PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PS/W 14/2011 (Rev. 2)
2 Annexes
1 January 2019

GUIDELINES FOR ACCESSION TO THE PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

Editor: Pharmaceutical Inspection Co-operation Scheme (PIC/S)
14, rue du Roveray
CH-1207 Geneva (Switzerland)
Tel. + 41 22 738 92 16 E-mail: info@picscheme.org
Web site: http://www.picscheme.org

GUIDELINES FOR ACCESSION TO THE

PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

TABLE OF CONTENTS

1. INTRODUCTION

1. The Pharmaceutical Inspection Co-operation Scheme (PIC Scheme) has been set up in order to provide, in the interest of public health, for the co-operation between pharmaceutical inspectorates with a view to

- fostering and maintaining mutual confidence;
- promoting quality management system for inspectorates and best practices and standards in the field of inspections; and
- contributing to global harmonisation of standards of good manufacturing practice (GMP) for medicinal products, as defined in paragraph 2 of the Scheme[1].

2. The Scheme is also a means of ensuring – through official inspections – that the quality of medicinal products (as defined in footnote No 1) is strictly in compliance with the marketing authorisation and GMP standards.

3. Paragraph 4 of the Scheme provides that "the Scheme is open for participation by competent authorities having the arrangements necessary to apply an inspection system comparable to that referred to in this Scheme and whose requirements and procedures could ensure the proper implementation of the Scheme and contribute to its effective operation".

4. The Scheme is primarily based on mutual confidence between Participating Authorities (PA). Such confidence can only be achieved on the basis of a thorough knowledge of each other's inspection systems and inspection practice and standards as well as through personal contacts between representatives (including inspectors) of the different national competent authorities.

5. The procedure of accession to the Scheme is not only designed to ensure that the Authority applying for participation complies with the conditions laid down in the Scheme; it also aims at fostering and maintaining the necessary mutual confidence between all authorities concerned.

6. Against this background and in line with the general objectives of the Scheme, the Committee set up under the Scheme (hereafter referred to as "the Committee") has – on the basis of practice and experience – agreed on the following guidelines for the procedure of accession. This procedure is, however, meant to remain flexible in the sense that the sequence of events should not necessarily have to follow the order set out below.

---

[1] Paragraph 2 of the Scheme reads as follows: “For the purpose of this Scheme "medicinal product" means:

(a) any pharmaceutical, medicine or similar product intended for human or veterinary use which is subject to control by health legislation in the manufacturing country or in the importing country, and

(b) any active pharmaceutical ingredient (API) or excipient which the manufacturer uses in the manufacture of a product referred to in sub-paragraph (a) above.”

7. In addition, in order to guarantee the equivalence of the Accession Guidelines with the PIC/S Joint Reassessment Programme (JRP) [2], the same procedures shall apply to both.

8. Considering (i) the many differences in GMP regulations for medicinal products; (ii) the various Quality Systems (QS) applied by interested Competent Authorities; (iii) the limited resources available within PIC/S for the assessment of new membership applications; and (iv) the need to facilitate and accelerate the accession, the accession process has been split into two distinct phases, which are: "Pre-Accession Procedure" and "Accession Procedure".

9. The "Pre-Accession Procedure" (Chapter 2) should be followed if the interested Competent Authority:

a) does not apply the PIC/S GMP Guide; and/or

b) has not regularly participated in PIC/S training activities; and/or

c) is unsure whether it meets PIC/S requirements; and/or

d) has not yet introduced a QS similar along the lines of the PIC/S recommendation (PI 002); and/or

e) has requested to go through the pre-accession procedure.

10. The "Accession Procedure" (Chapter 3) should be followed in all other cases, notably if the interested Competent Authority is more familiar with the PIC/S Requirements and the PIC/S (or EU) GMP Guide is implemented.

