Proposed Framework of Characteristics that Define the Quality Conduct of a Clinical Trial

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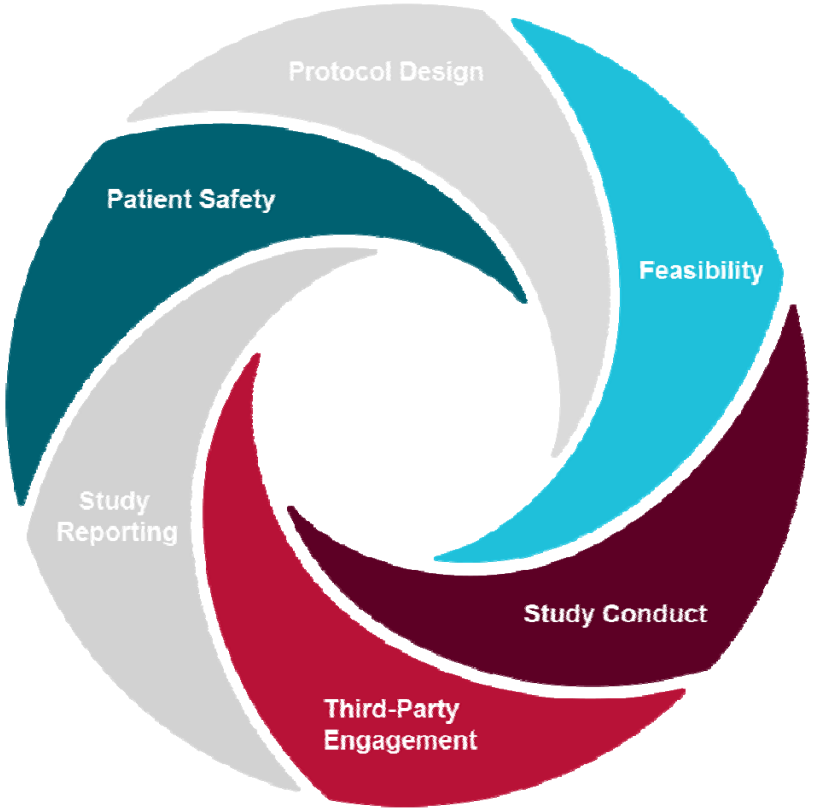
Proposed Draft Framework

- Intended to describe the characteristics that are synonymous with the quality conduct of clinical trials.
- In scope are characteristics and indicators that are within the control of investigators and their delegates and that could be modified through training.
- Out of scope are characteristics that are beyond the control of sites, investigators and their delegates, including those characteristics that relate to protocol design and study reporting.
  - For more information on improving the quality of clinical trials through improved design, see CTTI's Quality by Design recommendations.

Organization of the Draft Framework

- The relevant categories of critical to quality factors as defined in CTTI's Principles Document
- The Donabedian model used to classify of different types of quality measure. This model has also been adopted by AHRQ.



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Feasibility

Structural Measures	Process Measures	Site Level Outcome Measures
Expertise ➢ Investigators and their delegates have sufficient experience in the specialty area of the study ➢ Investigators and their delegates have relevant research understanding and experience **Capacity** ➢ Sufficient and appropriate site staffing for the protocol. ▪ Are there sufficient team members with enough time to meet the responsibilities of the trial? ▪ Identify and resolve possible conflicts		

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Study Conduct

Structural Measures	Process Measures	Site Level Outcome Measures
Culture ➢ Presence of a participant centered culture ▪ A culture that values and promotes partnership between investigators & their delegates and patients and their families in order to align decisions with patients' wants, needs, and preferences. ➢ Cooperative institutional environment ➢ Environment that emphasizes ethical conduct ➢ Culture of learning **Processes** ➢ Clear division of roles and responsibilities ➢ Clear and effective lines of communication with ▪ Other site staff ▪ The sponsor/CRO **Systems** ➢ Ability to assess whether it is possible to recruit/conduct protocol • Example: a thorough review of the protocol against patient charts to determine if site can really enroll the patients ➢ Ability to develop / existence of a clear recruitment plan likely to be successful in the environment of the site ➢ Ability to identify and address issues through process improvement	**Pre-Trial Planning** ➢ Appropriate planning • Investment in time needed to understand thoroughly the study design, study procedures and protocol ➢ Development of an accurate and useable study process map, to lay-out clearly the steps needed for all trial processes, start to finish. Ex: who receives study documents, who files them with the IRB, who will handle drugs/devices, who will administer Informed Consent, etc, etc **Recruitment** ➢ Optimized enrollment • Time to enrollment (knowing subject pool, defining recruitment methods in advance, contingency plans if enrollment not progressing) • Eligible patients) • Evaluable patients • Absence of selection bias **Protocol Compliance** ➢ Minimal preventable protocol deviations ➢ Correct assessment of outcomes **Retention** ➢ Subject follow-up • Adequate • Appropriate • Minimal loss to follow-up **Data Quality** ➢ Quality and completeness of data • No missing data ➢ Data integrity • Data in EDC system consistent with source documents; entries and corrections are timely • Critical data completely in the EDC, esp safety and primary efficacy within X timeframe • Allied data (labs, images, etc) not directly controlled by the PI is accurate, complete, timely ➢ Time to crf completion ➢ Resolution of monitoring visit action items by the next visit **Quality Control** ➢ Establishment of key performance and quality indicators appropriate for and aligned with the trial objectives. These could include, for example: • Absence of critical findings and less than three major findings • Absence of IRB reprimand letters • Absence of suspension or termination of investigators or sites • Absence of ineligible subjects enrolled • Informed consent available for subject prior to intervention • x% of subject visits scheduled in visit window • Data queries resolved within x weeks of issue ➢ Review of those KPIs and KQIs periodically, as appropriate for the trial ➢ Rapid corrective and preventive action/continuous improvement cycle	**Trial Conduct & Administrative** ➢ Complete Investigator Site File (ISF) ➢ Minimal subjects lost to follow-up ➢ Protocol compliance rate greater than xx (may vary with therapeutic area). Examples: • Study visits • Procedures • Dosing ➢ Complete IP reconciliation / accountability for all IP **Data** ➢ Rapid data entry and query resolution ➢ Query free data at the end of the trial ➢ Site data reliable (can be included in the study without concern)

