Role of Core Lab in Clinical Trial

M. Therese Tupas-Habib, RDCS
Manager, Cardiovascular Core Lab
MedStar Health Research Institute
American Society of Echocardiography
Recommendations for Use of Echocardiography in Clinical Trials

A Report from the American Society of Echocardiography’s Guidelines and Standards Committee and The Task Force on Echocardiography in Clinical Trials

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Why Echo?

- non-invasive diagnostic tool
- Assess cardiac structure, function and hemodynamics
- Essential data on safety and efficacy of drugs and devices
- Assess enrollment eligibility
Application of Echo

- Prosthetic valves
  - assess valve hemodynamics

- Myocardial infarction and CAD
  - assess disease impact on LV remodeling and function

- Heart failure
  - Assess LV systolic and diastolic function, LV remodeling; assess treatment effects

- Hypertension
  - assess effects of treatment on cardiac structure and function
Recommendation for use of echo in clinical trial:

- Use of central reading/core lab
What is a core lab?
Why a Core Lab?

- Reduces variability in interpretations
- Use of limited number experienced observers
- Standardization of training and acquisition
- Monitor of image quality
Goals

To provide central reading/analysis for images generated at enrolling centers

To standardize variables to be analyzed

To standardize the way these variables will be analyzed

To generate a database of high quality that can be integrated to the clinical data.
Responsibilities and Organization
Core Lab Requirements for Single Study

- Clinical study protocol
- Echo Core Lab SOP (study specific procedures)
- Laboratory QPM
- Equipment logs, inventory and maintenance
- Personal records (training logs and certifications)
- Institutional Policies and Procedures
What Is an SOP?

Study-specific Manual of Operations
- Responsibilities of the research team
- Site Visit
- Training
  - Image acquisition protocol (Site manual)
- Image Analysis
  - completion of case report form
- Data management
  - tracking of images and forms
  - data checking and data transfer
- Document control
- Audit
Research Team

Director
Associate Director
Manager
Project Leader or Technical Manager
Interpreting sonographers
Admin support staff
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Site Visit

- Feasibility of conducting the study
- Personnel resources
- Review processes
- Equipment
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Acquisition protocol

- Standardized acquisition protocol
  - ‘menu’ of echo views necessary
  - training – written material, training CD, webex, investigators’ meetings and/or on-site
- limit number of sonographers
- responsible physician must review
- perform validation / qualification echo
Reduction in Echo Variability

Echo quality, Echo quality and Echo quality!!!

- Modern machine (within approx 5 years)
- Experienced sonographer
- MOTIVATED echocardiographer
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Image Analysis

- Steps for performing measurements
- Qualitative
  - Categorical assessment
- Quantitative
  - