EUROPEAN COMMISSION
ENTERPRISE and INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Pharmaceuticals

GUIDANCE DOCUMENTS CONTAINING THE COMMON PROVISIONS ON THE CONDUCT OF GCP INSPECTIONS BY COMPETENT AUTHORITIES OF THE DIFFERENT MEMBER STATES

GUIDANCE FOR THE PREPARATION OF GOOD CLINICAL PRACTICE INSPECTIONS

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This document forms part of the guidance documents containing the common provisions on the conduct of GCP inspections . Please check for updates in the Volume 10 of the Rules Governing Medicinal Products in the European Union.
http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol10_en.htm

1 INTRODUCTION

The scope of this document is to provide guidance for the preparation for GCP inspections carried out by competent authorities of the different Member States, which may take place on any of the following occasions:

(a) before, during or after the conduct of clinical trials;
(b) as part of the verification of applications for marketing authorisation;
(c) as a follow-up to the granting of authorisation.

The responsibilities set out in this guidance are outlined in the guidance for coordination/co-operation with other organisations involved in assessing Good Clinical Practice requirements. This guidance on preparing for the inspection may be used in preparing for any type of inspection (see guidance for the conduct of GCP inspections, including its annexes).

2 INSPECTION INITIATION

The appointment of the inspection team and acceptance of each role is part of the guidance for coordination/co-operation with other organisations. Prior to, or during the process of requesting a GCP inspection, informal contacts and assessments (phone, fax, email) and an evaluation of the EudraCT/national inspection databases will have helped define the context of the request. A decision on the scope of the inspection, the centres/sites and the composition of the inspection team will also have been made. This will have resulted in the definitive inspection request/assignment.

The involved MS Inspectorate(s) will subsequently designate the Lead Inspector (LI) and the other members of the inspection team. In those cases where more than one MS is involved and more than one site is inspected, a Reporting Inspector (RI) could be appointed and acceptance of that role is part of the guidance for coordination/co-operation. In this latter case, communication between the RI and the LI(s) will result in the definition of the site inspection team and formal assignment of the LI(s). The language of the inspection at each site will be in general the local language.

The dates and places of each inspection site are set by the LI(s) according to the local procedures. The LI(s) communicate this information to the RI, when applicable, who checks that the formal timelines are not endangered. Subsequent changes in the composition of each local team should be communicated to the RI.

At the moment the formal inspection request is issued, the LI(s) or RI when applicable, has been appointed, arrangements/contracts between the involved parties (i.e MS Inspectorates for joint inspections, etc.) have been drawn up and contact points within the Inspectorate(s) have been identified.

The LI(s) or the Reporting Inspector, when applicable, formally receives a copy of the inspection request according to the co-ordination/ co-operation procedure. This is the formal start of this guidance for the preparation of the inspection. The preparation of the inspection should be completed within a deadline according to the local procedures

A contact point at the sponsor/applicant should be identified .The inspection will be announced to the sponsor/applicant in writing and additional documents/information requested (see more details in section 7). To note that in some cases inspections may be unannounced.

3 REVIEW OF DOCUMENTS AND INFORMATION

Essential information and documentation required for preparing the inspection need to be identified, obtained and reviewed. The information needed to conduct the inspection, may be derived from a number of sources eg. the inspection request, MA dossier, reference documents, guidelines,

legislation, inspection SOPs (EU, local), international standards (ISO/NEN), local legal requirements (EU, third country), local field standards, additional documents requested from the sponsor/inspectee etc. A guide to the documentation that may be used for review prior to the start of an inspection is listed in the appendix 1 to this procedure.

This information should be reviewed and evaluated by the LI(s) and by the RI when applicable. The inspection request should be evaluated on the basis of the applicable/available documents and information. Results of this review will be incorporated into the inspection plan(s).

In case the sponsor/applicant fails to provide the inspection team with the requested documents, or the submitted documentation is below the required standard, these objections will be notified to the sponsor/applicant in writing, with a deadline for remedial action. If a response is not received, the necessary measure should be taken according to the local procedures.

The review of information on all aspects of the inspection could lead to the identification of additional technical and logistical needs (e.g. translation in case of language problems, transport feasibility), or other sites requiring inspection to achieve the objectives of the request.

