to the Secretariat and
23 accompanied by information on the relevant experience of the nominee (*curriculum vitae*)
24 and by a declaration of interests. The nomination form, *curriculum vitae* and the declaration
25 of interests are held by the Secretariat. The nomination form and *curriculum vitae* are
26 provided to the Presidium. The declarations of interests are managed as described in the
27 Code of practice for the work of the European Pharmacopoeia.

28 1.2.4 On request the *curriculum vitae* and the declaration of interests of experts and *ad hoc*
29 specialists might also be provided to Chairs of Groups of Experts or Working Parties.

30 1.2.5 When proposing an Expert or an *ad hoc* Specialist for re-nomination, the delegation should
31 consider the past contribution of the nominee and may consult the Chair of the Group of
32 Experts or Working Party concerned, the Secretariat and the Presidium for advice on this.

33 1.2.6 Delegations should make every effort to send their comments or other contributions to
34 matters to be treated by correspondence within the agreed deadlines. A delegation failing to

1 observe a deadline should consider the disadvantages involved in delaying adoption of a text
2 before asking the Commission to make a comment or contribution into consideration.

3 1.2.7 Delegations should send to the Chair of the Commission copies of all correspondence
4 relevant to the work of the Commission.

5 **2 GROUPS OF EXPERTS AND WORKING PARTIES**

6 2.1 Activities

7 2.1.1 The procedures for elaboration of monographs and general chapters of the European
8 Pharmacopoeia are described in Annex 3.

9 2.1.2 During the work, due consideration is taken of the relevant Technical Guide(s) for the
10 Elaboration of Monographs wherever applicable. Editorial style is taken care of by the
11 Secretariat.

12 2.1.3 Where relevant, draft monographs, general chapters or other texts submitted must be
13 accompanied by validation reports relating to the methods proposed together with batch
14 analysis for the full range of tests. Validation reports are archived at EDQM and are not
15 released to third parties. The tests should be verified in at least a second laboratory.
16 Specifications in monographs should be based on those for products approved in Member
17 States.

18 2.1.4 Monograph proposals should be submitted together with a report including experimental
19 results and summarising all available scientific information, including validation data.

20 2.1.5 Wherever possible work should proceed by correspondence between a limited number of
21 Experts and *ad hoc* Specialists-(co-ordinator and co-workers). Copies of all relevant
22 correspondence are sent to the Chair of the Group of Experts or Working Party and to the
23 Secretariat. The aim of the preliminary exchange by correspondence between the co-
24 ordinator and co-workers is to provide a good basis for the Group of Experts or Working
25 Party to finalise the drafts as promptly as possible.

26 2.1.6 A member of the Commission's Secretariat shall attend each meeting of a group. The
27 member of the Secretariat in attendance may at any time contribute to the work of the
28 group.

29 2.2 Chairs of Groups of Experts and Working Parties

30 2.2.1 Proposals for new appointments and for re-appointment should be submitted not later than
31 28 days before the beginning of the Session at which the appointment is to be made. Not
32 later than 21 days before the beginning of the Session, the Secretariat should notify the
33 delegations in writing of candidatures received.

34 2.2.2 The Chair, with the support of the Secretariat, is responsible for the progress of the work
35 allocated to the Group of Experts or Working Party and to this end establishes a plan for

- 1 carrying out the work, distributes the work in consultation with the members and ensures
2 that time limits set for assignments are respected.
- 3 2.2.3 Wherever possible, the Chair holds a preparatory meeting with the Secretariat prior to the
4 meeting.
- 5 2.2.4 The Chair, with the support of the Secretariat, ensures that drafts are based on the
6 Commission's relevant Technical Guides and are supported by the necessary documentation
7 in the form of experimental results, reports of group meetings, validation data and an
8 explanatory note, particularly for revision proposals.
- 9 2.2.5 The Chair ensures that scientific grounds are adequately reflected in the decisions of the
10 Group of Experts or Working Party.
- 11 2.2.6 The Chair monitors, together with the Secretariat, that the present Guide for the Work is
12 respected.
- 13 2.2.7 The Chair, with the support of the EDQM, follows up the appropriate work for establishing
14 the reference standards.
- 15 2.2.8 The Chair decides, in consultation with the members, when a draft can be published in
16 Pharmeuropa for comment.
- 17 2.2.9 Comments received after publication in Pharmeuropa are considered by the Group of Experts
18 or Working Party concerned. The Chair ensures that the comments are considered according
19 to their merits. Wherever a proposal for change is not accepted, the Chair ensures that the
20 reasons are clearly formulated. When a substantial change is introduced in the light of the
21 results of the enquiry, the text is published in Pharmeuropa again for comment.
- 22 2.2.10 The Chair decides, in consultation with the members, when a draft for a monograph, general
23 chapter or other text can be submitted to the Commission for adoption. The Chair should be
24 prepared, on behalf of the Group of Experts or Working Party, to resolve in session minor
25 points raised by delegations of the Commission.
- 26 2.2.11 The Chair decides, in consultation with the Secretariat, the agenda for a meeting. Normally
27 documents should be received by members a week in advance of the meeting.
- 28 2.2.12 The Chair ensures that only authorised persons are attending the meeting.
- 29 2.2.13 The Chair ensures that impartiality is maintained in case an interest is declared.
- 30 2.2.14 Where necessary, the Chair refers to the Commission in writing any question requiring a
31 decision of principle prior to continuation of work on a given item.
- 32 2.2.15 Chairs (except those of "dormant" working parties), who are not part of Commission
33 delegations, should attend a session of the European Pharmacopoeia Commission at least

1 once a year to have the opportunity to see how Commission works and to present the
2 progress of the work carried out by their Group.

3 2.2.16 Chairs report regularly to the Commission on progress with the work programme,
4 highlighting items where the work has not advanced as expected and the reasons for this.

5 2.2.17 Chairs of Groups of Experts and Working Parties should be prepared to attend and play an
6 active role in conferences organised by EDQM on subjects relevant for the activities of their
7 Group of Experts or Working Party.

8 2.2.18 Chairs may be convened to special meetings subject to the approval of the Commission,
9 which shall also determine the date and agenda of such meetings.

10 2.2.19 When a Chair attends and plays an active role in conferences organised by third parties on
11 subjects relevant for the activities of the Ph. Eur. Commission, he shall keep informed the
12 Chair of the Commission and the Secretariat prior to the conference.

13 2.2.20 In the absence of the Chair, the Group of Experts or Working Party shall agree on an acting
14 Chair from amongst its experts from Ph. Eur. Member States.

15 2.3 Experts

16 2.3.1 Proposals for new appointments and for re-appointment should be submitted not later than
17 28 days before the beginning of the Session at which the appointment is to be made.

18 2.3.2 Experts should meet the selection criteria approved by the Commission. They contribute on a
19 voluntary basis having fully understood the commitment involved.

20 2.3.3 Experts shall be appointed by the Commission for their personal competence and if
21 applicable, have at their disposal the facilities necessary to contribute to the Group of
22 Experts or Working Party. They shall be allocated to Groups of Experts or Working Parties on
23 the proposal of the Presidium according to the selection criteria approved by the
24 Commission. For each Group, the Secretariat shall provide the Commission with the
25 geographical distribution of the already appointed (if applicable) and proposed members.
26 Based on this information, the Commission shall ensure a fair and appropriate balance of the
27 geographical distribution between the experts from Ph. Eur. Member States but also
28 between the experts from Ph. Eur. Member States and the experts from non-Ph. Eur.
29 Member States.

