Clinical Quality Assurance and Control

Module 7 Topic 1

Learning Objectives

- What is Quality Control and Assurance?
- What is the difference between the two?
- Importance of QC and QA in Clinical Trials
- What is an Audit?
- Types of Audit?

Need for QC/QA in a Changing Clinical Trial "Landscape"

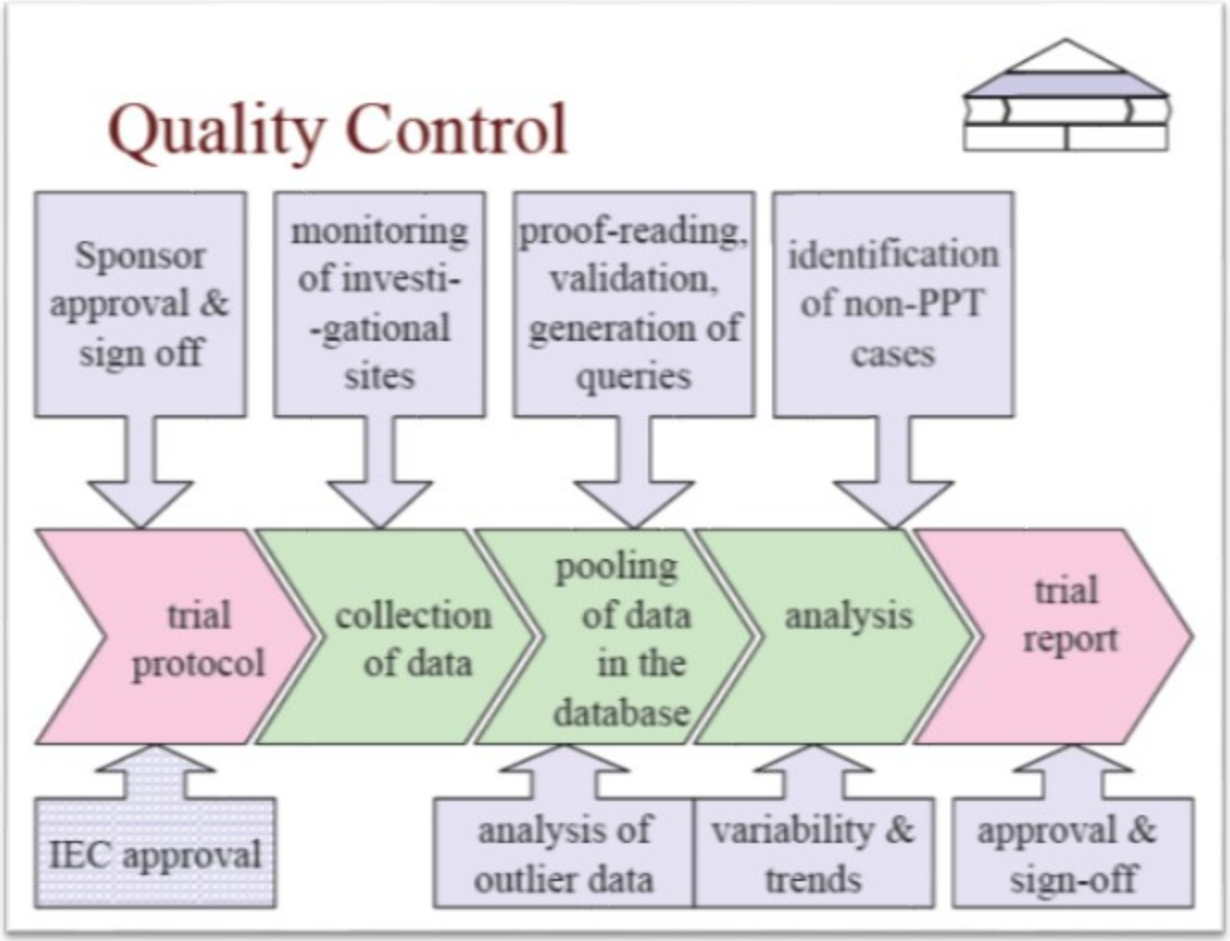
- More studies; more sites; greater volume at each site
- Expansion and fluidity of clinical investigator pool
- "New" players in new roles (CRO's, SMO's)
- New technologies (electronic record-keeping)
- More participation by "vulnerable" subjects
- Global expansion (areas new to GCP)
- Above all, outsourcing boom in India

Quality Control (QC)

- Periodic functional checks within each functional department to verify that clinical data are generated , collected, handled, analysed and reported according to protocol, SOPs and GCP.

