FDA Pharmaceutical Industry Guidance Review:
ICH E8 & ICH E6 (R2)

E8(R1) General Considerations for Clinical Studies

Focuses on designing quality into clinical studies (medicinal products in humans)

➢ Quality should still ensure:

- Protection of subjects
- Generation of meaningful & reliable results
- Management of risks
- Quality should rely on proper design and execution rather than retrospective activities such as auditing.

Critical Quality Factors

- Each study should include a set of quality factors
- Researchers should seek to emphasize factors that stand out as critical to study quality.
  - Critical factors: attributes related to good protection of subjects, reliability, interpretability
    - If these quality factors integrity were "undermined by errors, the reliability or ethics of decision-making would also be undermined"
    - Include risk that threaten their integrity

Proactivity: ensure all staff have training on the critical factors and why it is important to report risks/issues immediately

Approach to Identifying Critical Quality Factors

1. Are the objectives clearly stated?
2. Is the study designed to meet the need it intends to?
3. Are the needs meaningful to patients?
4. Is/are the hypothesis(es) specific, timely and scientifically valid?
5. Can the objectives be met by the design planned?
6. Is it operationally feasible?

Overview

- Be proactive about quality factors and risk: train everyone
- Cut out *nonessential activities* to promote focus on critical quality factors
- Include stakeholders in design planning
  - Everyone involved should be encouraged to participate in quality building activities (coordinators, site, staff, patients, organizations, etc.)

Drug Development Planning

- Includes all aspects of development of a product from "target product profile through post-approval activities".
- Non-clinical information (physiological and toxicological aspects) should be included.

Additional Detailed Resources

E8(R1) includes detailed information on:

- Design elements for clinical studies
- Conduct and reporting guidelines
- Considerations in identify critical quality factors
  - Proactive, cross-functional
  - Occurs at time of study planning and throughout study, etc. (p. 26)
- Critical quality factors grid (Annex 3)
  - Contents of other E-documents in relation to others

E6(R2) Good Clinical Practice; Integrated Addendum to ICH E6(R1) Guidance for Industry

- Good Clinical Practice (GCP): "international ethical and scientific quality standard for designing, conducting, recording and reporting" human trials.

  - Compliance assures subjects are protected and the trial data is ultimately credible.
  - Applies to: US, EU and Japan
  - Facilitates mutual acceptance of clinical data by regulatory authorities
  - Guidance should be followed when generating clinical data to summit to regulators.

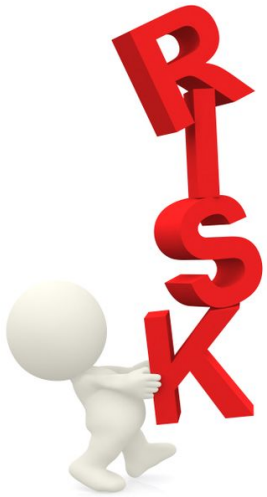
Content Summary

- Contains clinical trial *definitions* as expected to be interpreted by a regulator
- Addendum created to address increased scale, complexity, cost and technology availability/use
- Use in conjunction with other ICH guidelines such as:
  - E2A: Clinical Safety Data Management
  - E3: Clinical Study Reporting
  - E7 Geriatric Populations
  - E8 General Considerations for Clinical Trials
  - E9: Statistical Principles
  - E11: Pediatric Populations

Detailed information on: Investigator qualifications, Sponsor roles, trial design, monitoring, auditing, noncompliance/suspension, an investigator's brochure and more.

Principles of GCP

- Declaration of Helsinki
- Risks and inconveniences weighed against benefit before trial begins
- Submit rights, safety and well-being is top priority
- Available nonclinical and clinical data on investigational products support trial
- Scientifically sound, protocol detailed



Principles of GCP Continued

- IRB or IEC approval
- Care provided by qualified medical personnel
- Conductors of the trial must be qualified by education, training and experience
- Consent should be freely given by all participants
- All clinical trial information should be recorded, handled and stored in away that allow accurate reporting, interpretation and verification

Principles of GCP (Addendum items)

- Confidentiality of records that identify patients should be protected according to applicable regulatory requirements
- Follow Good Manufacturing Practice (GMP)