Building Quality into Clinical Trials
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Objective

- Introduction
- Quality in Clinical Trials
- Changing Landscape
- Forces for Change/Quality Issues
- Elements of Quality Clinical Trials
- Building Quality into Clinical Trials
Introduction

- Safe & Effective Medical Products
- Trial Complexity
- Industry Challenges
  - Rising Costs
  - Delays
  - Compliance to Global Quality
- Globalization and outsourcing
- Aligning industry practices with FDA Compliance
Concept of Quality in Clinical Trials

- Increases concerns and decreased confidence
- FDA promotes quality from start and ongoing
- Quality in clinical trials
- Quality’s characterization
Regulatory and Industry Goals

- Produce and approved high quality products
- With minimal regulatory oversight
- High benefits and lower risks
- By ensuring protection and welfare of our patients
Expectations of Regulatory Authorities

FDA:

Can’t “inspect in” quality retrospectively – need to build in prospectively

Expect shift from data-heavy IDE/IND submissions to “knowledge-rich”, i.e. with insights gained from Quantitative Risk Management (QRM) approaches

Involve regulators proactively in agreeing quality definitions for programs
**Expectations of Regulatory Authorities from Quality Risk Management (QRM)**

**EU:**
- Identify risks prospectively

  **Comprehensive/holistic approach:**
  - Organizational level
  - Project level

  In clinical program, apply concept at early program design stage, before individual trials are running
Both are working on moving quality by design (QbD) into studies in humans

This is part of the strategy of the agency to “develop more robust clinical infrastructure” – Janet Woodcock.

Provide “high-quality data” – strong enough to support the sponsor’s labeling claims.
Well recognized and in place for manufacturing of products.

Implementing QbD system prospectively into clinical development is more effective than overhauling of processes, changing SOP’s and resources retrospectively.

Increasing focus on having quality systems in place during planning stages.

Systematic approach will produce more reliable and useful data.
Clinical Trials Transformation Initiative (CTTI)

- Established out of shared vision

**Mission/Scope:**

- To identify practices that through broad adoption will increase the quality and efficiency of clinical trials
- Generate evidence how to improve design and execution
Clinical Trials Transformation Initiative (CTTI)

Projects
- QbD is a major current interest since August 2011.
- Plan to expand beyond drug studies and sponsors.

Principles
- Protect and promote public health.
- Generate adequate and timely information:
  - Prevention, diagnosis, treatment.
- Need to protect human subjects and their privacy.
- Work together to move the system forward.
Quality assurance has relied on audits and inspection but now under scrutiny

- Protocol complexities and decline in study performance, subject recruitment and retention
- Globalization
- Multiple outsourcing partners
Forces for Change

- Increased mergers and acquisitions
- Digital revolution
  - Electronic medical records
  - Telemedicine
  - Mobile technology
  - Increased regulatory requirements
- Timelines
Forces for Change/Quality Issues

Consequences of poorly conducted research can be significant:
- Delay
- Potential harm
- Inaccurate product labeling
- Legal consequences
What Is Quality?

“Quality” is characterized by the ability to effectively and efficiently answer the intended question about the benefits and risks of a medical product (therapeutic or diagnostic) or procedure while ensuring protection of human subjects.

Oct. 2008, Dr. Rachel Behrman, CTTI and presently Director of CDE Office of Medical Policy
Elements of Quality Clinical Study

- Scientific valid and ethically sound protocol
  - Independent review prior to finalization
  - Inclusion/exclusion unnecessarily restrictive
  - Feasible to carry out protocol requirements in all regions trial may be conducted
  - Minimize protocol changes/amendments
- Adequate protection of subject‘s rights, safety, and welfare
Elements of Quality Clinical Study

Qualified personnel - not just a CV
- Adequate time, staff, equipment, etc.
- Knowledge of regulations and requirement
- Commitment to research
- Willingness to complete training requirements
Elements of Quality Clinical Study

- Adequate monitoring
  - Selection of monitors
  - Study Monitoring Plan
  - Study specific training
- Current complete and accurate data
Multidimensional Approach to Building Quality

Product Characteristics

- Indication
- Safety Profile
- Patient Population
- First in class vs. “me too”

Stakeholders

- Public
- Sponsors
- CROs
- Third parties
- Regulators
- IRBs
- Academia
- Institutions

Product Lifecycle

- Preclinical
- Preapproval
- Postmarketing
4 common problems in a clinical trial

- Protocol Design
- Procedural
- Recording (both random and fraudulent)
- Analytical
Building Quality in Clinical Trials

Focus on developing **Quality System** during clinical development

**Define quality objectives**
- Exam investigational product
- Plan clinical trials
- Exam existing clinical trial processes
- Identify potential risks
- Define controls to prevent errors
- Identify problems and intervene before serious
Building Quality in Clinical Trials

- Designing optimal infrastructure
- Optimizing processes and systems
- De-risking clinical programs
- “Fit-for-purpose” training and communication
- Enhancing GCP compliance and reducing audit/inspection findings
- Meeting health authority expectations
- Reduce costly errors
- Getting it right first time – minimizing need for laborious “fixes”
Building Quality in Clinical Trials

- FDA recommends
  - Say what you do
  - Do what you say
  - Prove it
  - Improve it
Say what you do

- Qualified management team to govern whole clinical trial process
- Robust oversight of outsourced activities
- Policies and procedures for key clinical processes
  - Protocol development to clinical study reports
  - Good procedures can mitigate potential risks
Building Quality in Clinical Trials

- Do what you say
  - Education and training
  - Protocol and study requirements
  - System and standardization
    - Policies and procedures
  - All team members know their responsibility
  - Monitors it’s not just matching data
  - Site selection and learning curve
  - Protection of clinical trial subjects
  - Quality assurance and auditing
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Prove It - Requires new approaches:

- Risk-based monitoring
  - Process management & verification of critical activities including quality controls
  - Co-monitoring to ensure compliance to monitoring plan
  - Repeat/supplemental training as necessary
  - Replacement of monitors as necessary

- Trend analysis
  - Looks at data as compliance intelligence
  - Statistical monitoring
Building Quality in Clinical Trials

- Enabled an integrated, cross-functional approach to proactively build quality into the clinical trials
- The team, collectively, developed a much better appreciation for what could go wrong
- Resulted in greater ability to systematically manage quality
- Enabled the team to take ownership of quality
Cost vs. Quality

- There is a cost to poor quality
- Higher quality leads to lower costs
- This can be a win-win if done prospectively and correctly
- Continuously improve!
Conclusion

- Build quality into scientific and operational design
  - Focus on what matters – subject safety and data integrity
  - Develop a quality management plan
  - Prospectively measure the error rates of important parameters
  - Monitoring tailored to trial design and quality objectives
  - Improve training and procedures
  - Report quality issues found, action taken, understand impact on analysis and interpretation of results

Clinical Research and Compliance Consulting
Conclusion

Innovations in study designs are critical for success of clinical development:
- Simulations
- Adaptive Designs
- Bayesian Networks

New initiatives to translate animal data into early human testing

Build in quality in advance instead of fixing things afterwards
Compliance to quality requirements is the cornerstone of a scientifically valid and ethically sound clinical trial.

Continuous vigilance and continuous process improvement

Overall objective

- Subject protection
- Data quality/integrity
- Protocol compliance
QUESTIONS?
Thank You

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http://dugasclinicalresearch.com/
References:


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