

## Module II: The Trial Landscape

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- Why clinical trials?
- Main features of clinical trial design
- The history of clinical trials
- The drug development process
- Phases of clinical trials
- Clinical trial players
- Trial guidelines - GMP, GLP and GCP
- **Quality assurance – audits and inspections**
- Research ethics
- Risk and benefits of trial participations

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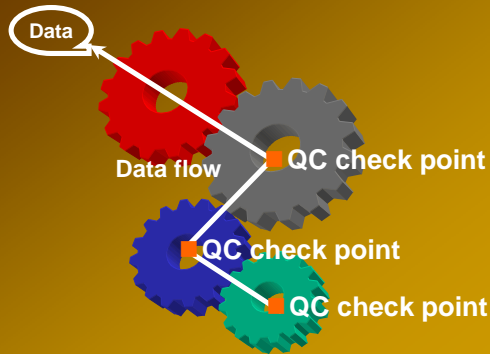
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## Quality assurance – audits and inspections

### Quality Control (QC) & Assurance (QA)



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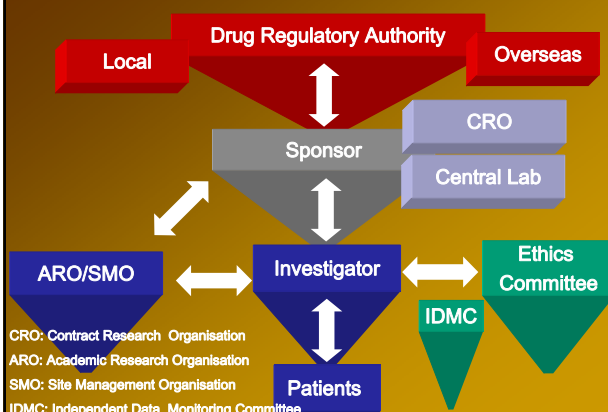
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## Quality assurance – audits and inspections



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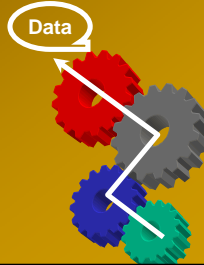
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## Quality assurance – audits and inspections

### Quality Assurance - QA

In the context of clinical research:

- “All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).”



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## Quality assurance – audits and inspections

What is the difference?  
Inspection versus Auditing

- **Inspection** is by Governmental Agencies, Health Authorities and the Drug Regulatory Authorities
- **Auditing** is by pharmaceutical, devices companies, CROs, and others



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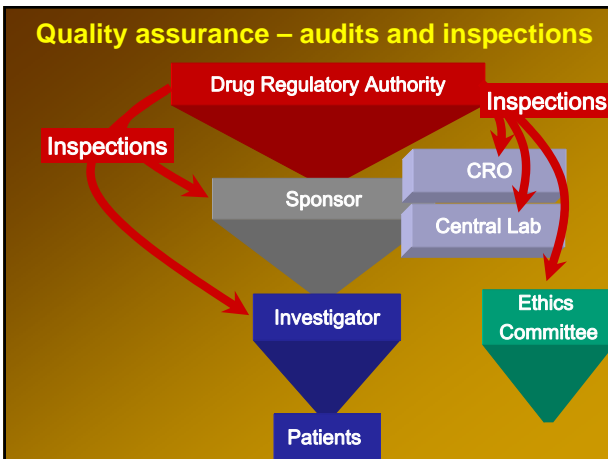
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## Quality assurance – audits and inspections



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**Quality assurance – audits and inspections**

Local  
Drug Regulatory Authority  
Overseas  
Inspections

- Sponsors
- CROs
- Central Laboratories
- Clinical Investigators
- Ethics Committees

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**Quality assurance – audits and inspections**

Local  
Drug Regulatory Authority  
Overseas  
Inspections

- Clinical Investigators

Agenda

- Introduction
- Interview
- Review of study files
- Review of medical records and CRFs
- Exit interview

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**Quality assurance – audits and inspections**

Local  
Drug Regulatory Authority  
Overseas  
Inspections

- Clinical Investigators

Areas of Questioning

- Protocol
- Subject's records
- Informed Consent
- IRB approval
- Reports to sponsor
- Test article accountability
- Records retention
- Computer/electronic data system

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### Quality assurance – audits and inspections

Drug Regulatory Authority (Local, Overseas) → Inspections → Clinical Investigators

**Inspections Findings**

Most Common Deficiencies	%
Inadequate Patient Consent Form	44
Failure to adhere to protocol	51
Inadequate and inaccurate records	51
Inadequate drug accountability	28

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### Quality assurance – audits and inspections

Drug Regulatory Authority (Local, Overseas) ↔ Trial Specific Inspections → Clinical Investigators

