



PHARMACEUTICAL INSPECTION CONVENTION  
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PI 002-3  
25 September 2007

**RECOMMENDATION**  
**ON**

**QUALITY SYSTEM REQUIREMENTS  
FOR PHARMACEUTICAL INSPECTORATES**

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## 1. DOCUMENT HISTORY

Adopted by the PIC/S Committee on	24 October 2000
Entry into force of PI 002-1 on	1 January 2001
Entry into force of PI 002-2 on	1 October 2004

## 2. INTRODUCTION

- 2.1 One of the main purposes of the Pharmaceutical Inspection Co-operation Scheme is to facilitate the exchange of information on national inspections in respect of the manufacture and, where relevant, wholesale distribution of medicinal products. The general requirements for National Pharmaceutical Inspectorates are to fulfil the requirements of National Legislation and of the relevant EU Directives for EU/EEA countries. Specific obligations of inspections as contained in national law and if any European Directives (for the EU/EEA countries), must be included in the National Inspectorate's quality systems.
- 2.2 This document outlines the quality system requirements for GMP Pharmaceutical Inspectorates. It is intended that each GMP Pharmaceutical Inspectorate uses the document as the basis for developing and implementing its own quality system and for preparing its own quality manual. In addition to providing a basis for self-assessment and a reference document for use by external assessors, establishing and maintaining an effective quality system will generate confidence within and between GMP National Pharmaceutical Inspectorates in the assessment of compliance with good manufacturing practice and/or good wholesale distribution practice.
- 2.3 National GMP Pharmaceutical Inspectorates, the European Commission (EC), the European Medicines Agency (EMA) and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) should co-operate with one another in exchanging experiences in the maintenance and operation of quality systems and in the further development of this document.
- 2.4 Only on a voluntary basis, this document could be useful for other inspectorates assessing compliance with GXP or for the inspection of pharmacies.
- 2.5 In preparing this text, the following documents were used (or noted):
- |                 |   |
|-----------------|---|
| EN 45004 : 1995 | General criteria for the operation of various types of bodies performing inspections;                   |
| EN 45012 : 1998 | General requirements for bodies operating assessment and certification/ registration of quality system; |
| ISO 9001-2000   | Quality management systems-Requirements;  |
| ISO 9004-2000   | Quality management systems: guidelines for performance improvements;                                    |

ISO 19011 : 2002	Guidelines for quality and/ or environmental managerial systems auditing;
PI 002-1 : 2000	PIC/S Recommendations on quality system requirements for pharmaceutical inspectorates;
October 2003	EU Revised Compilation of Community procedures on administrative collaboration and harmonisation of inspections;
1998	Proceedings of the PIC-PIC/S seminar on quality systems for pharmaceutical inspectorates.

### **3. PURPOSE**

- 3.1 The primary purpose of a quality system is to ensure that adequate quality standards are maintained. The purpose of adopting a common standard for quality system requirements is to achieve consistency in inspection standards between GMP National Pharmaceutical Inspectorates and thus to facilitate mutual recognition of and mutual confidence between those Inspectorates. This standard should help facilitate the implementation of the EEA Joint Audit Programme and PIC/S Joint Re-assessment Programme.
- 3.2 Each GMP national inspection service should use this document as the basis for developing its own quality system, so that inspection activities within each inspection service are carried out in accordance with a system which is compatible with systems of the other Participating Authorities.

### **4. SCOPE**

- 4.1 This document specifies the quality system requirements for National pharmaceutical inspection services concerned with good manufacturing practice activities.
- 4.2 Where wholesale inspections are required by national legislation to be carried out by GMP National Pharmaceutical Inspectorate Service, this document specifies the quality system requirements for National Pharmaceutical Inspection Services competent for the inspection of good wholesale distribution practice of medicinal products.
- 4.3 The quality system should include all activities involved in the GMP inspection process.