ICH-GCP section 1.47

Quality Control



Quality Control and Quality Assurance

- Quality Control (QC)
- Daily, ongoing, “real time” activities
- Usually 100 %

Quality Control in Clinical Trials

- Pre trial Quality Control activities
- Ongoing Quality control activities

Quality Assurance (QA)

Systems and processes established to ensure that the trial is performed and the data are generated in compliance with GCP.

Quality Assurance is mentioned in ICH-GCP

- Chapter 5 : Sponsor
  - Section 5.1 Quality assurance & quality control
    - The sponsor is responsible for implementing & maintaining quality assurance & quality control systems with written SOPs to ensure that trials are conducted & data are generated, documented (recorded) in compliance with protocol, GCP & applicable regulatory requirement(s)

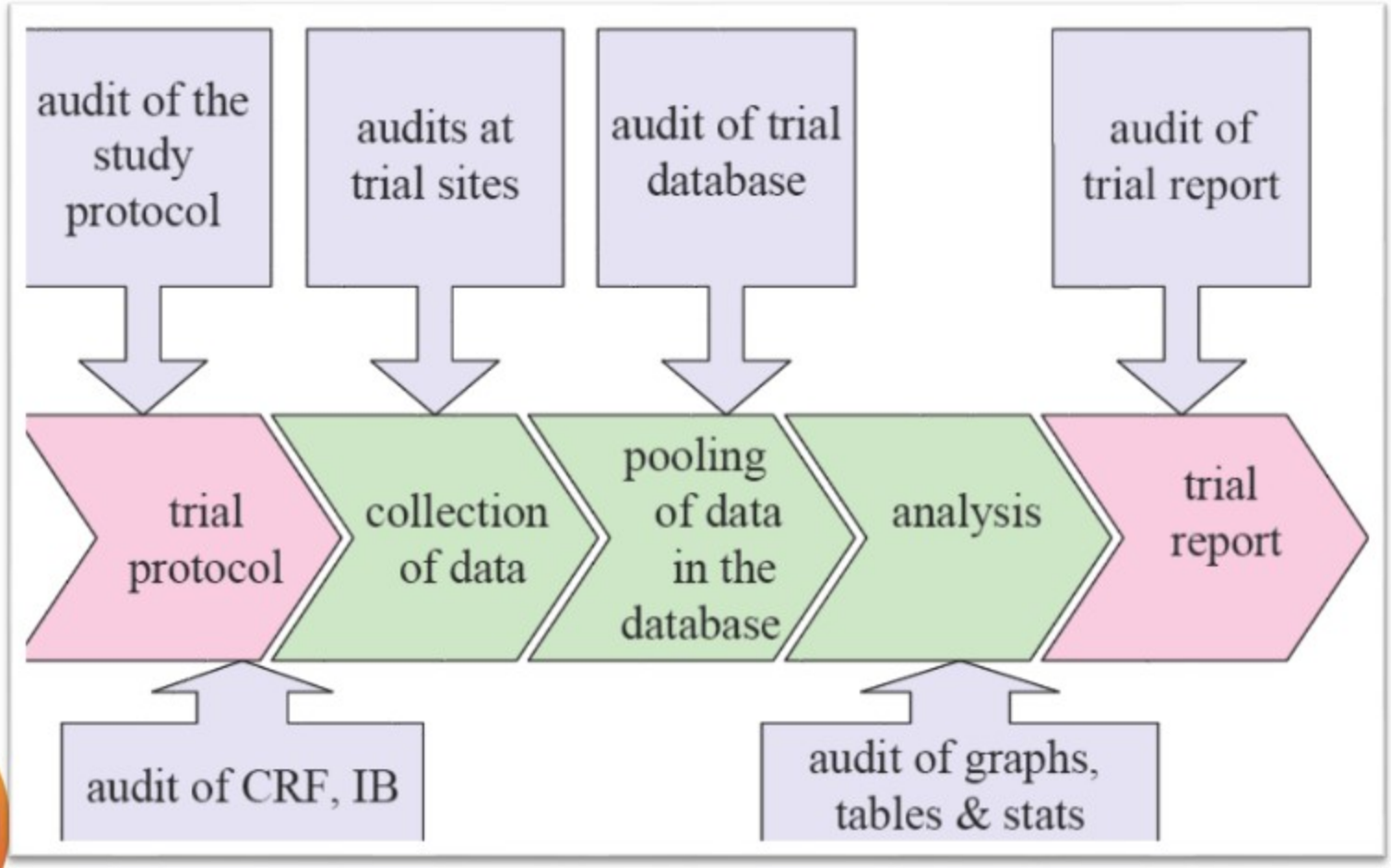
ICH GCP 1997

The Quality Assurance Procedure?

- Audit
  - The independent, systematic action to ensure the quality of study, data generated, is accurate, reliable, patient's safety and right is protected and followed GCP, SOPs & applicable regulations in the country

ICH-GCP 1997

QA, Trial Specific Audits



Types of Audits

Investigator site audit	Off site archiving
Database audit	Laboratory
Clinical study report audit	Clinical supplies
System audit	Clinical Research Organisation (CRO)
Protocol, protocol amend, consent forms, patient/volunteer information leaflet and CRFs	Validation of computer systems
IRB Audit	

Difference b/w QC & QA

QC: Routine checks, an ongoing process.