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Study Conduct – Structural Measures

- Culture
  - Participant centered
  - Partnerships - Investigators; their delegates, patients, families
  - Values scientific inquiry, research integrity and methods
  - Supportive and cooperative institutional
  - Integrity and Ethical conduct
  - Inquiry and learning
- Processes
  - Clear division of roles and responsibilities
  - Clear and effective lines of communication with:
    - Other site staff
    - The sponsor/CRO
  - Established study conduct systems (record mgmt., IP mgmt., etc)

Study Conduct – Structural Measures

- Systems
  - Ability to critically assess protocol accrual requirements to determine and demonstrate existence of required patient population AND participation
  - Ability to establish of a clear recruitment, retention and adherence plan based on understanding of clinical realties, patient behaviors and Institutional requirements
  - Ability to identify and address issues through process improvement

Study Conduct – Process Measures

- Pre-Trial Planning
  - Investment in training for understanding the study design as it prescribes study procedures
  - Protocol specific training of outcome definitions, major protocol definitions, patient safety, etc.
  - Quality plan / map for study condut
- Recruitment
  - Time to enrollment Eligible patients
  - Evaluable patients
  - Absence of selection bias

Study Conduct – Process Measures

- Follow-up and Protocol Compliance
  - Procedures to prevent and/or identify protocol deviations
  - Procedures to support correct assessment of outcomes

- Retention and Adherence
  - Subject follow-up for data integrity and patient safety
  - Teaching for participant compliance, adherence
  - Practices to establish open discussions with participants to maintain participant engagement

Study Conduct – Process Measures

- Data Recording and Reporting
  - Procedures to achieve data quality, integrity and completeness:
    - Attributable
    - Legible
    - Contemporaneous
    - Original
    - Attributable
  - Timely and comprehensive resolution of monitoring visit action items

Study Conduct – Process Measures

- Quality Control
  - Establishment of key performance and quality indicators:
    - aligned with the trial objectives
    - Eg:
      - Informed consent available for subject prior to intervention
      - x% of subject visits scheduled in visit window
      - Data queries resolved within x weeks of issue
      - Absence of ineligible subjects enrolled
  - Systematic monitoring and review of those KPIs and KQIs
  - Integrated corrective and preventive action/continuous improvement cycle

Study Conduct –Outcome Measures

(Site Level)

- Trial Conduct & Administrative
  - Complete Investigator Site File (ISF)
  - Minimal subjects lost to follow-up
  - High protocol compliance for:
    - study visit schedules
    - Accuracy and completeness of procedures
  - Complete IP reconciliation / accountability
- Data
  - Rapid data entry and query resolution
  - Query free data at the end of the trial
  - Site data reliable

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Third Party Engagement

Structural Measures	Process Measures	Site Level Outcome Measures
➢ Clear understanding, definition, and acceptance of the roles and responsibilities of allied personnel and departments (IRB, contracts, labs, etc) ➢ SOP's for site specific procedures exist including: ▪ how to identify and resolve problems ▪ how to elevate the awareness of problems to the investigator and project leadership at the sponsor		

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Patient Safety

Structural Measures	Process Measures	Site Level Outcome Measures
➢ Patient centered culture ➢ Knowledge-able staff	**Informed Consent** ➢ Effective communication during informed consent ➢ Informed consent available for subject prior to intervention	**Safety** ➢ Complete SAE / AE reconciliation ➢ Timely review/signatures/assessments of adverse events, procedure/lab results and other diagnostic testing ➢ Compliance with protocol safety algorithms, where applicable

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Discussion