In addition, as a result of the review of the documentation the inspection team members may conclude that additional (external) expertise is necessary to complete the inspection teams at the various sites. The information on the formal acceptance and the composition of the complete inspection team(s) will be added to the inspection files.

4 INSPECTION REQUEST VALIDATION

If the review of information and documentation results in a requirement for modification of the original request (scope of the inspection, sites for inspection, timelines), this must be communicated to the people responsible for the request of this inspection and the reasons substantiated according to the local procedures. This change must be agreed by all parties involved prior to incorporation into the inspection plan(s).

5 INSPECTION FILING AND ARCHIVING

The LI(s) participating in the inspection have to open Local Inspection Files. When a RI is applicable, he/she should also start the preparation of the central inspection file for the inspection as soon as the inspection is initiated. The format of these files should be in accordance with the format set out in the Guidance for Record keeping and archiving of documents obtained or resulting from the Good Clinical Practice inspection.

6 INSPECTION PLAN

An inspection Plan will be prepared for the inspected site. In those cases where a RI is appointed, a central inspection plan should be prepared by the appointed RI and finalised in agreement with the LIs. Based on the central inspection plan, the LIs will prepare local inspection plans for each selected site. The level of details in these inspection plans may vary. Routine inspection requests may need less detail than for cause inspections, or inspections for specific products or systems.

The inspection plan(s) will generally outline and define the relevant aspects of the clinical trial site(s) and scope that are to be covered during the inspection at the selected site(s). It will be based on the inspection request and the reviewed documentation.

The inspection plan(s) will incorporate the timelines for the practical organisation of the inspections at the site(s), the timelines for the preparation of local report(s), whereby the IIR, if applicable, will have to be finalised according to the guidance on coordination/co-operation with other organisations.

A checklist may be designed as part of the local inspection plan.

Elements to be taken into account when drafting the inspection plan are listed in Appendix 2.

7 INSPECTION ANNOUNCEMENT

The inspection team may announce the inspection to the applicant/sponsor (contact point). The responsible personnel of the selected site(s) will also be informed of the forthcoming inspection according to the procedures of the MS Inspectorate.

Inspection date(s) for the selected site(s) are communicated to the site(s), in accordance with the timelines in the site inspection plan(s).The relevant parts of the inspection plans will be communicated to the responsible personnel at the site.

Occasionally the sponsor/MAH may ask for a pre-inspection meeting to discuss the scope of the inspection. The LI(s) or, RI when applicable, are under no obligation to agree to such a meeting. In case the LI(s) or, RI when applicable, feel that a pre-inspection meeting would be useful (particularly to clarify aspects of the scope for a complex inspection), they have the discretion to arrange such a meeting as long as it does not affect the overall timelines for the inspection and the sponsor/MAH undertakes to pay the additional costs. The scope of the inspection as defined in the inspection request should not be affected by the results of this meeting.

8 PRACTICAL PREPARATION

The extent of preparation may differ between inspections, depending on the type of inspection, type of trial, therapeutic area and product, location of the inspection, number of selected sites, etc.

For third country inspections it may be convenient to have the sponsor or applicant company helping with the provision of air tickets, local transport and accommodation according to the itinerary set out by the inspection team.

For EU inspections, the LI may facilitate the practicalities for the other team members as much as possible.

For third country inspection it may be essential to establish contact with the local inspectorates/authorities to inform them of the proposed inspection.

There may also be a need to ensure the availability for a translator in case the language used locally is not available within the inspection team. This service may be requested from the sponsor.

9 RESPONSIBILITIES

9.1 Responsibilities of the Lead Inspector (LI)

- The communication with the parties involved in the request for the inspection.
- The verification of the location of the site(s) and for the co-ordination, organisation and validation of the inspection team.
- The preparation of the local inspection plan.
- The preparation, upkeep, quality and security of the local inspection files and for keeping the archives according to the local procedures
- Starting the preparation of the inspection after formally receiving a copy of the request according to the set procedures.
- Proposing and setting the timelines for the inspection activities (preparation, conduct, reporting).
- Initiating the formal information flow to the inspection team.
- The review of the quality and completeness of the information
- The sending of the submitted documentation and information to the inspection team without delay.
- Deciding whether more information is needed from those parties involved in the request for the inspection.

