



**PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME**

PS/W 14/2011 (Rev. 3)
2 Annexes
19 April 2022

**GUIDELINES FOR ACCESSION
TO THE
PHARMACEUTICAL INSPECTION
CO-OPERATION SCHEME**

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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: <https://www.picscheme.org>

**GUIDELINES FOR ACCESSION TO THE
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME**

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1. INTRODUCTION

1. The Pharmaceutical Inspection Co-operation Scheme (PIC/S) 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 Scheme¹.
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. In order to facilitate the accession process, the Committee set up under the Scheme (hereafter referred to as "the Committee") decided to introduce a pre-accession process to allow interested National Competent Authorities (NCA) willing to be PIC/S Participant Authorities (PIC/S PA) to better understand what PIC/S is and what are the expectations for becoming such a PA.
6. Against this background and in line with the general objectives of the Scheme, 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.
7. In addition, in order to guarantee the equivalence of the Accession Guidelines with the PIC/S Joint Reassessment Programme (JRP) (see PS/W 9/2000), the same procedures shall apply to both. Refer to the JRP procedure for the list of definitions.

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."

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” (see PS/W 12/2019) and “Accession Procedure” (see below).

2. ACCESSION PROCEDURE FOR APPLICANT AUTHORITIES

9. An Authority applying for participation in this Scheme should address itself first to the Scheme's Secretariat preferably by e-mail. In case of multiple authorities responsible for covering all elements of the GMP regulatory compliance programme, they all have, and together, address themselves to the PIC/S's Secretariat. In this case, these authorities are hereafter referred to as “the Applicant”. The Applicant shall then by the support of the Secretariat:

- Fill in and return the Questionnaire (PS/W 1/2011).
- Describe their GMP regulatory compliance programme by completing the Audit Checklist (PS/W 1/2005), together with the necessary supporting documents (see list at Annex III of PS/W 1/2011). Also refers as the self-assessment.

In the case where multiple authorities are responsible for covering various elements of the GMP regulatory compliance programme, they must all together as one fill in the Questionnaire and Audit Checklist, identifying for each item, “who” is responsible for “what”. All documents must be submitted in English and electronically, either as an attachment to an e-mail or via an electronic secured platform. Hyperlinks are not accepted. 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 regulatory compliance programme, which must be translated in all cases.

The Secretariat will then:

- (a) provide the Applicant with all other appropriate information, on (i) fees, (ii) total timeframe to join the Scheme; and (iii) the Applicant's responsibilities;
 - (b) 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;
 - (c) circulate the application to the Sub-Committee on Compliance (SCC) and Members of the Committee.
10. 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 six-year timeframe for the conclusion of the process, in particular the date when the six-year period will end.

11. In addition, during the whole assessment process, Applicants will have to pay an annual fee as defined in PS/W 17/2016.
12. A membership application is driven by the SCC. Depending on the size and the complexity of the Applicant's organisation and based on the recommendation provided by the SCC, the PIC/S Committee shall appoint (i) one Rapporteur and (ii) one or several Co-Rapporteur(s) to review and evaluate the membership application and additional team member(s) for the conduct of the observed inspections. The Rapporteur and Co-Rapporteur(s) may be proposed by the SCC or other members of the Executive Bureau to the Committee which will take the final decision. All the information from the Applicant referred in paragraph 9 shall be forwarded by the Secretariat to the Rapporteur and Co-Rapporteur(s) designated by the Committee.
13. The task of the Rapporteur, with the assistance of the Co-Rapporteur(s), is:
 - to create, coordinate and maintain the communication between the assessment/audit team and the applicant/auditee,
 - assign work within the audit team (including appointment as back-up)
 - evaluate together with the team the documentation submitted by the auditee,
 - 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 understands basic PIC/S requirements. In cases of doubt or if the Applicant is not understanding PIC/S requirements, the Applicant is invited to first go through the pre-accession procedure.
 - to send to the SCC a report on the progress of the evaluation,
 - to inform the SCC about facts needing immediate action,
 - to ask directly to the Applicant, where necessary, for additional information,
 - to inform the SCC and the Committee on his/her opinion on the gathered information,
 - to lead the discussion during a hearing of the Applicant's representative(s),
 - prepare the on-site visit,
 - prepare the audit plan,
 - share the duties among the audit team members,
 - prepare the draft report,
 - reach an agreement for the preliminary report to be sent to the auditee,
 - send the report to the auditee,
 - receive and distribute answers/ CAPA plan from the auditee,
 - ensure the evaluation of responses/CAPA from the auditee,
 - prepare and reach an agreement for the final report to be sent to the auditee and the SCC,
 - send the report to the auditee and the SCC,

- In the event that a rapporteur leaves the PIC/S PA in which he works before the process has been completed and validated, it is his responsibility to inform his hierarchy and the SCC as soon as possible so that the accession process can be satisfactorily completed and within the time limits.

Some of these tasks could be done remotely, if agreed between the SCC and the Applicant.

14. The SCC is in charge to assess the final evaluation report through direct contacts with the Rapporteur (including a possible hearing during a SCC teleconference). If necessary, the Rapporteur can involve the Audit Team. An agreement between the SCC and the Rapporteur has to be reached before submitting the final evaluation report to the Committee.
15. The final decision is made by the Committee.
16. If an Applicant has been assessed or reassessed by two other PIC/S PAs under other programmes within the past 5 years and based on the recommendation issued by the SCC, 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 (including reports of the observed inspections) with the PIC/S Committee. In this case and based on recommendation issued by the SCC, 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.