30 2.3.4 At the end of the term of office the appointment of each expert may be renewed. Where an
31 expert is appointed during the three-year period, his term of office shall end at the same
32 time as that of other members. At a time sufficiently before the end of the term of office, the
33 Commission shall review the Terms of Reference and the necessity to reappoint Groups of
34 Experts and Working Parties for a new period. Based on the results of this review, the
35 Secretariat of the Commission shall update the Terms of Reference and ask each Contracting
36 Party for its proposals, in writing, for the designation of experts.

- 1 2.3.5 Experts receive the basic documents decided by the Commission (see Annex 4).
- 2 2.3.6 Each Expert should make a fair contribution to the work of the Group of Experts or Working
3 Party, including the provision of results of experimental work, where required, and respect
4 the time limits set for assignments.
- 5 2.3.7 Experts receive all documents and other written communications intended to be studied by
6 the Group of Experts or the Working Party. They should maintain confidentiality concerning
7 the work of the group.
- 8 2.3.8 An Expert should maintain proper communication either with the National Pharmacopoeia
9 Authority if he is nominated by a Contracting Party or with the Secretariat if he is nominated
10 from a non-Ph. Eur. Member State, for example by making regular reports on the progress of
11 work.
- 12 2.3.9 An Expert should attend all meetings of the Group of Experts or Working Party. An expert
13 nominated by a Contracting Party should inform the National Pharmacopoeia Authority and
14 the Secretariat in good time if he is unable to attend a meeting. An expert from non-Ph. Eur.
15 member state should inform the Secretariat in good time if he is unable to attend a meeting
- 16 2.3.10 If an expert fails to attend three consecutive meetings, the Chair of the Group of Experts or
17 Working Party and the Secretariat may decide to stop sending documents and other written
18 communications to this expert. The relevant NPA needs to be consulted beforehand in case
19 of experts nominated by a Contracting Party.
- 20 2.3.11 Experts may involve other persons in their work for the Pharmacopoeia where this is useful
21 for the advancement of the work and are responsible for ensuring that these persons are
22 aware of the confidential nature of provided information and data and that the results of the
23 work shall only be used by the Pharmacopoeia.
- 24 2.3.12 When an expert attends and plays an active role in conferences organised by third parties on
25 subjects relevant for the activities of the Ph. Eur. Commission, he shall keep informed the
26 Chair of the Commission and the Secretariat prior to the conference.
- 27 2.4 Ad hoc Specialists
- 28 2.4.1 Proposals for new appointments and for re-appointment should be submitted not later than
29 28 days before the beginning of the Session at which the appointment is to be made.
- 30 2.4.2 Subject to the prior approval of the Chair of the Group and of the Secretariat, *ad hoc*
31 specialists having a current scientific and/or technical knowledge in a specific aspect of the
32 work or a specific topic may assist a Group even if such a need has not been raised in the
33 *Terms of reference and profile for members* document.
- 34 2.4.3 *Ad hoc* specialists should meet the selection criteria approved by the Commission. They
35 contribute on a voluntary basis having fully understood the commitment involved.

- 1 2.4.4 *Ad hoc* specialists receive part or all of the basic documents decided by the Commission (see
2 Annex 4) as considered appropriate by the Chair of the Group of Experts or Working Party
3 and by the Secretariat.
- 4 2.4.5 *Ad hoc* specialists do not have access to other documents intended to be studied by the
5 Group of Experts or Working Party unless decided so, on a case-by-case basis, by the Chair of
6 the Group of Experts or Working Party and by the Secretariat i.e. if considered necessary for
7 the *ad hoc* specialist to fulfil their role.
- 8 2.4.6 The Secretariat provides all documents and other written communication intended to be
9 studied by the *ad hoc* specialist at the relevant meeting.
- 10 2.4.7 *Ad hoc* specialists should maintain confidentiality concerning his work for the group.
- 11 2.4.8 *Ad hoc* specialists will be invited to attend meetings where his expertise is relevant and
12 needed. *Ad hoc* specialists may then attend the whole meeting.
- 13 2.4.9 An *ad hoc* specialist should inform the National Pharmacopoeia Authority and the Secretariat
14 in good time if he is unable to attend a meeting.
- 15 2.4.10 At each Commission session, a list of *ad hoc* specialists having participated in the work of the
16 Groups since the previous session will be provided to the Commission.
- 17 2.4.11 *Ad hoc* specialists may involve other persons in their work for the Pharmacopoeia where this
18 is useful for the advancement of the work and are responsible for ensuring that these
19 persons are aware of the confidential nature of provided information and data and that the
20 results of the work shall only be used by the Pharmacopoeia.
- 21 2.4.12 When an *ad hoc* specialist attends and plays an active role in conferences organised by third
22 parties on subjects relevant for the activities of the Ph. Eur. Commission, he shall keep
23 informed the Chair of the Commission and the Secretariat prior to the conference.

24 2.5 Substitutes

- 25 2.5.1 The substitute should have a similar knowledge and expertise to the appointed expert or *ad*
26 *hoc* specialist and his *curriculum vitae* as well as a declaration of interest should be sent by
27 the Contracting Party to the Secretariat.
- 28 2.5.2 The Contracting Party provides all documents and other written communication intended to
29 be studied by the substitute at the relevant meeting.

30 **3 EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES AND HEALTHCARE**

31 3.1 European Pharmacopoeia Department (EPD)

- 1 3.1.1 The Secretariat of the European Pharmacopoeia and its Groups of Experts and Working
2 Parties is performed by the European Pharmacopoeia Department (EPD) of EDQM. The Head
3 of this Department acts as scientific Secretary to the Commission.
- 4 3.1.2 The Secretariat arranges Sessions of the Commission and meetings of the Groups of Experts
5 and Working Parties and any other meetings asked for by the Commission. Convocations,
6 which should indicate the venue and duration of a session or a meeting are sent to the
7 Delegates and/or Experts/*ad hoc* Specialists, to Liaison Sections of the European Committee
8 on Pharmaceuticals and Pharmaceutical Care and to central addresses of National
9 Pharmacopoeia Authorities in adequate time, normally not less than 4 weeks before the
10 meeting or session, to allow appropriate arrangements to be made.
- 11 3.1.3 For Sessions of the Commission, the Secretariat draws up a draft agenda, in consultation with
12 the Chair. This draft agenda is sent to delegations so as to be available not less than 6 weeks
13 before the Session. The agenda is drawn up taking into account comments received from
14 delegations normally by the deadline indicated on the draft agenda. The agenda is sent to
15 delegations such as to be available at least 3 weeks before the Session. An addendum to the
16 agenda is prepared and provided to delegations at the beginning of the Session. The final
17 agenda is adopted by the Commission at the beginning of the Session on the basis of the
18 agenda and the addendum. If the addendum to the agenda contains an item submitted for
19 adoption at the Session, this item may be deleted from the agenda on request of a
20 delegation or adopted subject to confirmation by delegations following the Session.
- 21 3.1.4 For meetings of Groups of Experts and Working Parties, the Secretariat draws up a draft
22 agenda, in consultation with the Chair of the Group of Experts or Working Party. This draft
23 agenda is sent to Experts and *ad hoc* Specialists so as to be available not less than 3 weeks
24 before the Meeting. The agenda is regularly updated based on the contributions of members.
25 The final agenda is presented for adoption by the members at the beginning of the meeting.
- 26 3.1.5 Documents for adoption at a Session of the Commission are normally sent so as to be
27 available not less than 14 days before the Session. Documents submitted for adoption are
28 posted on the DRT (Document Review Tool) of the EDQM to allow Delegations to enter their
29 comments (if any). Comments are entered either in English or in French, in the English
30 version of the text.
- 31 3.1.6 The Secretariat draws up an annual plan for the meetings of the Groups of Experts and
32 Working Parties, in consultation with the Presidium. The Secretariat may propose, in
33 consultation with the Presidium, to hold additional meetings if needed.
- 34 3.1.7 The Secretary to the Commission issues a summary of proceedings of each session within 14
35 days. The summary of the session shall briefly indicate for each item on the agenda the
36 decision taken (adoption, adoption subject to confirmation by one, several or all
37 delegations).
- 38 3.1.8 The Secretariat issues a summary of proceedings of a meeting within one week of the
39 meeting. The summary of the meeting of a Group of Experts or Working Party shall briefly