**Why or when do a Regulatory Authority inspect investigators overseas?**

- Importance of Data to a product evaluation
- Suspicious data
- More patients with disease than seems normal
- Significant media attention
- Complaints
- Investigator working outside speciality
- Site location

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### Quality assurance – audits and inspections

#### Definition of an “audit”

- “A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and .... standard operating procedures (SOPs) .... regulatory requirements.” ICH/CPMP GCP/135/95
- Planned and systematic actions = Quality

Data → [Gear Mechanism]

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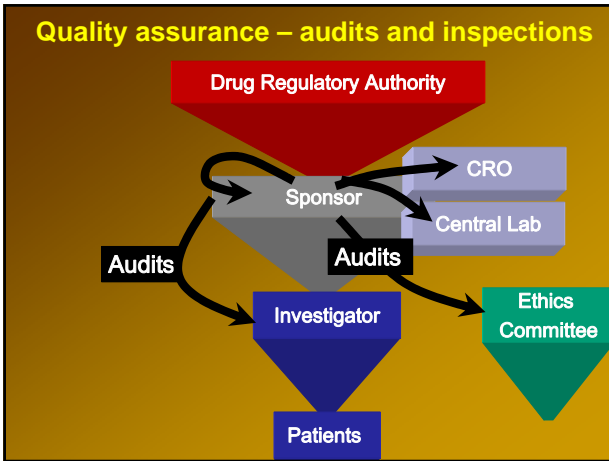
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### Quality assurance – audits and inspections

#### Responsibilities of the Sponsor in QA & QC

- Implementing and maintaining QA and QC systems with written SOPs
- Securing agreement from all involved parties to ensure direct access to trial-related information
- QC at each stage of data handling
- Agreement with all involved parties should be documented in the protocol and/or in the contract

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### Quality assurance – audits and inspections

#### Responsibilities of the Sponsor in QA & QC

- Regulatory Authorities Contacts
- Financing
- Trial Design / Protocol Development
- CRO selection
- Central Lab selection
- Investigator selection
- Trial Management
- Allocation of responsibilities
- Audit
- Trial Monitoring
- Clinical Data Management
- Medical Statistics

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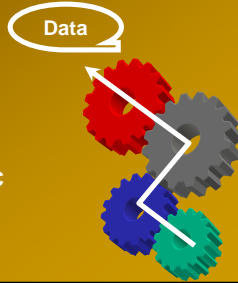
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## Quality assurance – audits and inspections

### Responsibilities of the Sponsor in QA & QC

- Manufacturing, packaging, labelling and coding investigational products
- Information on Investigational Products
- Supplying and handling Investigational Products
- Safety information
- Adverse drug reaction reporting
- Confirmation of review by IRB/IEC
- Clinical Trial Reports



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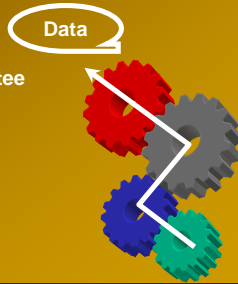
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## Quality assurance – audits and inspections

### Type of Audits

- Internal
- CRO
- Central Lab
- Manufacturing
- Investigator site + Ethics Committee



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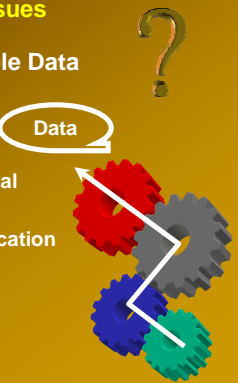
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## Quality assurance – audits and inspections

### Audit Critical Issues

Investigator site → Questionable Data

- Not Following Inclusion Criteria
- Missing Serious Adverse Events
- Missing Informed Consent
- Missing Ethics Committee approval
- Poor Drug Accountability
- Not Recording Concomitant Medication
- Abnormal Laboratory Values
- Fraud



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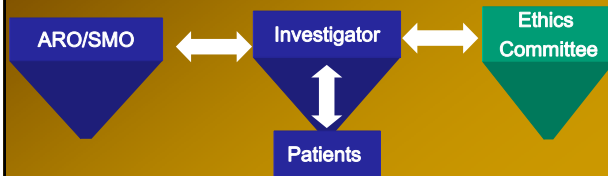
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## Quality assurance – audits and inspections

### Quality Assurance at Investigator Sites

Investigator Team and Ethics Committee:

- Education
- Standard Operating Procedures



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## Conclusion

### Quality assurance – audits and inspections

Quality Assurance of clinical trials is crucial.

The Quality Control is made by means of:

- Drug Regulatory Authority Inspections
- Sponsor Audits

Institutions with clinical trial activities should also implement a QA programme to ensure that also investigator-initiated clinical trials follows international trial guidelines:

- Education
- SOPs
- Audits



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