2. PRE-ACCESSION PROCEDURE FOR INTERESTED AUTHORITIES

11. An Authority complying with the conditions of paragraph 9 above (hereafter referred to as "the Pre-Accession Applicant") should address itself first to the PIC/S Secretariat, which shall

(a) provide the Pre-Accession Applicant with all appropriate information, in particular the pre-accession process, information on fees and timeframe ;

(b) inform Members of the Committee of the above;

(c) ask the Pre-Accession Applicant to complete the Questionnaire (PS/W 1/2011) and the Audit Checklist (PS/W 1/2005) and return them to the Secretariat. (Note: all documents must be submitted in English and electronically, either as attachment to an e-mail or on a CD-ROM; hyperlinks are not accepted).

12. The Committee shall then appoint a Rapporteur (and Co-Rapporteur(s) if needed) for the pre-assessment of the Pre-Applicant. The Rapporteur is not obligatorily a member of the Committee but must belong to a PIC/S PA.

2 see Joint Reassessment Programme (PS/W 9/2000)

13. The task of the Rapporteur is:

- to review the documentation submitted by the Pre-Accession Applicant;
- to examine whether there are major gaps between (i) the Pre-Accession Applicant's legislation and quality system and (ii) basic PIC/S requirements;
- to carry out a short visit (if needed) to the Pre-Accession Applicant to discuss and complete the gap analysis;
- to prepare a short report based on PS/W 12/2002;
- to give a recommendation to the Committee regarding the readiness of the Pre-Accession Applicant to apply for PIC/S membership.

14. The Committee shall then decide on the next steps, e.g.:

- To invite the Pre-Accession Applicant to apply for membership;
- To ask the Pre-Accession Applicant to first comply with PIC/S requirements before applying;
- To conclude a partnership agreement with the Pre-Accession Applicant.

15. The maximum timeframe for the pre-accession process is 2 years upon receipt of the completed Audit Checklist and Questionnaire.

16. The Pre-Accession Applicant does not have to pay a pre-accession application fee. However, during the whole pre-accession process, it will have to pay an annual fee, as defined in the PIC/S Financial Rules (PS/W 1/2004) and the PIC/S Fees (PS/W 17/2016). Derogations are decided by the PIC/S Committee.

17. In the event that an on-site visit is recommended in order to complete the gap analysis, the Pre-Accession Applicant should normally also cover the related travel costs.

3. ACCESSION PROCEDURE FOR APPLICANT AUTHORITIES

18. An Authority applying for participation in this Scheme (hereafter referred to as "the Applicant") should address itself first to the Scheme's Secretariat preferably by e-mail. The Secretariat shall:

(a) provide the Applicant with all appropriate information, in particular the Questionnaire and the Audit Checklist, information on (i) fees, (ii) total timeframe to join the Scheme; and (iii) the Applicant's responsibilities;

(b) ask the Applicant to fill in and return the Questionnaire (PS/W 1/2011) and the Audit Checklist (PS/W 1/2005), together with the necessary supporting documents (see list at Annex III of PS/W 1/2011). All documents must be submitted in English[3] and electronically, either as an attachment to an e-mail or on CD-ROM. Hyperlinks are not accepted;

---

3 If the language of the Applicant is the same as one of the spoken languages by a PIC/S PA, some of the supporting documents (e.g. legislation) can be submitted in the original language with the exception of excerpts dealing with the GMP inspection system, which must be translated in all cases.

(c) check that the submitted application is complete, in particular that all necessary supporting documents have been submitted. If the application is complete, the Applicant will be requested to pay the relevant application fee (corresponding to the annual membership fee paid by PA). Incomplete applications will be returned to Applicants;

(d) circulate the application to Members of the Committee.

19. A membership application will only be considered complete and the assessment process will only start once the complete application and all supporting documents have been received and the Applicant has paid the application fee. The Secretariat will inform the Applicant about the starting date of the procedure and remind the Applicant of the 6-year timeframe for the conclusion of the process, in particular the date when the six-year period will end.

20. In addition, during the whole assessment process, Applicants will have to pay an annual fee, as defined in the PIC/S Financial Rules (PS/W 1/2004) and the PIC/S Fees (PS/W 17/2016).