- 1 indicate for each item on the agenda the decision taken (discussion during the next meeting,
2 Pharmeuropa, Commission) and any follow-up to be made.
- 3 3.1.9 The Secretary to the Commission issues the draft records of sessions of the Commission in
4 the two official languages within 4 weeks. A deadline for comments on the draft record is set
5 at not more than 6 weeks before the beginning of the next session. The record, amended if
6 necessary, is issued promptly after the deadline.
- 7 3.1.10 The Secretariat issues the reports of group meetings within 8 weeks unless otherwise agreed
8 with the Chair. Each report shall indicate inter alia the names of the participants and the
9 duration of the meeting; it shall have the summary of proceedings as a preface and the work
10 programme of the group on new and revised texts, with the state of advancement, as an
11 appendix. When a change proposed in writing by a National Pharmacopoeia Authority or by a
12 manufacturer is not agreed, the Secretary clearly indicates the reasons for non-acceptance of
13 the proposal in the report.
- 14 3.1.11 The Secretariat prepares new versions of working documents as necessary and sees to it that
15 the correct editing style is used in draft monographs, general chapters and other texts of the
16 Pharmacopoeia using the *Style Guide*.
- 17 3.1.12 Where a document is to be adopted by the Commission by correspondence, the Secretariat
18 distributes the document to all delegations and to National Pharmacopoeia Authorities and
19 indicates a deadline for adoption. If no delegation opposes adoption by the deadline, the
20 Secretariat forwards the document for publication and informs the Commission at the next
21 Session.
- 22 3.1.13 The Secretariat, in consultation with the appropriate Chair, makes the necessary contacts
23 with manufacturers or other suppliers in order to obtain samples of material needed for
24 work on monographs, general chapters and other texts and for use as reference standards
25 and to request proposals for specifications and validated methods to be included in
26 monographs, general chapters or other texts.
- 27 3.1.14 The Secretariat submits to the Commission any proposals made in accordance with Rule 19
28 of the Rules of Procedure for elaboration, revision or suppression of monographs, general
29 chapters or other texts.
- 30 3.1.15 The Secretariat provides to the Commission, National Pharmacopoeia Authorities and
31 delegations at regular intervals a document showing the state of advancement of all items
32 (new and revised) on the work programme.
- 33 3.1.16 The Secretariat organises public conferences on subjects related to the work of the
34 Commission where this is useful for achieving progress.
- 35 3.1.17 The Secretariat maintains suitable liaison with other parts of EDQM to ensure proper co-
36 ordination of work.

- 1 3.1.18 Following the decision of the Commission to create a Group of Experts or Working Party, the
2 Secretariat sends to National Pharmacopoeia Authorities and delegations an invitation to
3 submit proposed nominations, indicating the terms of reference of the group and the profile
4 expected for its members.
- 5 At each Commission session, the Secretariat shall provide the Commission with a list of *ad*
6 *hoc* specialists having participated in the work of the Groups since the previous session of the
7 Commission.
- 8 3.1.19 Not later than 6 months before the end of the term of office of Groups of Experts and
9 Working Parties, the Secretariat sends to National Pharmacopoeia Authorities and
10 delegations an invitation to submit proposed nominations, indicating the terms of reference
11 of the group and the profile expected for its members.
- 12 3.1.20 Where a change to the work programme is proposed (addition or deletion of an item), the
13 Secretariat sends a questionnaire to National Pharmacopoeia Authorities to determine
14 whether they are in favour of the proposed change. Where deletion of an item is proposed
15 because of lack of information on producers, if a National Pharmacopoeia Authority is in
16 favour of maintaining the item on the work programme, the Authority shall endeavour to
17 provide the information needed.
- 18 3.1.21 Where it is proposed to suppress a published monograph, a general chapter or another text,
19 the Secretariat sends a questionnaire to National Pharmacopoeia Authorities to determine
20 whether they are in favour of the proposed suppression.
- 21 3.1.22 The Secretariat organises an annual meeting of Secretaries of National Pharmacopoeia
22 Authorities to facilitate and co-ordinate the activities of common interest and to provide a
23 forum for exchange of information. This meeting is normally hosted by one of the Authorities
24 on a rotation basis.
- 25 3.1.23 When needed, the Secretariat may organise hearings of relevant industry associations.
26 Wherever possible, the Chair of the Commission and, where applicable, the Chair of the
27 Group of Experts or Working Party concerned attend the meeting.
- 28 3.1.24 The Secretariat maintains the Knowledge database on the EDQM website, providing
29 supplementary information on monographs, general chapters and other texts for the
30 assistance of users.
- 31 3.1.25 The Secretariat participates in the activities of the Pharmacopoeial Discussion Group
32 together with representatives of the Japanese Pharmacopoeia and the United States
33 Pharmacopoeia and ensures that work is carried out with due respect for the Commission's
34 established procedures. The Secretariat makes liaison with the relevant Groups of Experts
35 and Working Parties and informs the Commission of the state of work.
- 36 3.1.26 The Secretariat participates in the work of other bodies which have an impact on the work of
37 the Commission, notably relevant committees of the European Medicines Agency (EMA), the
38 Commission of the European Union, the World Health Organization and the Organisation

1 Mondiale de la Santé Animale (OIE). Reports are made to the Commission on this
2 participation.

3 3.1.27 The EPD arranges for publication of Pharmeuropa, which contains all texts issued for public
4 enquiry and comment together with scientific notes, general information on the work of
5 EDQM, etc.

6 3.1.28 Corrections made to definitive texts before publication are notified to the interested parties,
7 notably delegations and National Pharmacopoeia Authorities.

8 3.1.29 The EPD exercises general oversight for the drafting style of texts to be published. To this
9 end, the EPD prepares and updates the Style Guide.

10 3.2 Laboratory Department (also called "Laboratory") (DLAB)

11 3.2.1 The Laboratory contributes to the work on elaboration of monographs, general chapters and
12 other texts at the request of the Commission or of a Group of Experts or Working Party.

13 3.2.2 The Laboratory Department (DLAB) organises the adoption of reference standards.

14 3.2.3 A member of the scientific staff of the Laboratory should, wherever possible, attend the
15 meetings of groups to advise on aspects related to reference standards and for the
16 discussion on work in which they have participated and on which they have reported to the
17 group.

