ICH E8(R1) Final Version

GENERAL CONSIDERATIONS FOR CLINICAL STUDIES

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1 QUALITY BY DESIGN

FOCUS ON CRITICAL TO QUALITY FACTORS TO:

- PROTECT PATIENTS
- GENERATE RELIABLE & MEANINGFUL DATA

2 QUALITY RELIES ON

GOOD DESIGN

Clear objectives and endpoints that address the primary scientific questions; selection of appropriate subjects & sites; approaches that minimize bias.
(randomization, blinding or masking, control of confounding)

GOOD DESIGN EXECUTION

Ensuring feasibility quality of facilities everywhere, procedures & processes.

Overreliance on retrospective documents checking, monitoring, auditing, inspections.

3 RISK TO QUALITY

1. Identify clear critical to quality factors when designing a study
2. Determine the risks threatening their integrity
3. Determine the probability and impact of those risks
4. Implement control process to manage risks

4 CONSIDERATIONS IN IDENTIFYING CRITICAL TO QUALITY FACTORS

- Engagement of all relevant stakeholders during study planning
- Study design supports a meaningful comparison with the chosen control group
- Number of subjects, duration of study & frequency of visits are sufficient to support the study objective
- Choice of response variables and assessment methods support the drug effect evaluation
- Systems and processes are in place to ensure the integrity of critical study data
- Non-clinical and clinical studies are complete and adequate to support the study being designed
- Adequate measures are used to protect subjects (informed consent, IRB/IEC review, pseudonymisation, etc.)
- Eligibility criteria reflect study objectives and are well documented in the protocol
- Procedures include adequate measures to minimize bias
- Extent and nature of study monitoring are tailored to specific study design & objectives
- Study objectives address relevant scientific questions
- Feasibility assessment confirmed the study operational viability
- Information about subjects important to understanding risk/benefit is specified in protocol, design, conduct & analysis
- SAP is pre-specified and defines the analysis methods appropriate for the endpoints and populations
- Need for a data monitoring committee is assessed

5 KEY ASPECTS OF A QUALITY APPROACH TO STUDY DESIGN

- Clearly articulated objectives of the study
- The objectives can be met by the chosen design and data sources
- Study is designed to meet the need it sets out to address
- These needs are meaningful to patients
- Study hypotheses are specific, timely and scientifically valid
- Study design is operationally feasible
- Protocols and case report forms/ data collection methods enable the study to be conducted as designed

6 QUALITY CULTURE

- Encourage proactive open dialogue
- Discourage "one size fits all" approach
- Engage broad range of stakeholders (including external ones)
- Train stakeholders prior to the first subject enrolment and during the study
- Go beyond the reliance on tools and checklists
- Choose quality measures and performance indicators that are aligned with a proactive approach to design
- Build on experience and knowledge
- Periodically review critical to quality factors to determine whether adjustments to risk control are needed
- Use innovative methods for ensuring quality

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