21. Depending on the size and the complexity of the Applicant's organisation and application, the PIC/S Committee shall appoint (i) one Rapporteur and (ii) one or several Co-Rapporteur(s) to review and evaluate the membership application. The Rapporteur and Co-Rapporteur(s) may be proposed by the Chair of the Compliance Group or other members of the Executive Bureau to the Committee which will take the final decision. All the information in paragraph 18b shall be forwarded by the Secretariat to the Rapporteur and Co-Rapporteur(s) designated by the Committee.

22. The task of the Rapporteur [4], with the assistance of the Co-Rapporteur(s), is:

- to control that the application is complete,
- if the Applicant has not gone through a pre-accession, to carry out a quick pre-assessment of the application to make sure that the applicant meets basic PIC/S requirements. In cases of doubt or if the Applicant is not complying with PIC/S requirements, the Applicant is invited to first go through the pre-accession procedure.
- to evaluate the information contained in the application,
- to send to the Secretariat, no later than one month before a Committee meeting, a report on the progress of the evaluation,
- to inform the Chair of the Compliance Group about facts needing immediate action,
- to ask, where necessary, for additional information,
- to inform the Committee on his/her opinion on the gathered information,
- to lead the discussion during a hearing of the Applicant's representative(s),
- to lead the on-site assessment of the Applicant by a PIC/S Audit Team,
- to write a final evaluation report with a recommendation for action to be taken by the Committee.

4 This is equivalent to the task of the Team Leader under the JRP (see PS/W 10/2005)

23. The final evaluation and decision is made by the Committee.

24. If an Applicant has been assessed or reassessed by two other PIC/S PA under other programmes within the past 5 years, the PIC/S Committee may decide on a partial assessment based on the review by the Rapporteur of the evaluation reports issued by these PA. The Applicant shall share these reports with the PIC/S Committee. In this case, the on-site assessment shall be waived. If necessary, the Committee may however decide on a follow-up visit to check the implementation of possible recommendations made by the Rapporteur.

4. PARTICIPATION IN TRAINING ACTIVITIES

25. The Applicant shall be invited to attend PIC/S seminars and other training activities. The contribution fee to the PIC/S Secretariat, which is collected as part of the seminar registration fee (see para. 5.20 of PI 003-4), shall be CHF 100 per participating inspector from an Applicant Authority (NB: CHF 75 for Members and CHF 150 for Non-Members).

26. The Applicant may also invite representatives of the PIC/S Committee to participate as speakers in GMP training seminars organised by the interested Authority for its inspectors.

5. PARTICIPATION IN PIC/S COMMITTEE MEETINGS

27. Applicants shall have the right to attend non-restricted parts of Committee meetings as observers (no voting right). Applicants are entitled to one representative; the latter should be familiar with GMP inspections (e.g. Chief Inspector or Senior Inspector); additional representatives may be allowed if seats are available. To ensure consistency in the discussion of the application, the same representatives shall attend Committee meetings.

6. VISIT (i.e. ON-SITE ASSESSMENT) OF THE APPLICANT

28. Unless subject to a partial assessment (as described at paragraph 24), an Audit Team[5] of the PIC/S Committee shall be invited to the country of the Applicant in order to make an on-site assessment of the inspection system, inspection practice and standards (including the licensing system for manufacturers and the handling of suspected quality defects), as well as to observe, in the course of inspections to one or more representative pharmaceutical firms, the application of GMP rules in the manufacture of pharmaceutical products. (Details on the organisation of the visit to the country of the Applicant by an Audit Team of the PIC/S Committee are contained at Annex 1. See also PS/W 10/2005 “JRP Procedure”)

---

[5] An Audit Team consists of a Team Leader, who is normally the Rapporteur during the paper evaluation, as well as, Audit Team Members who will observe GMP inspections during the on-site assessment visit.

29. The Audit Team shall prepare a report on the on-site visit (as described in PS/W 10/2005) and present it to the Committee. The report shall contain a recommendation on the acceptance (or rejection) of the application as well as on expected corrective action. On the basis of this recommendation, the PIC/S Committee may decide that a follow-up visit is necessary to verify that appropriate remedial actions have been taken following the first visit.