18 3.3 Reference standards

19 3.3.1 The Laboratory Department (DLAB) and the Department of the Biological Standardisation
20 and OMCL (DBO) participate in the establishment and monitoring of reference standards.

21 3.3.2 The DLAB, in co-operation with the relevant Groups of Experts or Working Parties,
22 undertakes work necessary for establishing reference standards. It carries out the
23 establishment of reference standards and reports to the relevant Group of Experts or
24 Working Party on work done.

25 3.3.3 The DBO, in co-operation with the relevant Groups of Experts or Working Parties, undertakes
26 work necessary for establishing Biological Reference Preparations. It carries out the
27 establishment of reference preparations and reports to the relevant Group of Experts or
28 Working Party on work done.

29 3.3.4 The DLAB and the DBO ensure that the work for establishing any new reference standard is
30 carried out so that the standard can be made available in good time for the entry into force
31 of the monograph, preferably at the time of publication.

32 3.3.5 The DLAB and the DBO ensure that the work for establishing any replacement batch of
33 reference standard is carried out so as to ensure continuous supply to users.

1 3.3.6 Reference standards are adopted by correspondence. Reference standard establishment
2 reports are approved by correspondence, unless an issue has arisen which makes the
3 approval by the Experts possible only after discussion in a meeting.

4 3.3.7 For adoption of reference standards by correspondence, the members of the relevant Group
5 of Experts or Working Party are alerted by the DLAB and requested to approve the reference
6 standard laboratory report within 3 weeks. In case of urgency, this deadline might be
7 shortened. The reference standard establishment report is considered approved by the
8 Group of Experts/Working Party when no objection is received within the given deadline. The
9 delegations are contacted after that by the DLAB for agreement of the adoption of the
10 reference standard within 14 days, after which the reference standards are considered
11 adopted and will be released. At each Session of the Commission, a document is presented
12 which gives the detail of substances adopted, with the dates of approval by the groups and
13 adoption by the Commission.

14 3.4 Publications and Multimedia Department (DPM)

15 The Publications and Multimedia Department (DPM) arranges for the publication in suitable form of
16 monographs, general chapters and other texts adopted by the Commission.

17 3.5 Certification of Substances Division (DCEP)

18 3.5.1 As stated in the Code of Practice for the Certification Procedure and in the terms of reference
19 of the Certification of suitability to the Monographs of the European Pharmacopoeia, the
20 Governing Body of the Certification activities is the Certification Steering Committee.

21 3.5.2 The Certification of Substances Division (DCEP) runs the Certification of suitability to the
22 monographs of the European Pharmacopoeia (CEP) procedure which is intended to be used
23 for substances for which a monograph (general monograph and/or specific monograph) has
24 been adopted by the European Pharmacopoeia Commission: organic or inorganic substances
25 (active or excipients), manufactured or extracted; substances produced by fermentation as
26 indirect gene products; herbal drugs or herbal drug preparations and products with risk of
27 transmitting agents of animal spongiform encephalopathies (TSE).

28 3.5.3 The CEP ensures that by applying the relevant monographs of the European Pharmacopoeia,
29 if necessary with additional tests appended in an annex to the respective CEP, it is possible to
30 fully control all possible impurities and contamination from the particular route of
31 manufacture (including source materials) for which the CEP has been granted.

32 3.5.4 If the assessment of the respective quality dossier submitted by the applicant has identified
33 the need to update the monograph due to impurities that are not adequately controlled by
34 the current version of the monograph, the DCEP may request the revision of this monograph.
35 The request for revision contains the information that the relevant Group of Experts of the
36 European Pharmacopoeia needs to update the monograph which has been shown to be
37 inadequate. It is prepared so as not to divulge the confidential information in the dossier.

1 3.6 Quality management system

2 The EDQM maintains a quality management system for its work in each of its departments according
3 to an internationally acknowledged standard .

4 **4 NATIONAL PHARMACOPOEIA AUTHORITIES**

5 4.1 General role

6 The general role of the National Pharmacopoeia Authorities is outlined in Annex 1.

7 4.2 Activities

8 4.2.1 The National Pharmacopoeia Authority is the department within each Contracting Party,
9 responsible for maintaining proper communication with the EDQM. By virtue of Rule 8.1 of
10 the Rules of Procedure, each National Pharmacopoeia Authority must have (a) qualified
11 person(s) (pharmacist or equivalent), responsible for the implementation of the decisions of
12 the Commission.

13 4.2.2 The necessary secretarial support is provided to the National Pharmacopoeia Authority to
14 fulfil and assure the co-ordination of the following essential functions:

- 15 • preparation of and/or implementation of the European Pharmacopoeia and its
16 supplements at national level;
- 17 • responding to questionnaires from EDQM on the work programme of the European
18 Pharmacopoeia;
- 19 • provision of information on local manufacturers and other interested parties who wish to
20 contribute to the work;
- 21 • inform their Expert Committees and local manufacturers, where necessary, on advanced
22 drafts considering the necessary degree of confidentiality,
- 23 • forwarding to EDQM of national comments on Pharmedropa drafts,
- 24 • briefing of Commission members before sessions;
- 25 • forwarding proposals for Experts and *ad hoc* Specialists as members of Groups of Experts
26 and Working Parties;
- 27 • provision of information on the European Pharmacopoeia to local users, in addition to
28 the user support provided by EDQM (HelpDesk);
- 29 • attendance at annual meetings of National Pharmacopoeia Authorities to promote
30 exchange on working methods, etc., within Member States;
- 31 • notification of elaboration of national texts to the Commission.

1 4.3 Duties

2 4.3.1 National Pharmacopoeia Authorities are required to send their comments on a draft for a
3 monograph or other text to the Secretariat within the indicated deadline. The deadline is
4 usually 60 days from the deadline for public comment indicated in Pharmeuropa. If an
5 amended draft is resubmitted for comment, no new matters can be raised in the comments.
6 Comments are entered on the DRT (Document Review Tool) of the EDQM. Comments
7 received after the deadline will be taken into account at the discretion of the Chair of the
8 Group of Experts/Working Party and only where it is indispensable to do so.

9 4.3.2 Proposals for a fundamental change in a draft text should be well-founded and should be
10 supported, wherever necessary, by experimental evidence. Proposals that are not well-
11 founded or not supported by experimental evidence are considered but normally rejected on
12 these grounds.

13 4.3.3 Any comment on a document should contain a substantiated proposal for its improvement
14 or should clearly state the action expected and the reasons for this. Comments which do not
15 fulfil these requirements will be considered but will normally be rejected on these grounds.

16 4.3.4 National Pharmacopoeia Authorities should maintain communication with the Experts and *ad*
17 *hoc* Specialists from their country whilst respecting their independent position as scientific
18 advisers to the Commission.

19 **5 OTHERS**

20 5.1 Manufacturers and other interested parties from Member States of the Ph. Eur. Convention

21 5.1.1 Comments on Pharmeuropa texts should be submitted via the National Pharmacopoeia
22 Authority.

23 5.1.2 Proposals for new items for the work programme or for revision of monographs or general
24 chapters should be submitted via the National Pharmacopoeia Authority.

25 5.1.3 Technical enquiries on monographs and other texts should be submitted, preferably in
26 writing, either to the National Pharmacopoeia Authority or via the EDQM HelpDesk.

