



PIC/S 1/98 (Rev. 4)  
Annex  
13 December 2007

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

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

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## 1. DOCUMENT HISTORY

Adoption by Committee	14-15 June 2004
Entry into force	1 July 2004

## 2. 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 assurance of inspections, and
- contributing to global harmonisation of standards of good manufacturing practice (GMP).

2. The Scheme is also a means of ensuring, through official inspections, that strict quality control of the manufacture of pharmaceutical products is carried out in accordance with appropriate 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 the Participating Authorities. 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 pharmaceutical inspectorates.

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 is also aiming at the fostering of 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 "PIC/S Committee"), on the basis of practice and experience, has 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) <sup>1</sup>, the same procedures shall apply to both.

8. Applications for participation are normally considered by the PIC/S Committee one at a time.

### **3. ACCESSION PROCEDURE**

9. An authority applying for participation in this Scheme (hereafter referred to as “the Applicant”) should address itself first to the Scheme's Secretariat.

10. On receipt of the authority’s letter of intent to participate in the Scheme, the Secretariat shall:

- (a) provide the Applicant with all appropriate information, in particular the application and information on fees;
- (b) ask the Applicant to fill in and return the application and questionnaire (PS 2/99-2), together with the necessary supporting documents in English (see list at Annex III of PS 2/99-2);
- (c) check that the submitted application and questionnaire is complete, in particular that all necessary supporting documents have been submitted. If the application is complete, the Applicant must be requested to pay the relevant application fee. Incomplete applications will be returned to the Applicant;
- (d) circulate the completed application and questionnaire to Members of the Committee.

11. 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 Co-ordinator responsible for Membership Applications in the Executive Bureau. All the information in paragraph 10b shall be forwarded by the Secretariat to the Rapporteur and Co-Rapporteur(s) designated by the Committee.

12. The task of the Rapporteur <sup>2</sup>, with the assistance of the Co-Rapporteur(s), is:

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<sup>1</sup> see Joint Reassessment Programme (PS/W 9/2000)

<sup>2</sup> This is equivalent to the task of the Team Leader under the JRP (see PS/W 10/2005)

- to control that the application and questionnaire is complete,
- to evaluate the information contained in the application and questionnaire,
- to send to the Co-ordinator, no later than one month before a PIC/S Committee meeting, a report on the progress of the evaluation,
- to inform the Co-ordinator about facts needing immediate action,
- to ask, where necessary, for additional information,
- to inform the PIC/S 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.

13. The Co-ordinator's task is to:

- propose to the PIC/S Executive Bureau candidates for Rapporteur and Co-Rapporteur(s) for new Applicants,
- draft a status report for the PIC/S Committee on the basis of progress reports prepared by the Rapporteur,
- in the event of problems needing immediate action, prepare with the assistance of the Rapporteur a proposal for the Executive Bureau's attention and action,
- monitor the timeframe of the accession process (see paragraph 25 - 28).

14. The final evaluation and decision is made by the PIC/S Committee.

15. If an Applicant has been assessed or reassessed by two other PIC/S Participating Authorities (PAs) 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 PAs. 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**

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

17. 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. MEETING WITH PIC/S COMMITTEE**

18. Following discussion in the PIC/S Committee, the Applicant shall be invited to send representatives to meet the members of the PIC/S Committee for an informal exchange of views and a discussion on the inspection system applied under the Scheme as compared to the national system of the Applicant. This will provide for an opportunity to ask questions on the documentation received and to obtain clarification on uncertain points. Several meetings can be held if necessary.

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

19. Unless subject to a partial assessment (as described at paragraph 15), an Audit Team of the PIC/S Committee shall be invited to the country of the Applicant in order to become better acquainted with its inspection system and inspection practice and standards, as well as to observe, in the course of visits 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.)

20. On the basis of a recommendation of the Audit Team, 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. PARTICIPATION IN PIC/S COMMITTEE MEETINGS AS GUEST**

21. Representatives of the Applicant may, if appropriate, be invited to attend meetings of the PIC/S Committee as "Guests".

#### **8. DECISION BY THE PIC/S COMMITTEE**

22. When the compliance with the provisions of the Scheme has been assessed and provided that all the Participating Authorities have given their consent during

a restricted meeting of the PIC/S Committee (i.e. without Guests), the Applicant shall be accepted as a Participating Authority.

23. The Secretariat should formally invite the new Participating Authority to accede to the Scheme. The latter should in turn accept to participate in the Scheme.

## **9. TIMEFRAME AND APPLICANT'S RESPONSIBILITIES**

24. The total timeframe for the application process should not exceed six years (from the time of the acceptance of the application until the PIC/S Committee's decision on acceptance as a Participating Authority). Any application which exceeds this limit and/or the above deadlines should be rejected.

25. The Applicant shall provide the Rapporteur with progress reports on a regular basis.

26. 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.

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

## **10. REVISION HISTORY**

<b>Date</b>	<b>Version number</b>	<b>Reasons for revision</b>
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 PAs - To delete the status of Observer for Applicants

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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 become better acquainted with the quality system of the Applicant, to observe two or more GMP inspections to pharmaceutical companies, as well as the methods of GMP inspection applied by the Applicant's inspectors in those companies.

2. Generally, travel costs to the visiting country and accommodation are covered by the Audit Team; the rest is provided by the Applicant. For countries located outside Europe, which involve higher travel costs for the Audit Team, the interested authority may consider providing, through the PIC/S Secretariat, financial assistance to help cover the travel costs of the Audit Team.

**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 system,
- a review of the companies to be visited, 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:

- quality management of the Inspectorate,
- manufacturer licensing system,
- communication with pharmaceutical assessors, laboratories, enforcement body and other bodies of the Agency,
- suspected quality defect management and Rapid Alert system,
- training of inspectors; and
- detailed information and the inspection plan and strategy for each company to be visited.

## **OBSERVED INSPECTIONS**

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

## **CLOSING MEETING & CONCLUSION**

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 interpretation of the GMP rules,
- make proposals for correcting these differences, 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 PIC/S 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 PIC/S 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.

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

- (a) the Applicant needs to modify its system of inspection/licensing 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.

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