



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

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Defining Quality Conduct of Clinical Trials

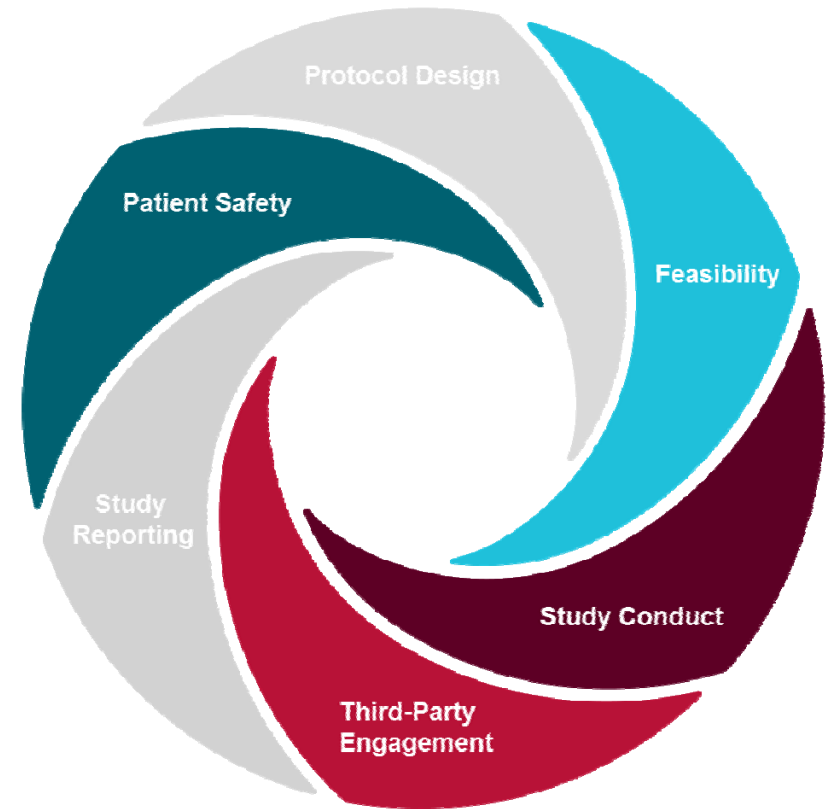
- ▶ Rationale: If you don't know where you're going, anywhere will get you there
- ▶ We are defining quality as the absence of errors that matter
 - Errors which have a meaningful impact on the safety of trial participants or credibility of the results (and thereby the care of future patients).

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](#).



Feasibility

Structural Measures	Process Measures	Site Level Outcome Measures
<p><u>Expertise</u></p> <ul style="list-style-type: none">➤ Investigators and their delegates have sufficient experience in the specialty area of the study➤ Investigators and their delegates have relevant research understanding and experience <p><u>Capacity</u></p> <ul style="list-style-type: none">➤ Sufficient and appropriate site staffing for the protocol.<ul style="list-style-type: none">▪ Are there sufficient team members with enough time to meet the responsibilities of the trial?▪ Identify and resolve possible conflicts		

Study Conduct

Structural Measures	Process Measures	Site Level Outcome Measures
<p>Culture</p> <ul style="list-style-type: none"> ➤ Presence of a participant centered culture <ul style="list-style-type: none"> ▪ 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 <p>Processes</p> <ul style="list-style-type: none"> ➤ Clear division of roles and responsibilities ➤ Clear and effective lines of communication with <ul style="list-style-type: none"> ▪ Other site staff ▪ The sponsor/CRO <p>Systems</p> <ul style="list-style-type: none"> ➤ Ability to assess whether it is possible to recruit/conduct protocol <ul style="list-style-type: none"> • 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 	<p>Pre-Trial Planning</p> <ul style="list-style-type: none"> ➤ Appropriate planning <ul style="list-style-type: none"> • 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 <p>Recruitment</p> <ul style="list-style-type: none"> ➤ Optimized enrollment <ul style="list-style-type: none"> • 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 <p>Protocol Compliance</p> <ul style="list-style-type: none"> ➤ Minimal preventable protocol deviations ➤ Correct assessment of outcomes <p>Retention</p> <ul style="list-style-type: none"> ➤ Subject follow-up <ul style="list-style-type: none"> • Adequate • Appropriate • Minimal loss to follow-up <p>Data Quality</p> <ul style="list-style-type: none"> ➤ Quality and completeness of data <ul style="list-style-type: none"> • No missing data ➤ Data integrity <ul style="list-style-type: none"> • 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 <p>Quality Control</p> <ul style="list-style-type: none"> ➤ Establishment of key performance and quality indicators appropriate for and aligned with the trial objectives. These could include, for example: <ul style="list-style-type: none"> • 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 	<p>Trial Conduct & Administrative</p> <ul style="list-style-type: none"> ➤ Complete Investigator Site File (ISF) ➤ Minimal subjects lost to follow-up ➤ Protocol compliance rate greater than xx (may vary with therapeutic area). Examples: <ul style="list-style-type: none"> • Study visits • Procedures • Dosing ➤ Complete IP reconciliation / accountability for all IP <p>Data</p> <ul style="list-style-type: none"> ➤ 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)



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 realities, 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 conduct

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

Third Party Engagement

Structural Measures	Process Measures	Site Level Outcome Measures
<ul style="list-style-type: none">➤ 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:<ul style="list-style-type: none">▪ how to identify and resolve problems▪ how to elevate the awareness of problems to the investigator and project leadership at the sponsor		

Patient Safety

Structural Measures	Process Measures	Site Level Outcome Measures
<ul style="list-style-type: none">➤ Patient centered culture➤ Knowledgeable staff	<p><u>Informed Consent</u></p> <ul style="list-style-type: none">➤ Effective communication during informed consent➤ Informed consent available for subject prior to intervention	<p><u>Safety</u></p> <ul style="list-style-type: none">➤ 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



Discussion