27 5.2 Manufacturers and other interested parties from non-Member States of the Ph. Eur. Convention
28 or multinational interested parties:

29 5.2.1 Comments on Pharmeuropa texts should be submitted preferably via the National
30 Pharmacopoeia Authority of one of the Member States where the product is authorized.

31 5.2.2 In case comments on Pharmeuropa texts (preferably as attachments to the enquiry form) are
32 submitted via the EDQM HelpDesk; the Member State(s) where the product is authorized
33 should be indicated.

1 5.2.3 Proposals for new items for the work programme or for revision of monographs or general
2 chapters should be submitted to the Secretariat in Strasbourg. According to the Rules of
3 Procedures (§19.1) proposals from manufacturers and other interested parties from
4 Observer States can also be made via a NPA.

5 5.2.4 Technical enquiries on monographs and other texts should be submitted via the EDQM
6 HelpDesk.

7 5.3 International organisations

8 Communications should be made via the Secretariat in Strasbourg.

9 5.4 Industry associations or other associations

10 Communications should be made via the Secretariat in Strasbourg.

11 **6 REVISION OF TEXTS**

12 6.1 Technical revisions

13 6.1.1 Routine revision of the texts of the Pharmacopoeia shall be effected as follows:

14 (a) a delegation or the Chair of the Commission or of a Group of Experts or Working Party or
15 the Secretariat, having noted the need for revision, shall present a reasoned request for
16 the revision of a text;

17 (b) when the Commission has decided on the priority to be accorded to the proposed
18 revision, the Group of Experts or Working Party concerned shall be informed;

19 (c) the usual working procedure shall then be followed and the revised text shall be
20 published after adoption by the Commission;

21 (d) the revision of texts for the purpose of correcting errors in the text or editorial style
22 modifications shall be done by the Secretariat without a discussion by the Commission.
23 However, Contracting Parties shall be informed promptly of the correction of errors or
24 style modifications made and its effective date, which shall be the date of publication.

25 6.1.2 Requests for revision should be submitted using the standard form (see Annex 5) for this
26 purpose. The parts of the text to be revised should be clearly identified and where possible a
27 concrete proposal should be formulated. The Group of Experts or Working Party may make a
28 preliminary evaluation of the revision request before examination by the Commission if this
29 is convenient taking account of meeting dates.

30 6.1.3 However, work on the revision should not start before the Commission has decided to add
31 the item to the work programme.

32 6.1.4 Requests for revision should be accompanied by sufficient information to enable the
33 Commission to decide whether revision is justified and necessary and to accord the

1 appropriate priority. Where a request for revision does not fulfil the above criteria, after
2 consultation with the Chair of the Group of Experts or Working Party and/or the Chair of the
3 Commission, the Secretariat may refer the matter back to the originator with a substantiated
4 request for further information.

5 6.1.5 Technical revisions submitted to the Commission are accompanied by a briefing note that
6 summarises the revision. The briefing note is later posted in the "View History" field of the
7 Knowledge database, after editorial adaptation where necessary, to inform users of the
8 reasons for the changes and of the changes.

9 6.2 Minor revisions

10 6.2.1 In the interest of simplification of working procedures, minor revisions may be submitted
11 directly to the Commission where the Chair of the Group of Experts/Working Party or the
12 Secretariat considers that prior publication in Pharmeuropa is not needed.

13 6.2.2 Submission of a minor revision implies that the change is not controversial and that the
14 Commission will be able to decide simply on the basis of the briefing note to the monograph
15 that the revision is justified and necessary. Therefore, no request for revision is necessary to
16 start the work on a minor revision.

17 6.2.3 The briefing note mentioned above is later posted in the "View History" field of the
18 Knowledge database, after editorial adaptation where necessary, to inform users of the
19 reasons for the change.

20 6.3 Rapid revision

21 When it is necessary to make a rapid revision of a Ph. Eur. text (including the suspension of the whole
22 or part of a text) the following procedure shall be followed:

- 23 (a) a delegation or the Chair of the Commission or of a Group of Experts or Working Party or
24 the Secretariat, having noted the need for rapid revision, shall present a reasoned
25 proposal for the revised text and, where appropriate, data supporting the proposed
26 revision;
- 27 (b) the Secretariat shall inform the Commission and the Group of Experts or Working Party
28 concerned. The Group or Working Party shall be consulted promptly by a written
29 procedure and, if necessary, be convened as soon as possible and shall take the necessary
30 action concerning the problem. The Secretariat shall prepare all necessary documents and
31 send them to the delegations;
- 32 (c) the Commission shall take a decision at its next Session or by correspondence;
- 33 (d) if the Commission decides that the revised text shall be published and implemented
34 rapidly, outside the normal publication cycle of the European Pharmacopoeia, this text is
35 published in the form of a Resolution of the European Committee on Pharmaceuticals and
36 Pharmaceutical Care with a view to its rapid implementation.

1 **7 CORRECTIONS OF ERRORS**

2 The Secretariat arranges for prompt republication of a text wherever notification of an error in the
3 text or editorial style modification is received and informs the Commission and National
4 Pharmacopoeia Authorities. Corrections that can be made with simple notification include:
5 differences between the English and French texts where the correct version is evident; items that
6 clearly do not correspond to the decision of the Group of Experts, the Working Party and/or the
7 Commission.

8 **8 SUPPRESSION OF THE TEXTS OF THE EUROPEAN PHARMACOPOEIA**

9 When it is necessary to suppress a text of the Pharmacopoeia, the following procedure shall be
10 followed:

- 11 (a) a delegation or the Chair of the Commission or of a Group of Experts or Working Party or
12 the Secretariat, having noted the need for suppressing a Ph. Eur. text, shall present a
13 reasoned proposal;
- 14 (b) the Secretariat shall transmit the proposal to all the delegations;
- 15 (c) the Commission shall decide whether the monograph shall be suppressed;
- 16 (d) if the Commission decides that the monograph shall be suppressed it shall recommend to
17 the European Committee on Pharmaceuticals and Pharmaceutical Care in accordance with
18 paragraph 3 of Article 4 of the Convention the date at which the suppression shall take
19 effect.

20

1 **ANNEX 1**

2 USE, ELABORATION AND UPDATING OF THE EUROPEAN PHARMACOPOEIA

3 INTRODUCTION

4 The European Pharmacopoeia is elaborated under an international convention of the Council of
5 Europe. The Convention has been signed by 37 States and by the European Union. The signatories to
6 the Convention undertake:

7 “to take the necessary measures to ensure that the monographs which ... constitute the European
8 Pharmacopoeia shall become the official standards applicable within their respective countries”.

9 The purpose of the European Pharmacopoeia is to promote public health by the provision of
10 recognised common standards for use by healthcare professionals and others concerned with the
11 quality of medicines. Such standards are to be of appropriate quality as a basis for the safe use of
12 medicines by patients and consumers. Their existence:

13 – facilitates the free movement of medicinal products in Europe;

14 – ensures the quality of medicinal products exported from Europe.

15 European Pharmacopoeia monographs and other texts are designed to be appropriate to the needs
16 of:

17 – regulatory authorities;

18 – those engaged in the control of quality;

19 – manufacturers of starting materials and medicinal products.

