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Guidance for the conduct of good clinical practice inspections

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Guidance for the conduct of good clinical practice inspections

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1. Introduction

The scope of this document is to provide guidance for the conduct of Good Clinical Practice (GCP) inspections that are carried out by competent authorities of the different Member States, which may take place on any of the following occasions:

- Before, during or after the conduct of clinical trials.
- As part of the verification of applications for marketing authorisation.
- As a follow-up to the granting of authorisation.

The guidance is applicable for any site to be inspected and may involve inspection in one Member State only or several Member States.

This guidance takes into account the following procedures:

- *'Guidance for the preparation of GCP inspections'* (EMA/165056/2016) which describes the steps immediately before the conduct of an inspection and particularly the inspection plan.
- *'Guidance for the preparation of GCP inspection reports and communication of inspection findings'* (EMA/359269/2016) which describes the contents of GCP inspection reports and the procedure for their approval.

During the preparation of the inspection an inspection plan is established. This plan will depend on the scope of the inspection. The lead inspector (LI) will conduct the inspection at the selected site.

Inspections will be conducted within the framework of this document and national procedures. The emphasis of the inspection may vary depending on whether or not the inspection is related to the assessment of a Marketing Authorisation Application, to the routine surveillance of clinical trials performed in the Member States, or to another specific purpose.

As the Regulation (EU) No 536/2014 provides the basis for the application of a risk proportionate approach to the design and conduct of clinical trials, inspectors should take this into account during the inspection when such an approach is implemented in the conduct of the clinical trial inspected. Risk adaptations should be clearly described and justified in a risk assessment and mitigation plan (see reference iv for further information).

2. Opening meeting

Before the start of the inspection an opening meeting must take place between the inspector(s) and the inspectee(s).

The purpose of an opening meeting is to:

- introduce the inspector(s) to the inspectee(s);
- explain the regulatory framework for the conduct of the inspection;
- be informed of any national, departmental or other practices which affect the implementation of quality systems or GCP compliance by the inspectee(s);
- introduce the inspectees and identify their roles and responsibilities, including distribution of duties and functions for the conduct of the trial, if applicable Review the scope and the objectives of the inspection;

- provide a short summary of the methods and procedures to be used for the conduct of the inspection;
- confirm that the resources, documents, electronic systems and facilities needed by the inspector(s) are available;
- confirm the time and date for the closing meeting and any interim meetings;
- clarify the inspection plan provided to the site, if necessary.

3. Conduct of the inspection/collecting information

The main inspection activities should be detailed on the inspection plan. Nevertheless during the inspection, the inspector(s) may adjust the plan to ensure the inspection objectives are achieved.

Sufficient information to fulfil the inspection objective(s) should be collected through examination of relevant documents with direct access, interviews and observation of activities, equipment and conditions in the inspected areas. The names and titles of persons interviewed or present during the inspection meetings and the details of the inspected organisation should be documented.

If access to records or systems, or copying of documents is refused for any reason or there is any withholding of documents or denial of access to areas to which the inspector has legal access, these refusals should be documented and included in the inspection observations, as well as challenged and escalated where appropriate.

For each type of site to be inspected as well as for the archiving, an annex identifies detailed items that may be checked during the inspection.

- Annex I: conduct of the inspection at investigator site.
- Annex II: conduct of the inspection at clinical laboratories.
- Annex III: conduct of the computer systems inspection.
- Annex IV: conduct of the inspection at sponsor site and/or Contract Research Organisations.
- Annex V: conduct of inspection of phase I units.

For each item it should be checked, if applicable, how data was generated, collected, reported, analysed, modified and archived.

4. Inspection observations and minutes of the inspection

All inspection observations should be documented. If appropriate, copies should be made of records containing inconsistencies or illustrating non-compliance.

At the end of the inspection, the inspector(s) should review all observations to determine which are to be reported as findings. The inspector(s) should then ensure that the findings are documented in a clear, concise manner and are supported by objective evidence. All reported findings should be identified with reference to specific requirements of the standard(s) or other related documents against which the inspection has been conducted. Observations not classified as findings may be documented as comments.

If required by national regulations, the inspection observations may be collected in minutes (or similar) to be written by the inspector(s) at the end of the inspection.

5. Closing meeting with the inspectee(s)

At the end of the inspection, the inspector(s) should hold a closing meeting with the inspectee(s). The main purpose of this meeting is to present inspection findings and comments to the inspectee(s) and appropriate management board, if necessary, to ensure that the results of the inspection are clearly understood and that there is no misunderstanding by either the inspector(s) or the inspectee(s).

Issues to be followed up by the inspectee(s) should be addressed, including any additional documents that may need to be sent to the inspection team.

During this meeting the inspector(s) should give details on the circulation of inspection reports (i.e. deadline to reply) according to the "Guidance for the preparation of GCP inspection reports and communication of inspection findings" (EMA/359169/2016), and national procedures, if applicable and any further planned inspections, for example associated investigator sites.

6. References

i. Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC

ii. Commission Implementing Act on detailed arrangements for clinical trials inspection procedures including the qualifications and training requirements for inspectors, pursuant to Article 78(7) of Regulation (EU) No 536/2014 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.

iii. 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.

iv. Risk proportionate approaches in clinical trials. Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use.

v. EUDRALEX "Guidelines for Clinical Trials", Volume 10 of the Rules Governing Medicinal Products in the European Union: http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol10_en.htm.