3. PARTICIPATION IN TRAINING ACTIVITIES

17. The Applicant shall be invited to attend PIC/S seminars and other training activities.
18. 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.

4. PARTICIPATION IN PIC/S COMMITTEE MEETINGS

19. 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 regulatory compliance programme (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.

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

20. Unless subject to a partial assessment (as described at paragraph 16) an Audit Team of the PIC/S Committee shall be invited to the country of the Applicant in order to make an on-site assessment of the GMP regulatory compliance

programme as well as to observe, in the course of inspections to one or more representative pharmaceutical or Active Pharmaceutical Ingredients (API) 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”.

21. The Audit Team shall prepare a report on the on-site visit (as described in PS/W 10/2005) and present it to the SCC. The report shall contain a recommendation on the acceptance (or rejection) of the application as well as on expected corrective and preventive actions (CAPA plan). The SCC is in charge to endorse this report (see paragraph 14). On the basis of this recommendation endorsed by the SCC, the PIC/S Committee may decide that a follow-up visit is necessary to verify that appropriate CAPA plan has been implemented following the first visit on which the report is based.

6. DECISION BY THE PIC/S COMMITTEE

22. 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 other Applicants, pre-Applicants and 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.
23. In the case of a negative outcome, the Committee shall explain the reason why during a hearing with the concerned Applicant, in order to be sure that the two parties (the Committee and the Applicant) have a common and shared understanding of this outcome. The Applicant could be encouraged to submit a new application when ready. The Secretariat should formally notify the Applicant of the result of its application including the rationale for the decision
24. 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.

7. TIMEFRAME AND APPLICANT'S RESPONSIBILITIES

25. The total timeframe for the application process should not exceed six years (from the time of the acceptance of the application for the accession 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, based on recommendation issued by the SCC, on a case by case basis, by consensus and if duly justified.
26. “Clock-stops” not exceeding a total period of 12 months may be agreed by the Committee, based on recommendation issued by the SCC, 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.

27. In the event of “force majeure” (e.g. pandemic, natural disaster, armed conflict, etc.) as well as travel restrictions due to security or other reasons impacting the jurisdiction of the Applicant (or around), the Committee shall decide, upon recommendation of the SCC, to freeze the application process for a period, which cannot exceed the total timeframe, as defined in paragraph 25. During this period, the Applicant is exonerated from paying the annual fee and attending PIC/S meetings and events. It is the responsibility of the Applicant to provide assurances that the application process can resume, subject to review by the SCC. Upon recommendation of the SCC, the Committee shall decide on the unfreezing of the application process and related conditions, in particular the date. Once unfrozen, the Applicant must indicate whether it wishes to update its application or re-apply.
28. The Applicant shall provide the Rapporteur with progress reports on a regular basis regarding the implementation of CAPA plan. This obligation shall continue even after the Applicant’s accession to PIC/S.
29. 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.
30. It is desirable for relevant staff of the Applicant to participate in PIC/S Seminars; participation in Expert Circles is recommended.

8. 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-Accession 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 with the revised PIC/S Financial Rules
19 April 2022	PS/W 14/2011 (Rev. 3)	- To remove the pre-accession process which is moved to separate Guidelines on Pre-Accession (PS/W 12/2019)

		<ul style="list-style-type: none">- To adapt the Accession Guidelines to situations where a request for Accession is made by multiple competent authorities- To better define the role of the Rapporteur, the SCC and the Committee- To better define the scope of the assessment (based on the GMP regulatory compliance programme ("GRCP"))- To introduce the possibility to freeze a membership application
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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 GMP regulatory compliance programme (GRCP) in place 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 and API 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 be covered by the Applicant. One auditor trainee should also be paid by the Applicant. Observers are allowed after approval of SCC. Expenses for observers are for their own budget (see Travel Guidance PS/W 9/2014).

PROGRAMME

3. A programme should be prepared jointly by the Applicant and the Team Leader of the Audit Team. The programme of the visit should be comparable to the PIC/S Joint Re-assessment Programme (see PS/W 10/2005), the EU Joint Audit 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 with the Applicant's Management, Head of each part of the GRCP, including a general presentation, not exceeding 1 hour, on the national GRCP,
 - a meeting with the Head of Inspectorate and inspectorate staff (see item 5 below),
 - an examination of the GRCP'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 and relevant staff to review the visit and to make comments and recommendations.

GENERAL INFORMATION

5. The concerned Heads of GRCP staff of the Applicant should provide an overall information about the 78 indicators (Audit Checklist PS/W 1/2005) and PIC/S specific requirements listed at Annex of the Audit Checklist.

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 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),
- asking for corrective and preventive actions and their timeframe, and
- appraise the overall impressions.

8. The Audit Team should prepare a report to the Sub-Committee on Compliance (SCC) after the visit in which the recommendation concerning the accession to the Pharmaceutical Inspection Co-operation Scheme should be given. For the format of the Audit report, see PS/W 12/2002.

9. 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

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

- (a) the Applicant needs to address concerns raised before any follow-up visit is arranged;
- (b) a follow-up visit should take place before further consideration, with a report of this visit provided to the Committee for its decision;
- (c) the accession process should proceed subject to a follow-up visit with a report of this visit provided to the Committee, 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(ies)]

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)

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

- expresses / express the willingness of *[name of Authority(ies)]* 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 / undertake 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 / agree to] contribute to the effective operation of the Scheme by means of constructive co-operation with the other Participating Authorities and participation in the meetings and financing of PIC/S.

The name and address of *[name of Authority(ies)]* 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]