20 The European Pharmacopoeia can only fulfil its role properly when each of the interested parties
21 participates actively in the process of elaboration and updating of standards. This note is intended to
22 outline the elements of active participation.

23 EXCHANGES BETWEEN THE PHARMACOPOEIA AND STAKEHOLDERS

24 The Pharmacopoeia, an integral part of the regulatory control system for the quality of medicines,
25 will remain useful only if it is promptly adapted to the needs of its users, notably the experts dealing
26 with applications for marketing authorisation (assessed by the competent authorities and prepared
27 by the manufacturers). Hence, the Pharmacopoeia has taken measures to respond promptly to
28 requests from competent authorities.

29 First, the role of the Pharmacopoeia with respect to that of licensing authorities should be recalled:

30 Unlike licensing dossiers, which are prepared and assessed for an individual product, the
31 Pharmacopoeia is the indispensable communication and standardisation tool that allows a uniform
32 standard to be applied; it should be maintained up-to-date to avoid duplication of work (and
33 therefore increases in costs) and above all anarchy or differences in requirements; by providing
34 harmonised, validated analytical methods, specifications and units, by establishing common

1 reference standards for all users from Europe and beyond, it acts as a reliable reference tool for
2 communication, it links individuals, and it facilitates national and international administrative,
3 commercial and scientific exchange between all the partners responsible for the design, manufacture
4 and quality control of medicines, in both the public and private sectors.

5 This common tool continues to serve its users only if they wish and are able to make their opinions or
6 needs for adaptation known.

7 The tripartite relationship between the Pharmacopoeia, Licensing Authorities and Manufacturers
8 may be clarified by national or supranational legislation. EU directives (currently 2001/82/EC,
9 2001/83/EC and subsequent amendments) summarize the principles for example as follows:

10 Principle no. 1: the European Pharmacopoeia and its standardised and validated specifications,
11 adopted unanimously by the national delegations, are binding.

12 This was codified in Annex 1 to Commission Directive 2001/83/EC as amended,

13 - Introduction and general principles, (5): "With respect to the quality part (chemical, pharmaceutical
14 and biological) of the dossier, all monographs including general monographs and general chapters of
15 the European Pharmacopoeia are applicable."

16 - Chapter 3.2(5): "The monographs of the European Pharmacopoeia shall be applicable to all
17 substances appearing in it..."

18 - "In the case of analytical procedures included in the European Pharmacopoeia, this description shall
19 be replaced in each relevant section "remark: of an application for a marketing authorization" by the
20 appropriate detailed reference to the monograph(s) and general chapter(s)."

21 Principle no. 2: In exceptional cases, if it appears that the control of a product or specific preparation
22 in a licensing dossier is inadequate, the licensing authority and the applicant for marketing
23 authorisation must have additional tests.

24 "However, where a starting material in the European Pharmacopoeia or in the pharmacopoeia of a
25 Member State has been prepared by a method liable to leave impurities not controlled in the
26 pharmacopoeia monograph, these impurities and their maximum tolerance limits must be declared
27 and a suitable test procedure must be described..."

28 In case where a specification contained in a monograph of the European Pharmacopoeia or in the
29 national pharmacopoeia of a Member State might be insufficient to ensure the quality of the
30 substance, the competent authorities may request more appropriate specifications from the person
31 responsible for placing the product on the market..."

32 Principle no. 3: Where it has been found that a monograph is not sufficient to cover all products on
33 the market, the licensing authority must inform the European Pharmacopoeia in general terms
34 without breaking confidentiality and must ask the manufacturer to contact the Pharmacopoeia to
35 update the monograph.

1 "...The competent authorities shall inform the authorities responsible for the pharmacopoeia in
2 question. The person responsible for placing the product on the market shall provide the authorities
3 of that pharmacopoeia with the details of the alleged insufficiency and the additional specifications
4 applied..."

5 Practically, the conditions for achieving these three principles merit clarification.

6 Regarding Principle no. 1:

7 It is clear that application of principles 2 and 3 will be needed less if the texts of the European
8 Pharmacopoeia are updated regularly. This means setting up a mechanism in the European
9 Pharmacopoeia Commission allowing rapid updating and, outside the European Pharmacopoeia, the
10 organisation of frequent, regular and effective communications with its different partners involved.

11 Within the European Directorate for the Quality of Medicines and HealthCare (Council of Europe,
12 Strasbourg), the European Pharmacopoeia has a permanent Scientific Secretariat and a Laboratory
13 dedicated to the elaboration and updating of monographs and general chapters.

14 The principles applied in elaboration of monographs are outlined in a series of Technical Guides,
15 available for download from the EDQM website (www.edqm.eu). The methods included are
16 validated according to current guidelines. The monograph specifications are based on currently
17 approved medicinal products in Member States. This applies in particular to impurity profiles and all
18 specified impurities in monographs can be considered to be qualified at or above the level of the
19 acceptance criterion.

20 In view of the above, it is essential that manufacturers respond to invitations from the Secretariat to
21 participate in the work of elaboration and revision by providing samples and data. The Secretariat
22 regularly sends out such invitations via industry associations and via individual pharmacopoeia liaison
23 persons notified by manufacturers.

24 Different procedures are applied for elaboration of monographs but in all cases draft new
25 monographs and drafts of revision proposals are published in Pharmeuropa for public consultation.

26 It is essential that competent authorities have in place a system for critical examination of
27 Pharmeuropa drafts and generation of comments to be provided to the Secretariat. Similarly,
28 manufacturers should have in place a system of alert for identification of drafts that are of interest
29 and development of comments.

30 EDQM sends notifications to interested parties whenever an item is added to the work programme
31 (new monograph or revision proposal). Interested parties are invited to contact EDQM and
32 participate in the work, notably by providing data and samples of their product.

33 It is essential that interested parties have in place a system for identification of items of interest and
34 that they contact EDQM in a timely manner. Appointment of a pharmacopoeia liaison within the
35 company and notification of EDQM of the contact details is the most effective means.

36 Regarding Principle no. 2:

1 A monograph may be incomplete and not cover an impurity present in a product manufactured by a
2 new route of synthesis or of purification. When a marketing authorization is requested for a
3 medicinal product containing such a substance for reasons of public health the applicant must submit
4 additional information and the licensing authority must demand it.

5 The National Pharmacopoeia Authority is the most effective liaison for notification of suspected
6 deficiencies in monographs. The form shown in the Annex 2 can be used for brief notification of a
7 suspected deficiency in a monograph. The HelpDesk on the EDQM website can also be used for
8 communication of this type.

9 In the light of the international growth of trade, which is likely to make this situation more common,
10 the demonstration that the reference to the Pharmacopoeia is suitable for a given source is
11 requested by current guidelines of the Quality Working Party established under the Committee for
12 Medicinal Products for Human Use and the Committee for Veterinary Medicinal Products (EMA).

13 To simplify the compilation of the marketing authorisation dossier and to make the reference to the
14 Pharmacopoeia directly usable, the procedure for certification of suitability has been set up; this
15 procedure allows the manufacturers to demonstrate the applicability of the monograph to their
16 product whilst protecting the confidentiality of intellectual property. If the monograph does not
17 provide adequate control, the certificate will be accompanied by additional requirements, pending
18 revision of the monograph.

19 Regarding principle no. 3:

20 As the Pharmacopoeia is the instrument shared by the three partners (two use it, one elaborates and
21 updates it), the existing means of communication between them should be optimised to respond
22 better to the specific needs of each partner whilst respecting its constraints.