- The conduct of the inspection at the site in accordance with the local SOPs and legal requirements.
- Checking that the timelines are kept throughout the duration of all inspection facets.
- Checking that the confidentiality requirements are adhered to.
- Keeping the inspection documentation up to date and secure.
- Ensuring that all local relevant reference documents are available and important local details/differences communicated to the inspection team.

- **Responsibilities of the Reporting Inspector (RI), when applicable**

- The communication with the parties involved in the request for the inspection.
- The verification of the location of the site(s) and for the co-ordination of the inspection team.
- The preparation of the central inspection plan.
- The preparation, upkeep, quality and security of the central inspection files and for keeping the archives according to the local procedures
- Starting the preparation of the inspection after formally receiving a copy of the request according to the set procedures.
- Proposing and setting the timelines for the inspection activities (preparation, conduct, reporting).
- Initiating the formal information flow to the inspection team.
- The review of the quality and completeness of the information
- The sending of the submitted documentation and information to the inspection team without delay.
- Deciding whether more information is needed from the parties involved in the request for the inspection.
- The conduct of the inspection at the site in accordance with the local SOPs and legal requirements (applicable when there is also LI).
- Checking that the timelines are kept throughout the duration of all inspection facets.
- Checking that the confidentiality requirements are adhered to.
- Keeping the inspection documentation up to date and secure.

APPENDIX 1: DOCUMENTS/INFORMATION THAT MAY BE USED FOR REVIEW PRIOR TO THE START OF THE INSPECTION

1. **Parties involved in the request of the inspection**
   Inspection Request
   Inspection Procedures
   Assessment Reports, when applicable
   List of Questions, response to the LoQ, when applicable

2. **Overview of the conduct of the study:**
   total number of sites/locations/countries
   inclusion rate, screening, randomisation, etc.
   SAEs, ADRs
   drop out frequency
   time frame of trial
   annual reports, final report
   presence of a similar/extension protocol

3. **Sites**
   investigator(s)/co-investigator(s) CVs and qualifications
   information on sites involved/selected (including e.g. pharmacy, clinical departments, X-ray, MRI, Echo, ultrasound, ECG, CT, CROs)

4. **Lab**
   local/central
   type of labs involved
   type of examinations/tests
   special equipment/procedures

5. **Sponsor**
   responsibilities defined in contracts
   CRO(s) involved
   protocol, amendments, investigator's brochure
   CRFs
   patient information and consent
   printout (of parts) of the clinical database
   quality management (QC, QA)
   sponsor SOPs related with the scope of the inspection
Monitoring procedures/reports
Monitoring Plan
Data management Plan
Statistical analysis Plan

6. **Trial Medication**
   GMP
   Manufacturing site information
   labelling
   blinding procedures
   randomisation list/procedures (eg. IVRS)
   quality documentation
   batch release certificate

7. **Ethics**
   patient information sheet/informed consent form
   patient recruitment process
   insurance documents

updates of safety information/IB
IEC opinion

8. Local inspectorate

availability of qualified inspectors
availability of qualified GMP inspectors (if the scope of the inspection covers IMP)
recruitment of external expertise
time schedule

9. Applicable regulations/guidelines

applicable GCP and legal requirements
notification/approval of protocol
importation of investigational products
announcement of inspection to the competent authority
insurance
trial medication: import license, labelling, storage, destruction
SAE reporting

10. Data

tabular listings of individual data

- per site
- the individual patient data listings for the patients recruited at this clinical trial site

APPENDIX 2: ELEMENTS TO BE TAKEN INTO ACCOUNT WHEN DRAFTING THE INSPECTION PLAN

1. General aspects

Items
Support
Timelines
Expertise
SOP
Legalities

2. General Content

Agenda, Dates
Sites, Facilities
Team Members
Systems
Specific contents

3. Layout options

Linear
Modules
Agenda with Addenda

APPENDIX 3: REFERENCES

- Directive 2001/20/EC on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
- Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such product.
- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the community code relating to medicinal products for human use, as amended.
- Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
- EUDRALEX Volume 10 - Clinical trials, of the Rules Governing Medicinal Products in the European Union: http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol10_en.htm