EUROPEAN COMMISSION
ENTERPRISE and INDUSTRY DIRECTORATE-GENERAL

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

Annex II
TO GUIDANCE FOR THE CONDUCT OF GOOD CLINICAL PRACTICE INSPECTIONS
Clinical Laboratories

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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

This guidance may be applied to the inspection of laboratories involved in clinical trials, e.g. analytical chemistry, clinical biochemistry, haematology, microbiology, histopathology, cytology, genetics.

As there is already a large volume of guidelines and other documentation available on the inspection applicable to laboratories, this guidance presents merely a general outline of the elements that have to be taken into account when inspecting such laboratories.

The following aspects should be checked during an inspection:

2. GENERAL ASPECTS

2.1. Background

2.1.1. Scope of work and responsibilities.
2.1.2. Accreditation status of the laboratory (the methods) e.g. GLP, GMP, ISO, EN.
- Fulfilment of national requirements of accreditation.
- Relevance of accreditation in the context of clinical trial(s).

2.1.3. Proportion of work in connection to clinical trials.

2.2. Organisation and Personnel

2.2.1. Organisation charts (facility management and scientific organisation charts).
2.2.2. Systems for QA and QC, including programmes for internal audits.
2.2.3. SOP system (distribution, relevant topics covered, like: availability including holidays etc., audit-trail, clinical trials, archiving etc).
2.2.4. Disaster plans, e.g. handling of defective equipment and consequences.
2.2.5. Staff – qualification, responsibilities, experience, availability, training programmes, training records, CV.

2.3. Contractual arrangements

2.3.1. Procedures, e.g. for contracts and sub-contracts, protocol, protocol amendments, definition of source data, agreements for reporting.
2.3.2. Specification of methods and procedures (including sample handling).
2.3.3. Agreed access and availability for monitoring, audit and inspection.
2.3.4. Data recording, handling and archiving.
2.3.5. Security and protection of subject confidentiality.

2.4. Facilities/ Premises

2.4.1. Suitability and adequacy of premises – e.g. adequate degree of separation of work areas to avoid mix-ups, contamination and interference.
2.4.2. Environmental conditions, e.g. temperature, airflow and air pressure, microbiological contamination.
2.4.3. Security and safety, e.g. fire, water and pest control.

2.5. Apparatus/ Equipment, Materials, Reagents

2.5.1. Apparatus available, in good working order and complies with relevant specifications.
2.5.2. Quality of general supplies including tap water, analytical water, gases etc.
2.5.3. Records of operation, maintenance, justification and calibration. Records of the validation for the methods used for the measuring equipment and apparatus (including computerised systems). Log books.
2.5.4. Materials and reagents are prepared, labelled and stored under appropriate conditions and adherence to expiry dates. Labels for reagents indicate their identity, source, concentration and expiry dates.
2.5.5. Apparatus and materials used do not alter to any appreciable extent the samples.
2.5.6. Definition of source data and source documents, retrieval and archiving. Data generated by automatic systems, e.g. listings, graphs, record traces or computer printouts, and their archiving.

3. TRIAL RELATED ASPECTS.

As part of the inspection all aspects applicable to the clinical trial, e.g. as listed under section 2, should be inspected.

3.1. Handling of samples

3.1.1. Pre-examination

- Samples obtained from subjects in the clinical laboratory, (date and time), identification, labelling, conditions, preparation, storage.
- Consideration for patient confidentiality in label details (where applicable, for example at laboratories remote from the investigator site).
- Documentation of receipt (date and time), identification, condition, re-labelling and storage of samples by identifiable person.
- Confirmation by the receiving laboratory that the samples were subject to appropriate handling and transfer prior to receipt for analysis.
- Procedures for acceptance or rejection of samples for analysis.
- Aliquotting and distribution for examination.

3.1.2. Examination

- Compliance with protocol and specified test methods.
- Traceability and identification of samples and controls.
- Recording of data, acceptance and release of results.
- Handling of non-conformance, repeat analysis / re-analysis, and results within critical / alert ranges.
- Competence, training and experience of personnel.

3.1.3. Procedures for disaster recovery

3.1.4. Post-examination

- Storage (anonymisation, decoding), retrieval and destruction of samples.

3.2. Material and methods

3.2.1. Material and methods according to the specification stated in the protocol / contract and/or required according to Ph Eur.
3.2.2. Validation status of the methods, appropriate setting of limits of detection / quantification, precision/accuracy, known inferences and specific control measures.
3.2.3. Participation in external control programmes, if applicable.

4. REPORTING OF LABORATORY RESULTS

Various systems for reporting of results may be required according to the protocol / contract e.g. report per sample (i.e. for immediate consideration in medical care of the subject) or on an integrated basis (i.e. to be used in the trial report). This will affect the procedures used by the laboratory and during the inspection.

4.1. Procedures for reporting and evaluation of results and for data transfer

4.2. Systems for alerting results that are unexpected and/or significant deviations from pre-specified limits

4.3. Transcription of raw data into the report

4.3.1. Identification of laboratory.
4.3.2. Unique identification and localisation of the subject.
4.3.3. Identification of investigator.
4.3.4. Date and time of sample collection, and time of receipt.
4.3.5. Date and time of examination and release of report.
4.3.6. Source of primary sample type and any comments of its quality.
4.3.7. Description of the examination and of its results.
4.3.8. If applicable, detection limit, uncertainty of each measurements, and reference intervals.
4.3.9. Where appropriate, interpretation of results and other comments.
4.3.10. Identification of the person releasing the report.

4.4. Attribution of review and release of the report(s) to the responsible personnel

4.5. Procedures for alterations and amendments of reports

4.6. Procedures for complaints and corrective actions

5. QUALITY ASSURANCE

5.1. Integrity of data reported by internal QA/QC and /or sponsor's QA/QC personnel, (audit certificate)

6. 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