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GCP Inspections

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PRINCIPLES OF EUROPEAN GCP INSPECTIONS

Clinical Trials Directive 2001/20/EU

- **Inspections shall be conducted by the competent authority of the Member State, in whose territory the site to be inspected is located**
- **They shall be carried out on behalf of the Community and the results shall be mutually recognised**
- **Inspections in relation to centralized authorization procedures (Regulation (EWG) Nr.2309/93) shall be coordinated by the Agency**

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PRINCIPLES OF EUROPEAN GCP INSPECTIONS

(cont.)

- **A Member State may request assistance from another Member State**
- **The Commission may request a new inspection should verification of compliance with this Directive reveal differences between Member States**
- **The Commission or a Member State may propose an inspection at the trial site and/or the sponsor's premises and/or the manufacturer established in a third country**

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REASONS TO PERFORM GCP INSPECTIONS

GCP inspections are routinely performed

- **to verify that organisations, institutions and facilities have quality assurance arrangements in place which ensure the conduct of clinical trials in compliance with applicable regulatory requirements and GCP**
- **to ensure that human subjects were protected from undue hazard or risk during the course of clinical trials and that internationally recognized ethical standards were applied**
- **to verify that clinical trial data and results are scientifically valid and accurate**

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REASONS TO PERFORM GCP INSPECTIONS

(cont.)

GCP inspection might be triggered due to

- **the recruitment of subjects from vulnerable groups or other ethical concerns**
- **their importance i.e. for an application for marketing authorisation**
- **concerns about the investigational medicinal product(s)**

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REASONS TO PERFORM GCP INSPECTIONS

(cont.)

- **concerns about the credibility and accuracy of the data e.g. when**
  - **the recruitment pattern appears to be unusual**
  - **the efficacy, biological or safety results are inconsistent with regard to results of other studies**
  - **the results of one site are significantly different from the others**
  - **serious and/or persistent GCP non-compliance was reported before for the site and/or organisation subject to inspection**

TYPES OF GCP INSPECTIONS

- Surveillance inspections (national)
- Inspections in relation to the clinical trial authorization (national)
- Inspections in relation to marketing authorizations (international)
  - national marketing authorization procedures
  - mutual recognition procedures (MRPs)
  - decentralized procedures (DCPs)
  - centralized procedures (CAPs)

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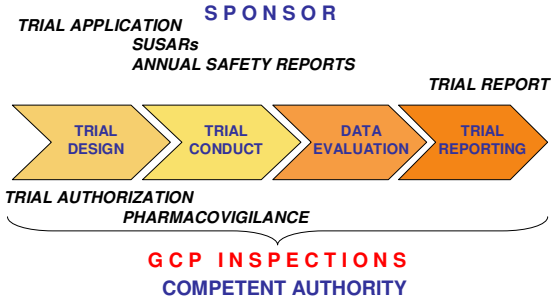
GOOD CLINICAL PRACTICE



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ESTABLISHMENT OF A GCP INSPECTORATE

Aspects to be taken into consideration

- Implementation of a Quality Management System
- Qualification of inspectors
- Estimation of the number of GCP inspections per year
- Participation in national and/ or European Working Groups (i.e. GCP Inspectors Working Group)
- Harmonization and Cooperation with other European Member State GCP Inspectorates and regulatory bodies (e.g. CTFG, CMDh)
- Interfaces

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ESTABLISHMENT OF A GCP INSPECTORATE

German Ordinance on GCP, chapter 15: Inspections

- *The competent authority and the competent Federal authority shall have a carefully designed and correctly managed quality assurance system which comprises at least the organisation structures, responsibilities and procedures*
- *The quality assurance system shall be fully documented and its ability to fulfil its functions shall be monitored*

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QUALITY MANAGEMENT SYSTEM (1)

- Definition of tasks and responsibilities
- SOPs
- Training
- QC measures e.g. review of inspection reports
- Internal audits

QUALITY MANAGEMENT SYSTEM (2)

GCP-Directive 2005/28/EU

- ***Member States shall establish the relevant procedures for verification of good clinical practice compliance***
- ***The procedures shall include the modalities for examining both the study management procedures and the conditions under which clinical trials are planned, performed, monitored and recorded, as well as follow-up measures***

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QUALITY MANAGEMENT SYSTEM (3)

EudraLex - Volume 10, Chapter IV

- ***Guidance for the preparation of GCP inspections***
- ***Guidance for the conduct of GCP inspections***
  - ***Annex I Investigator Site***
  - ***Annex II Clinical Laboratories***
  - ***Annex III Computerised Systems***
  - ***Annex IV Sponsor and CRO***
  - ***Annex V Phase I Units***
  - ***Annex VII Bioanalytical part, Pharmacokinetic and Statistical Analyses of Bioequivalence Trials***