23 Licensing authorities and manufacturers have similar needs:

- 24 • Reliable, accurate, transparent standards
- 25 • Up-to-date monographs
- 26 • Validated reference methods

27 Licensing authorities are constrained by the need for confidentiality of data submitted in licensing
28 applications. Manufacturers can submit data to EDQM knowing that it will be treated in confidence if
29 they so request, although the end result, a public standard will, of course, be freely available.

30 The Pharmacopoeia has its particular needs:

- 31 • Information on the market situation
- 32 • Information on the needs of licensing authorities in terms of general policy on safety and
33 efficacy and public health policy
- 34 • Data and samples representative of approved products on the market. The main constraints
35 for monograph development are:

- 1 ○ the work involved in development of validated and standardised methods that cover
2 the range of available products;
- 3 ○ availability of substances needed to prepare reference standards.

4 Each partner should clearly understand the needs and constraints of the other two. For its part,
5 EDQM, is committed to the following:

- 6 • Openness in monograph development based on the principles laid down in the relevant
7 Technical Guide, available on the EDQM website;
- 8 • Development of transparent monographs that can fully serve the needs of all users, with
9 support from the Certification Procedure;
- 10 • Priority drafting of monographs and general chapters requested by licensing bodies, notably
11 the Committees and Working Parties of EMA;
- 12 • Effective operation of the Certification Procedure to reduce the workload of assessors for the
13 relevant part of an application;
- 14 • Publication of monographs on active substances at least 2 years before patent expiry so that
15 a standard will be available when generic applications are made;
- 16 • Continuous development of the resources of the EDQM website as a support for all aspects
17 of the work;
- 18 • Organisation of hearings of interested parties at regular intervals or on request to promote
19 exchange on all aspects related to our work.

20 NATIONAL PHARMACOPOEIA AUTHORITIES

21 The process of monograph development is mainly undertaken at European level, with Member
22 States contributing resources to this collaborative process rather than developing national standards.
23 There is a consequent saving of resources and there is no subsequent need to harmonise national
24 positions. The role of national pharmacopoeia authorities has therefore evolved and they have
25 become part of an active network functioning in different directions for:

- 26 • Provision of expertise for European monograph development;
- 27 • Provision of information on the local market situation for medicinal products;
- 28 • Relaying of information on the pharmacopoeia at the local level;
- 29 • Liaison at local level between interested parties and EDQM.

30 EDQM organises an annual meeting of Secretaries of National Pharmacopoeia Authorities, to
31 facilitate and co-ordinate the activities of common interest and to provide a forum for exchange of
32 information.

33

1

ANNEX 2

2 NOTIFICATION OF A SUSPECTED DEFICIENCY IN A MONOGRAPH OF THE EUROPEAN
3 PHARMACOPOEIA

4 According to Directive 2001/83/EC as amended a licensing authority should inform the Secretariat of
5 the European Pharmacopoeia when, during the assessment of an application for marketing
6 authorization, requirements in a monograph of the European Pharmacopoeia have to be
7 supplemented in order to control sufficiently a raw material from a particular manufacturer.

8 Furthermore, the manufacturer has an obligation to co-operate with the European Pharmacopoeia
9 Commission with a view to updating the monograph.

10 The licensing authorities cannot submit to the Secretariat of the European Pharmacopoeia any
11 confidential information from a marketing authorisation application. Therefore, the information
12 submitted to the Secretariat of the European Pharmacopoeia, if possible with the help of the
13 National Pharmacopoeia Authorities, can be limited to a statement of the title of the monograph, the
14 name of the manufacturer, and the nature of deficiency in the monograph, etc. The Secretariat of the
15 European Pharmacopoeia will then contact the manufacturer to obtain the most detailed
16 information directly to allow initiation of the revision process.

17 When informing the Secretariat of the European Pharmacopoeia the following standard format may
18 be used:

19 The information should be sent to:

20 European Pharmacopoeia Department

21 EDQM

22 Council of Europe

23 7, allée Kastner

24 CS 30026

25 F – 67081 STRASBOURG

26 France

27 Fax: (+33) 3.88.41.27.71

28 Name of monograph

29 Problem encountered (e.g. test for related substances, insufficient, additional testing needed, test
30 replace due to malfunctioning etc.)

31 Name and address of manufacturer of finished product

32 Name and address of licensing authority and name of assessor

1 Name and address of the National Pharmacopoeia Authority

2

- 1 **ANNEX 3**
- 2 PROCEDURES FOR ELABORATION OF MONOGRAPHS FOR THE EUROPEAN PHARMACOPOEIA
- 3 The work programme is decided by the European Pharmacopoeia Commission. The Commission
4 considers for addition to the work programme monographs on active substances, excipients and, for
5 certain classes, medicinal products that are approved for use in Member States. In the interests of
6 public health, the Commission may decide to elaborate monographs on articles that do not meet
7 these criteria. At the time of addition to the work programme, a monograph or general chapter is
8 allocated to a procedure and to a Group of Experts or Working Party.
- 9 PROCEDURE 1
- 10 ELABORATION BY A GROUP OF EXPERTS
- 11 1. INITIATION
- 12 1.1 Following addition of an item to the work programme, for items to be dealt with by Procedure 1,
13 the Secretariat circulates information to the public via industry associations, pharmacopoeia liaison
14 persons of manufacturers, the EDQM website and Pharmeuropa Interested parties are invited to
15 contact the Secretariat with a view to providing samples and data and participating in the work.
- 16 1.2 The Secretariat identifies the manufacturers of the substance from information provided by the
17 National Pharmacopoeia Authorities and any other information it may have.
- 18 1.3 The Secretariat sends manufacturers/suppliers of the substance a standard letter informing them
19 of the procedure and the programme to be followed and asking them to:
- 20 i) supply current production batches and small amounts of the known impurities;
- 21 ii) supply in-house specifications for period-of-use for all grades, as accepted by the licensing
22 authorities, methods of analysis and analytical validation data;
- 23 iii) supply batch analysis data for stability batches;
- 24 iv) if possible, supply a batch which can be subsequently used as a chemical reference substance
25 (CRS), if required.
- 26 2. PREPARATION OF THE DRAFT MONOGRAPH
- 27 2.1 Each substance is attributed to a co-ordinator and if necessary a co-worker within the group.
- 28 2.2 After receiving the samples and documentation requested, the Secretariat sends copies of the
29 documentation and portions of the samples to the co-ordinator and, if necessary, to the co-worker.
- 30 2.3 After receiving the samples and the data, the co-ordinator agrees target dates for completion of
31 the laboratory work (preferably not more than 6 months) and initiates the work required, if
32 necessary, in collaboration with the manufacturer and the co-worker.

1 2.4 The co-worker or, in exceptional cases, the EDQM Laboratory carries out the necessary
2 verifications and sends comments to the co-ordinator who informs the Ph.Eur. Secretariat on
3 progress.

4 2.5 The first draft, conforming to the relevant Technical Guide for the Elaboration of Monographs
5 and the Style Guide is produced by the co-ordinator, ideally within 3 months after the completion of
6 the laboratory work.

7 2.6 The draft is then submitted to the Secretariat in one of the official languages, the Secretariat is
8 responsible for translation of the texts into the other official language and for final editorial
9 verification of the texts.