7. DECISION BY THE PIC/S COMMITTEE

30. When the compliance with the provisions of the Scheme has been assessed and provided that all PA have given their consent during a restricted meeting of the Committee (i.e. without Applicants and other guests), the Applicant shall be accepted as a PA. The Committee shall decide on the date of accession of the Applicant to the PIC Scheme.

31. The Secretariat should formally invite the new PA to accede to the Scheme and request the latter (a) to pay the membership fee and (b) sign a letter of accession (see Annex 2). The letter of accession, which should normally be signed prior to the accession date, will be circulated to all PIC/S PA.

8. TIMEFRAME AND APPLICANT'S RESPONSIBILITIES

32. The total timeframe for the application process should not exceed six years (from the time of the acceptance of the application until the Committee's decision on acceptance as a PA). Any application which exceeds this timeframe should be rejected. Exceptions should be decided by the Committee on a case by case basis, by consensus and if duly justified.

33. "Clock-stops" not exceeding a total period of 12 months may be agreed by the Committee upon request of the Applicant (e.g. if new legislation has been adopted in the fields covered by the application or if the Authority is subject to internal reorganisation). The annual fee must, however, be paid during the "clock-stop" period. In the event of a major reorganisation (e.g. merger or most inspectors leaving the Authority), the Applicant will be asked to re-apply.

34. The Applicant shall provide the Rapporteur with progress reports on a regular basis regarding the implementation of corrective action. This obligation shall continue even after the Applicant's accession to PIC/S.

35. An Applicant, which has been rejected by the Committee because the six-year timeframe has been exceeded, may at the discretion of the Committee be invited to re-apply.

36. It is desirable for relevant staff of the Applicant to participate in PIC/S Seminars; participation in Expert Circles is recommended.

9. REVISION HISTORY

Date	Version number	Reasons for revision
1 September 2006	PIC/S 1/98 (Rev. 3)	To adapt the Accession Guidelines to the JRP procedures
13 December 2007	PIC/S 1/98 (Rev. 4)	- To waive on-site assessment of Applicants recently audited by two other PA - To delete the status of Observer for Applicants
22 July 2011	PS/W 14/2011	To introduce a pre-accession process
1 December 2013	PS/W 14/2011 (Rev. 1)	- To use the term 'Pre-Accession Applicant' - To introduce the possibility for Pre-Accesion Applicant to pay an annual fee - To define the term 'Audit Team' - To amend the conditions on travel costs
19 December 2018	PS/W 14/2011 (Rev. 2)	To align paragraphs 16 & 20 to the revised PIC/S Financial Rules

* * * * * *

VISIT (i.e. ON-SITE ASSESSMENT) OF THE APPLICANT BY AN AUDIT TEAM OF THE PIC/S COMMITTEE

1. When the information provided has been considered sufficient by the PIC/S Committee and unless subject to a partial assessment, the Applicant is asked to invite a PIC/S Audit Team for a visit. The purpose of the visit is to allow the PIC/S Audit Team to ensure that the inspection system in place (including the licensing system for manufacturers and the handling of suspected quality defects) complies with the documentation received and is in line with PIC/S requirements. The Team will notably focus on the quality management system of the Applicant, observe two or more GMP inspections to pharmaceutical companies, as well as examine the methods of GMP inspection applied by the Applicant's inspectors in those companies. The visit is carried out in line with PS/W 10/2005. The present Annex is only a summary of various steps comprised in the on-site assessment.

2. Travel expenses relating to the on-site assessment visit undertaken by the Audit Team (including return flights to the visiting country, transport in the country, accommodation and food) should normally be covered by the Applicant. If the Applicant is unable to cover some of the costs (e.g. flights to the country), then it must inform the Committee well in advance of the on-site visit.

