Clinical Trial Oversight:
Ensuring GCP Compliance, Patient Safety and Data Integrity

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Overview

• The Principles of Good Clinical Practice (GCP)
• Sponsor & Investigator Responsibilities
• Clinical Trial Oversight
• Demonstrating Compliance
• Simple Rules to Follow
What is Good Clinical Practice?

• International **ethical** and **scientific quality standard** for designing, conducting, recording and reporting research involving humans.

• **1996 ICH GCP** - Unified standard across the European Union, Japan and the United States

• **2001/20/EC** – Principles of GCP are legal requirement in EU
What is the purpose of GCP?

‘Compliance with this good practice provides assurance that the rights, safety and well-being of trial subjects are protected, and that the results of the clinical trials are credible.’

Article 1, 2001/20/EC, EU clinical trials directive
13 Principles of GCP

Ethics:
1. Ethical conduct of clinical trials
2. Benefits justify risks
3. Rights, safety, and well-being of subjects prevail

Protocol and Science:
4. Adequate nonclinical and clinical information to support the trial
5. Scientifically sound, described in a clear and detailed protocol

Responsibilities:
6. IRB/IEC approval prior to initiation
7. Medical care/decisions by qualified physician
8. Each individual is qualified (education, training, experience) to perform his/her tasks
Principles of GCP Continued..

Informed Consent:
9. Freely given from every subject prior to participation

Data quality and integrity:
10. Accurate reporting, interpretation, and verification
11. Protects confidentiality of records

Investigational Products:
12. Conform to GMP’s and used per protocol

Quality Control/Quality Assurance:
13. Systems and procedures to ensure quality of every aspect of the trial
## Investigator Responsibilities

- Investigator qualifications
- Adequate resources
- Medical care of trial participants
- Compliance with the trial protocol, GCP, regulatory requirements
- Investigational product
- Randomisation procedures & unblinding

- Informed consent
- Records and reports
- Progress reports
- Safety reporting
- Premature termination or suspension of a trial
- Final report
- Investigators brochure

**Responsibilities**

- Responsible for conduct of trial and safety of patients
- Must have time, resources and adequate facilities
- Provide supervision and maintain oversight

Investigator may delegate some or all of their responsibilities **BUT** retains overall responsibility for the trial.
Sponsor Responsibilities

- **Clinical Trial Authorisation and Ethics Committee Opinion** (approvals, amendments and end of trial)

- **Good Clinical Practice and Conduct** (arrangements to adhere and ensure compliance with GCP and regulations)

- **Pharmacovigilance** (keep records of AEs, expedited and annual reporting of safety issues to REC and CA and other investigators)

Sponsor may delegate some or all of these responsibilities BUT retains overall responsibility for the trial and must maintain oversight to ensure trials are compliant
Monitoring

‘The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP and regulatory requirements.’

ICH GCP 1.38

• Risk-based approach
• Central and onsite monitoring
• Review of:
  – Facilities
  – IMP arrangements
  – Trial Master Files
  – Investigator Site Files
  – CRFs and Source documents
Compliance with the Protocol

‘The most important tool for ensuring human subject protection and high-quality data is a well-designed and articulated protocol.’


- Must be adhered to throughout the trial
- Basis for procedures to be followed and data which must be collected
- Authorised by the regulatory authorities and basis for regulatory inspections
- Amendments to the protocol must be approved
- Deviations, violations and serious breaches
Documentation is Essential

“Adhering to GCP is one thing, but proving that this has been done is another. For a trial to be credible in the eyes of the authorities, investigators must be able to show that the study is in compliance with GCP guidelines. This means documenting every study-related action”

(Hutchinson 2009).

Essential documents (ICH GCP 1.23)

‘Individually and collectively permit evaluation of the conduct of a study and the quality of the data produced’
Trial Master File – Essential Items

Scientific/Ethical Conduct:
1. Protocol
2. Ethics
3. Local Approvals
4. Regulatory
5. Correspondence
6. Research Team – staff and training
7. Participant Information
8. Data Management
9. Safety Reporting
10. Product Accountability
11. Monitoring and Audit

Management:
12. Contracts
13. Finance
14. Insurance
15. Committees
16. Local Sites/Laboratories
17. Study Meetings
18. Randomisations / Unblinding
19. Statistical Analysis
20. Publications
Trial Documentation

*If is isn’t written down it didn’t happen!*

*If it is not documented, it doesn’t exist!*
Ensuring Data Quality
Source Data Verification

- **Must be adequate information in the source documents**

  **Source Documents** = original documents, data and records, such as hospital records, lab reports, subjects’ diaries, pharmacy records, etc.

  - medical history, concomitant medication
  - informed consent discussions
  - every visit documented in detail
  - adverse events information
  - medical reports/lab reports signed off by clinician

- **Source Documents must be consistent with the CRF**

  **Case Report Forms** = tool used by the sponsor/investigator to collect trial data from each participating site.
Ensuring Patient Safety

- Compliance with the protocol
- All adverse event (AE) data in medical records
- AEs - record and report in line with protocol and SOPs
- PI or delegate assess events for seriousness, causality and expectedness
- Immediate reporting of Serious Adverse Events ~ 24 hours
- Follow up events and pregnancies
Regulatory Inspections

Inspection Process:
• Inspections are *audit* against regulatory requirements
• Review *systems* in place to manage the trial
• Review *trial documentation* and *source documents*
• *Interview* Staff

Inspectors right to:
• Suspend a trial or trial site on hold
• Terminate a trial or trial site
• Fine or imprison a person
10 Simple Rules for Investigators

1. Know and strictly **adhere to the protocol**

2. Select, train, log and **oversee study personnel**

3. **Record data accurately** and amend data correctly

4. Ensure **equipment is adequate**

5. Comprehensive **documented informed consent** process
10 Simple Rules for Investigators

6. Meticulously document **product accountability**

7. **Record all safety data** in medical records and report SAEs immediately to the sponsor

8. Maintain **good trial files** and source documents

9. Diligently **collect and record trial data**

10. **Keep everyone informed!**

   Adapted from Canary Books Publication ‘12 Golden GCP rules for Investigators’

Thank you for your attention!