### **5. DEFINITIONS**

- 5.1 Quality system: The sum of all that is necessary to implement an organisation's quality policy and meet quality objectives. It includes organisation structure, responsibilities, procedures, systems, processes and resources. Typically these features will be addressed in different kinds of documents as the quality manual and documented procedures, modus operandi etc

- 5.2 Quality Indicators Selected data intended to be periodically observed to assist in assessing trends in performance.
- 5.3 Pharmaceutical Inspectorate The National body responsible for co-ordinating and carrying out GMP inspections, including inspections of pharmaceutical manufacturers and/or wholesale distributors. If relevant, this could include making decisions concerning the issue or withdrawal of establishment licences or authorisations for their activities, the issue or withdrawal of GMP certificates, providing advice and handling suspected quality defects.
- 5.4 Licence: For the purposes of this document, a licence is defined as an authorisation to manufacture and/or distribute medicinal products

## **6. QUALITY MANUAL**

- 6.1 The Pharmaceutical Inspectorate should prepare and maintain a quality manual covering the elements described in this document. It is for each Pharmaceutical Inspectorate to decide on the format and style of their quality manual, but it must include, or make reference to, the quality system procedures which define the activities of the Inspectorate and the arrangements for maintaining the quality system. The reference used to complete it (as ISO or EN norms) must be quoted too.

## **7. ADMINISTRATIVE STRUCTURE**

- 7.1 The structure, membership and operation of the GMP Pharmaceutical Inspectorate should be such as to enable it to meet the objectives of quality management and to ensure that impartiality is safeguarded.
- 7.2 The personnel of the inspection service, including sub-contracted personnel and experts, should be free from any commercial, financial and other pressures which might affect their judgement and freedom to act. The Pharmaceutical Inspectorate should ensure that persons or organisations external to the inspection organisation cannot influence the result of inspections. The system for obtaining fees should not improperly influence the inspection procedure. Rules for deontology, ethics, conflict of interest and improper influence should be clearly defined.
- 7.3 The relationship of the Pharmaceutical Inspectorate to other agencies and to other organisations within and outside the Inspectorate should be described where relevant.
- 7.4 The Pharmaceutical Inspectorate should implement a policy which distinguishes between the process of inspection and that of issuing a manufacturing licence.
- 7.5 Where relevant, the Pharmaceutical Inspectorate should implement a policy which distinguishes between the process of inspection and that of providing an advisory service. This service should be of benefit to all of industry and not solely to individual organisations.

## **8. ORGANISATION AND MANAGEMENT**

- 8.1 Senior management of the Pharmaceutical Inspectorate should make a formal commitment to support the recommended principles embodied in this document by ensuring that the quality policy of the Inspectorate is documented, that it is relevant to the objectives of that organisation and that it is implemented.
- 8.2 The responsibility, authority and reporting structure of the Pharmaceutical Inspectorate should be clearly defined and documented. The structure should be defined in organisation charts and should be supported by written job descriptions for each member of staff.
- 8.3 There should be nominated an appropriately qualified and experienced person or persons with responsibility to carry out the quality assurance function, including implementing and maintaining the quality system. This person should have direct access to senior management.
- 8.4 The Pharmaceutical Inspectorate should have sufficient resources at all levels to enable it to meet its objectives effectively and efficiently. Senior management should ensure that all personnel are competent and qualified to carry out their assigned duties and that they receive appropriate training. Such training should be documented and its effectiveness assessed periodically.
- 8.5 There should be a system for periodic management review of the quality system. Such reviews should be documented and records should be retained for a defined period.

## **9. DOCUMENTATION AND CHANGE CONTROL**

- 9.1 The Pharmaceutical Inspectorate should establish and maintain a system for the control of all documentation relating to the inspection system. This should include policies, procedures, guidelines and any documents of external origin such as regulations and directives which may direct the activities of the Inspectorate or influence the quality of its operations.
- 9.2 The document control system should ensure that documents are authorised by appropriate persons prior to issue and that only current versions are held by nominated individuals. A record of all relevant documents and document holders should be maintained. The system should ensure that superseded documents are withdrawn from use. Superseded documents should be retained for an appropriate and defined period.
- 9.3 The documentation system should ensure that any changes to documents are made in a controlled manner and are properly authorised. There should be a means of identifying changes in individual documents.