QA: Periodic checks

QC: Can be carried out by functional personnel

QA: Should be carried out by an independent person/team

QC: Subpart of Quality Assurance System

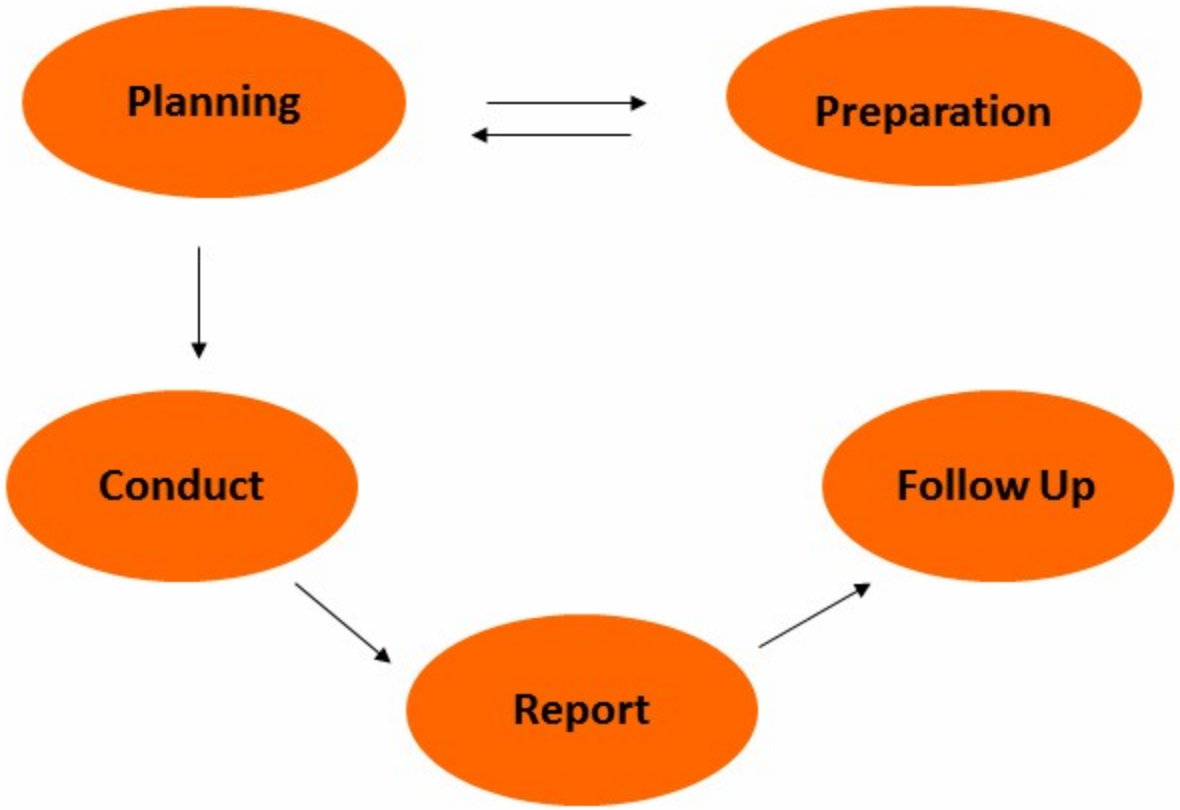
QC: Reports to the functional Head

QA: Reports to the higher management to avoid bias

Audit Process

- Main stages of an audit are as follows:
  - Planning
  - Performing
  - Reporting
  - Follow Up

Audit Process



Auditors- Where do they come from?

- Federal agency that oversees the research
- Sponsor (or their designee)
- In-house (QA)

Audits and Inspections

QA 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 to ensure that investigator initiate trials follows international trial guidelines:

- Education
- SOPs
- Audits

Difference between Audit and Inspection

In Audit, Inspectors are employed of the company who work for active clinical quality assurance (CQA) function (i.e. Sponsor/CRO)	In Inspection, Inspector are employed by government, through the agency of the regulatory or competent Authority (i.e. FDA/DCGI)

- Quality control is the responsibility of the people carrying out the work, such as the monitor, investigator or data manager.
- SOPs are provided to ensure that QC is built into the process.

ICH Quality Guidelines

- ICH has gradually evolved, to respond to the increasingly global face of drug development.
- Consists of Quality, Safety, Efficacy and Multidisciplinary guidelines.

ICH Quality Guidelines

Harmonization achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

ICH Quality Guidelines

Q 1 – Stability Testing

Q 2 – Analytical Validation

Q 3 – Impurities

Q 4 – Pharmacopoeias

Q 5 – Biotechnological Products

Q 6 – Specifications

Q 7 – Good Manufacturing Practices

Q 8 – Pharmaceutical Development

Q 9 – Quality Risk Management