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QUALITY MANAGEMENT SYSTEM (4)

(cont. EudraLex - Volume 10, Chapter IV)

- ***Guidance for the preparation of GCP Inspection Reports***
- ***Guidance for exchange of GCP Inspection Reports***
- ***Guidance for the communication on GCP inspections and findings***
- ***Procedure for standardisation of GCP inspection entries in EudraCT***

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ESTABLISHMENT OF A GCP INSPECTORATE

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QUALIFICATION OF GCP INSPECTORS (1)

GCP-Directive 2005/28/EU

- ***Member States shall ensure that inspectors have completed education at university level, or have equivalent experience, in medicine, pharmacy, pharmacology, toxicology or other relevant fields***

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QUALIFICATION OF GCP INSPECTORS (2)

GCP-Directive 2005/28/EU

- ***Member States shall also ensure that the inspectors have knowledge of the principles and processes that apply to the development of medicinal products and clinical research***
- ***Inspectors shall also have knowledge of applicable Community and national legislation and guidelines applicable to the conduct of clinical trials and the granting of marketing authorisations***

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QUALIFICATION OF GCP INSPECTORS (3)

GCP-Directive 2005/28/EU

- ***The inspectors shall be familiar with the procedures and systems for recording clinical data, and with the organisation and regulation of the healthcare system in the relevant Member States and, where appropriate, in third countries***

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QUALIFICATION OF GCP INSPECTORS (4)

German Ordinance on GCP, chapter 15

- ***The personnel responsible for carrying out the inspections shall be present in sufficient numbers and shall be qualified for their duties as well as independent and free from commercial, financial or other constraints which may affect their decision***
- ***The persons shall be given the opportunity to participate regularly in specialist training courses (10 days per year)***
- ***The qualifications of the personnel shall be verified.***

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ESTABLISHMENT OF A GCP INSPECTORATE

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ESTIMATION OF THE NUMBER OF GCP INSPECTIONS PER YEAR

The number of GCP Inspections to be performed depends on

- **the number of national clinical trials per year**
- **the number, type and GCP experience of institutions involved in the conduct of clinical trials (sponsor sites, CROs, phase I units, clinical sites, laboratories…)**
- **the number of marketing authorization procedures with involvement of the national agency (NPs, MRPs, DCPs, CAPs)**

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ESTIMATION OF THE NUMBER OF GCP INSPECTIONS PER YEAR

CAVE!

GCP Inspections are

- **only partly self-initiated but partly externally requested**
- **only partly voluntary but partly triggered**

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ESTABLISHMENT OF A GCP INSPECTORATE

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EMEA GCP INSPECTORS WORKING GROUP

Key objectives

- To advise Commission, CHMP, EMEA, CMDh and other WGs as requested on GCP and inspection related matters
- To contribute to the preparation and implementation of clinical trial related regulations
- To develop procedures and guidance
- To overview the conduct of inspections

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EMEA GCP INSPECTORS WORKING GROUP

(cont.)

- To develop communication and processes with assessors/CHMP
- To facilitate training and co-inspections/joint inspections
- To increase shared experience through review of anonymized inspection reports and findings
- To Prepare advice/position statements on common problem issues (raised by stakeholders) for public availability

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HARMONIZATION AND COOPERATION

- Final Draft of "Guidance for coordination / co-operation with other regulatory bodies involved in assessing GCP requirements in the context of marketing authorization applications for mutual recognition and decentralised procedures" to be published in EudraLex - Volume 10, Chapter IV

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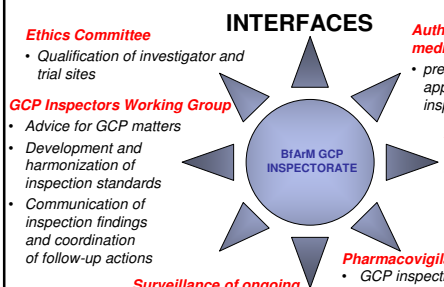
INTERFACES



Ethics Committee
- *Qualification of investigator and trial sites*

GCP Inspectors Working Group
- *Advice for GCP matters*
- *Development and harmonization of inspection standards*
- *Communication of inspection findings and coordination of follow-up actions*

Surveillance of ongoing clinical trials
- *actions to be taken due to serious GCP breaches*

Pharmacovigilance
- *GCP inspection of safety procedures and data (SUSAR reporting, ASRs)*

Authorization of clinical trials
- *GCP inspection of information and data submitted with the IMPD*

Authorization of medicinal products
- *pre and post approval GCP inspections*

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THANK YOU FOR LISTENING!