PROGRAMME

3. A programme should be prepared by the Applicant. The programme of the visit should be comparable to the PIC/S Joint Re-assessment Programme (see section 4.3 in PS/W 10/2005), the EU Joint Assessment Programme and EU MRAs. The Audit Team will use similar tools as mentioned in PIC/S procedures for observing inspections, i.e. PS/W 10/2002 (Procedure for Observing Inspections) and PS/W 11/2002 (Criteria for Observing Inspections).

4. The programme should include:

- an opening meeting (see paragraph 4.3.1 in PS/W 10/2005) with the Applicant’s Management, Head of Inspectorate and inspectorate staff, including a general presentation, not exceeding 1 hour, on the national GMP inspection system,
- a meeting with the Head of Inspectorate and inspectorate staff (see item 5 below),
- an examination of the Inspectorate’s quality management system,
- a cross-examination of the written documentation submitted (to ensure that e.g. a procedure is applied),
- observed inspections, and
- a closing meeting of the visit with the Applicant’s Management, Head of Inspectorate and relevant staff to review the visit and to make comments and recommendations.

GENERAL INFORMATION

5. The Head of Inspectorate and inspectorate staff of the Applicant should provide information about the inspectorate including notably:

- quality management system of the Inspectorate (including the quality manual),
- manufacturer licensing system,
- communication with pharmaceutical assessors, official medicines control laboratories (OMCL), enforcement body and other bodies of the Agency,
- suspected quality defect handling and Rapid Alert system,
- training of inspectors, and
- inspection strategy (e.g. based on quality risk management).

OBSERVED INSPECTIONS

6. The observed inspections should be performed following the procedure described in PS/W 10/2002.

CLOSING MEETING, CONCLUSION & REPORT

7. A closing meeting of the Audit Team and the Applicant's Management, Head of Inspectorate and appropriate staff should be held at the conclusion of the visits to the companies and this should be used to:

- outline any differences in the application and interpretation of GMP rules (including PIC/S recommendations),
- make proposals for corrective actions and their timeframe, and
- appraise the overall impressions.

8. For the closing meeting see also paragraphs 4.3.4 and 4.3.5 of PS/W 10/2005. N.B. Recommendations regarding corrective actions are normally made by the Audit Team, without consultation.

9. The Audit Team should prepare a report to the Committee after the visit in which the recommendation concerning the accession to the Pharmaceutical Inspection Co-operation Scheme should be given. For the format, see PS/W 12/2002.

10. The report to the Committee should include a recommendation on whether or not a follow-up visit should take place to verify that appropriate remedial actions have been taken by the Applicant Authority to bring its system up to a level equivalent to other PIC/S members.

DISCUSSION AT THE PIC/S COMMITTEE AND DECISION

11. The Committee should decide at its next meeting whether:

(a) the Applicant needs to modify its system of inspection, licensing or handling of quality defects before any follow-up visit is arranged;

(b) a follow-up visit should take place, with a report of this visit provided to the Committee for its consideration;

(c) the accession process should proceed subject to a follow-up visit confirming that appropriate remedial actions have been taken; or

(d) the accession process should proceed without the need for a follow-up visit.

* * * * * *

[Competent Authority]

Secretariat of the Pharmaceutical
Inspection Co-operation Scheme
(PIC/S)
Rue du Roveray 14
CH-1207 Geneva

[place, date]

Pharmaceutical Inspection Co-operation Scheme (PIC Scheme)

Dear Sirs,

I have the honour of informing you that *[name of Authority]*

- expresses the willingness of *[name of Authority]* to accede to the Pharmaceutical Inspection Co-operation Scheme, as contained in document PIC/S 1/95 (Rev. x) and to apply its provisions,

- undertakes to respect the confidentiality of all the information (written and oral) exchanged or shared under the Scheme in line with Chapter X of the Scheme, and

- will [agrees to] contribute to the effective operation of the Scheme by means of constructive co-operation with the other Participating Authorities.

The name and address of *[name of Authority]* to be considered as competent under the meaning of the Scheme is:

[Name
Address
Telephone:
Fax:
E-Mail:
Web site:]

Yours sincerely,

[Signature]

[Name & title]