Q 10 – Pharmaceutical Quality System

Synopsis

- A Clinical research set up (Sponsor/ CRO) has many functions which are essential for the smooth flow of activities.
- QA/QC is one of the mandatory functions without with Clinical Research cannot run.
- All Clinical trial Protocol, Clinical Trial Reports shall be treated as Final only when it is QA ed by Quality Assurance Department.

Synopsis

- All competent Regulatory authorities accept only QA ed Clinical Trial report
- QC, QA is mandatory for all CROs and Sponsors.
- For many companies, the failure of any audit may be not only become very costly, but also very concerning, because in an industry that is one of the largest in the world, the word of mouth is more worrisome. As large as the industry is, it is also very influential.

Exercise-1

- The auditor is performing an audit the site. The PI states that he has an adequate population for the study. As the auditor visits the center, he notices very few patients in the waiting room and the skeleton level of staffing. Are there any concerns?

Exercise-2

- The protocol and labelling require the IP to be stored at 2-8 degrees. Over the last month, the IP temperature logs at the investigational site indicated a temperature variation of 9-12 degrees for 10 separate days. When is this a deviation? A violation? An exception? How should this have been handled?

Exercise-3

- The PI did not consent subject # PMJ 21000. This subject went through screening procedures, but was eliminated from the study due to elevated BP. When is the lack of consenting (a) a violation, (b). A deviation (c) an exception or (d) not a problem? What steps shall auditor take here?

References

- www.pharmanet.com/pdf/whitepapers/QCQA.pdf
- www.ifapp.org
- Spiker B (1991). Guide to Clinical Trials, Raven Press, New York.