## **10. RECORDS**

- 10.1 The Pharmaceutical Inspectorate should establish and maintain a system of records relating to its activities which complies with any existing regulations. If relevant, the system should include documents received from licence applicants and licence holders as appropriate.
- 10.2 Records shall provide detailed information about the planning and scheduling of inspections, the way in which each inspection is to be conducted, a description of the inspection process, follow-up activities and recommendations to the body responsible for issuing licences.
- 10.3 All records should be handled in such a way as to prevent their damage or loss and should be retained for an adequate period consistent with any legal requirements. All records should be maintained in confidence to the inspected party unless otherwise required under freedom of information legislation, or unless required under exchange of information procedures and arrangements between National Pharmaceutical Inspectorates, the EU/EEA, the EMEA and Mutual Recognition Agreement (MRA) partners.

## **11. INSPECTION PROCEDURES**

- 11.1 The Pharmaceutical Inspectorate should conduct repeated inspections of manufacturers and/ or wholesale distributors and should issue inspection reports in accordance with National or European Community requirements as appropriate.
- 11.2 The Pharmaceutical Inspectorate should have the documented procedures and resources to enable inspection of manufacturing and wholesale distribution operations to be carried out in accordance with the official guidelines and National legislation and in accordance with a formal inspection plan. All instructions, standards or written procedures, worksheets, check lists and reference data relevant to the work of the Pharmaceutical Inspectorate should be maintained up-to-date and be readily available to staff.
- 11.3 When more than one inspector is involved in an inspection, a lead inspector should be appointed to co-ordinate inspection activities. The inspection report should normally be prepared by the lead inspector and should be agreed by all participating inspectors.
- 11.4 Inspection report format should be in compliance with the PIC/S procedure or European model.
- 11.5 Report should follow the procedure above. The inspection report should be sent to the responsible person of the inspected company (preferably the authorised person or qualified person). The lead inspector and all concerned inspectors should participate in assessing the eventual reply or replies to determine the appropriateness of corrective actions and the GMP status of the company.
- 11.6 Observations and/or data obtained in the course of inspections should be recorded in a timely manner to prevent loss of relevant information.
- 11.7 Completed inspections should be reviewed to ensure that the requirements are met.



## **12. INSPECTION RESOURCES**

### **12.1 Personnel**

- 12.1.1 The Pharmaceutical Inspectorate should possess the required personnel, expertise and other resources to perform inspections of manufacturers and/ or wholesale distributors to determine their compliance with the principles and guidelines of current good practices and with the relevant legislation.
- 12.1.2 The staff responsible for inspections should have appropriate qualifications, training, experience and knowledge of the inspection process. They should have the ability to make professional judgements as to the conformance of the inspected party with the requirements of good practices and the relevant legislation and be able to apply an appropriate degree of risk assessment. They should have knowledge of current technology, including computerised systems and information technology.
- 12.1.3 The Pharmaceutical Inspectorate should establish a documented system for recruiting and training its personnel and should carry out a regular review of the training received and the training needs for each member of staff. Individual training and qualification records should be maintained.

### **12.2 Resources and equipment**

- 12.2.1 The Pharmaceutical Inspectorate should have available the necessary resources and equipment to enable it to carry out its obligations effectively and efficiently.

## **13. INTERNAL AUDIT**

- 13.1 The Pharmaceutical Inspectorate should carry out and document periodic internal audits of its operations to assess compliance with the requirements of the quality system. Results of internal audits and associated corrective actions should be reviewed as part of the management review process.
- 13.2 Internal audit processes and documents, auditors qualifications should be clearly defined (e.g. reference to ISO 19011 : 2002).
- 13.3 Internal audit records should be retained for a defined period.

## **14. QUALITY IMPROVEMENT AND CORRECTIVE/PREVENTIVE ACTION**

### **14.1 Quality indicators**

- 14.1.1 The Pharmaceutical Inspectorate should establish and maintain quality indicators related to its activities notably in the area of timeframe mentioned in existing EU or national regulations (e.g. licensing system for manufacturing or marketing authorizations) and/ or documentation (e.g. writing reports).

- 14.1.2 Quality indicators should be reviewed as part of the management review process.
- 14.2 Corrective/ preventive action
  - 14.2.1 The Pharmaceutical Inspectorate should establish and maintain a procedure for the investigation of non-compliances with the quality system which are identified through internal or external audit of its activities. The procedure should include the prescribing, implementation and verification of corrective action. The procedure should cover also corrective actions arising from the investigation of complaints and other observations relating to the activities of the Inspectorate.
  - 14.2.2 The system should include a description of the steps to be taken in assessing the need for quality improvement and preventive action.
  - 14.2.3 Corrective and preventive actions should be documented and records should be retained for a defined period.