10 3. APPROVAL FOR PUBLICATION IN PHARMEUROPA

11 3.1 The draft monograph and a report of the studies carried out are presented to the Group of
12 Experts.

13 3.2 If the Group of Experts considers that further work is required, this should be undertaken by the
14 co-ordinator or the co-worker and, if necessary, the EDQM Laboratory and preferably the results
15 should be presented at the next meeting of the Group of Experts.

16 3.3 In general, the draft to be published in Pharmeuropa is approved by the group in not more than
17 two meetings.

18 3.4 If there are any non-scientific difficulties or differences in conception, the problem is immediately
19 submitted to the Commission.

20 4. PUBLICATION IN PHARMEUROPA

21 4.1 Once the Group of Experts has approved the draft monograph, the editorial amendments are
22 made by the Secretariat, and the monograph is published in Pharmeuropa and simultaneously sent
23 to the National Pharmacopoeia Authorities.

24 4.2 Whenever appropriate, the author of the monograph prepares an explanatory note to be
25 published at the same time as the monograph. The deadline for comment by the public is set at 3
26 months from the publication date of Pharmeuropa.

27 5. EXAMINATION OF THE COMMENTS

28 5.1 The Secretariat uses an electronic "Document Review Tool" to prepare the compilation of the
29 comments received which are made available to the co-ordinator/co-worker and to the Group of
30 Experts for the next meeting of the Group of Experts.

31 5.2 The co-ordinator reviews the comments, tries to resolve the difficulties by carrying out, where
32 relevant, any necessary laboratory work (the Ph. Eur. Laboratory may be asked to help) and submits
33 proposals to the group.

34 5.3 The comments are considered by the Group of Experts and the monograph is then approved for
35 adoption by the Commission. If necessary, to avoid delaying the publication of new texts, the Group

1 of Experts submits a text for adoption by the Commission while proposing further work on an
2 unresolved matter.

3 5.4 In cases where important modifications are foreseen in the light of the results of the enquiry
4 (change of a method, significant change of specifications), either a second publication is envisaged or
5 National Pharmacopoeia Authorities are consulted.

6 6. ADOPTION BY THE COMMISSION

7 6. 1 The Secretariat prepares the document for the Commission and submits it for adoption at the
8 next Session.

9

10 PROCEDURE 2

11 ADAPTATION OF NATIONAL MONOGRAPHS

12 Procedure 2 is no longer used since the programme of adaptation of national monographs has been
13 completed.

14

15 PROCEDURE 3

16 NATIONAL SECRETARIAT ACTING AS CO-ORDINATOR

17 This procedure has been integrated into the Procedure 4.

18

19 PROCEDURE 4

20 This procedure applies to substances for which a single interested party amongst manufacturers has
21 been identified. It is usually applied to substances still under patent protection where there is
22 potential for future production of generics. The aim of the procedure is to publish a monograph 5
23 years after the first approval in medicinal products in Europe, at latest 2 years or more before patent
24 expiry. The work is co-ordinated by EDQM and overseen by the Group of Experts P4. Data provided
25 by manufacturers is treated in confidence and access is allowed only to EDQM staff and members of
26 the Group of Experts P4, composed of representatives of Competent Authorities (national
27 pharmacopoeia authorities, regulatory authorities or OMCLs).

28 1. INITIATION

29 1.1 Following addition to the work programme, a co-ordinator in the Group of Experts P4 is
30 appointed and responsible persons in the Secretariat and Laboratory. Any member of the P4 group
31 may act as a co-ordinator and nominate a contact within the Competent Authority who for the
32 purpose of this monograph project becomes a member of the Group of Experts P4.

1 1.2 The Secretariat request data and samples from the manufacturer. Data are treated in confidence
2 and are accessible only to the Group of Experts P4 and EDQM staff members involved in the P4
3 Procedure.

4 1.3 The Secretariat reviews the data and samples received. If the data and samples are complete and
5 satisfactory, a first draft of the monograph is prepared by the responsible person within the
6 Secretariat. If the data and samples appear to be incomplete, the Secretariat requests further
7 data/samples before proceeding with the preparation of a first draft.

8 2. PREPARATION OF A FIRST DRAFT

9 2.1 The first draft is reviewed by the co-ordinator, the Secretariat and the Laboratory and questions
10 are compiled and forwarded to the manufacturer.

11 2.2 When all issues have been resolved with the manufacturer, the Laboratory tests one or more
12 batches according to the draft. Where necessary to confirm results from the EDQM Laboratory, the
13 tests are run in a second laboratory (of a national pharmacopoeia or OMCL).

14 If a National Pharmacopoeia Authority acts a co-ordinator, the draft is tested in its laboratories and
15 the confirmatory testing is carried out by the EDQM Laboratory.

16 2.3 Laboratory reports are sent to the manufacturer and further questions may be raised. The
17 responsible person with the Secretariat endeavours to resolve with the manufacturer all points of
18 difference, in collaboration with the co-ordinator and the responsible person in the Laboratory.

19 2.4 The amended draft, conforming to the relevant Technical Guide for the Elaboration of
20 Monographs and the *Style Guide*, is produced by the Secretariat in collaboration with the co-
21 ordinator, ideally within 3 months after the completion of the laboratory work.

22 2.5 The Secretariat is responsible for translation of the texts into the other official language and for
23 final editorial verification of the texts.

24 PUBLICATION IN PHARMEUROPA

25 3.1 Once the Group of Experts P4 has confirmed the draft monograph, the necessary amendments
26 are incorporated by the Secretariat. The monograph is published in Pharmeuropa and simultaneously
27 sent to the National Pharmacopoeia Authorities.

28 Whenever necessary, the author of the monograph prepares an explanatory note to be published at
29 the same time as the monograph. The deadline for comment by the public is set at 3 months from
30 the publication date of Pharmeuropa.

31 4. CONSIDERATION OF COMMENTS

32 4.1 The Secretariat uses an electronic "Document Review Tool" to prepare the compilation of the
33 comments received, which are made available to the co-ordinator and to the Group of Experts P4.

34 4.2 The co-ordinator and the responsible person in the Secretariat study the comments and prepare
35 a document showing the rationale for acceptance or non-acceptance of proposed changes.

1 4.3 A revised draft is prepared for confirmation by the Group of Experts P4 in the light of the
2 rationale document. If necessary, to avoid delaying the publication of the new texts, the Group of
3 Experts P4 submits a text for adoption by the Commission while proposing further work on an
4 unresolved matter.

5 4.4 In cases where important modifications are foreseen in the light of the results of the enquiry
6 (change of a method, significant change of specifications), either a second publication is envisaged or
7 National Pharmacopoeia Authorities are consulted.

8 5. SUBMISSION TO THE COMMISSION

9 The Secretariat prepares the document for the Commission and submits it for adoption at the next
10 Session.

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- 1 ANNEX 4
- 2 LIST OF BASIC DOCUMENTS PROVIDED TO THOSE INVOLVED IN THE WORK OF THE EUROPEAN
- 3 PHARMACOPOEIA COMMISSION
- 4 1. *Rules of procedure*
- 5 2. *Guide for the work of the European Pharmacopoeia*
- 6 3. *Code of Practice for the work of the European Pharmacopoeia*
- 7 4. Technical guide(s) (in the relevant field of work) for the elaboration of monographs
- 8 The *Style Guide* is made available on request.