## **15. COMPLAINTS**

- 15.1 The Pharmaceutical Inspectorate should establish and maintain a procedure for dealing with complaints relating to its activities, or those of its personnel, and any contracted persons or organisations. The procedure should describe the application and verification of corrective action arising from the investigation of complaints.
- 15.2 Records should be maintained of all complaints received and actions taken and should be retained for a defined period.

## **16. ISSUE AND WITHDRAWAL OF LICENCES AND GMP CERTIFICATES**

- 16.1 The Pharmaceutical Inspectorate should establish and maintain a system for the issue and withdrawal of licences and GMP certificates, or for advising about the issue and withdrawal of licences and GMP certificates, as appropriate.
- 16.2 Licence and GMP certificate applications should be assessed and determined in a timely manner and within any time limits imposed by National or European Community requirements. Where time limits are imposed, inspection activities should be included in the total time taken to determine the application.
- 16.3 There should be a documented system for taking appropriate action against a licence / or a GMP certificate notably in the event of an adverse inspection report. The system should include descriptions of the actions available to the Inspectorate; such actions may include suspension or revocation of the licence and/or the GMP certificate(s). There should be a system for assessing compliance of an organisation with imposed licensing action.
- 16.4 The system should include a description of the appeals procedure available to licence holders.

- 16.5 If the licensing system is not part of the Pharmaceutical Inspectorate, the latter should establish and maintain defined liaison with it to obtain and guarantee targets quoted in paragraphs 16.1 to 16.3.

## **17. HANDLING SUSPECTED QUALITY DEFECTS AND RAPID ALERT SYSTEM**

- 17.1 The Pharmaceutical Inspectorate should establish and maintain a system for handling of reports of suspected quality defects in medicinal products as defined in a related Standard Operating Procedure or the related Community procedure.
- 17.2 The Pharmaceutical Inspectorate should establish and maintain a system for issuing Rapid Alert as defined in a related Standard Operating Procedure or the related Community procedure.
- 17.3 The Pharmaceutical Inspectorate should establish and maintain an updated list of all performed recalls.
- 17.4 If the organization in charge of handling suspected quality defects and rapid alert system is not part of the Pharmaceutical Inspectorate, the latter should establish and maintain defined liaison with it to obtain and guarantee targets quoted in paragraphs 17.1 and 17.2.

## **18 LIAISON WITH THE OFFICIAL MEDICINE CONTROL LABORATORY (OMCL)**

The Pharmaceutical Inspectorate should establish and maintain defined liaison with the OMCL(s) of its own Participating Authority in order to exchange information concerning the quality of medicinal products existing on the national market. In particular, an SOP should define sampling processes for starting material and medicinal products.

## **19. SUB-CONTRACTING AND ASSESSING**

- 19.1 The Pharmaceutical Inspectorate should normally carry out the GMP inspections for which it is responsible and whilst it may sub-contract some of its work it cannot sub-contract any of its accountability. Sub-contracted personnel or experts may be employed as part of an inspection team to assist or advise in a technical capacity, but that team should normally be led by a GMP lead inspector. Sub-contracted personnel should be bound by the requirements of the quality system and there should be a written contractual agreement between the parties.
- 19.2 Persons or organisations to whom inspection activities are contracted out and experts should be free from any commercial or financial pressures which might affect their freedom to act. They should follow defined rules to avoid conflict of interests and regarding ethic and deontology. Senior management of the Pharmaceutical Inspectorate should ensure that these persons are appropriately qualified and experienced and that they are independent of any organisations which they might be asked to inspect.

## 20. PUBLICATIONS

- 20.1 The Pharmaceutical Inspectorate should have at its disposal an updated list of licensed manufacturers and/ or wholesale distributors. The list should be made available to authorised bodies when requested.

## 21 REVISION HISTORY

<b>Date</b>	<b>Version Number</b>	<b>Reasons for revision</b>
15.06.2004	PI 002-2	Amendment made to bring PIC/S recommendation in line with the EU document on quality system requirements; deletion of the Appendix (guidelines for documenting a quality manual); change in the Editor's co-ordinates.
25.09.2007	PI 002-3	Change in the Editor's co-ordinates.

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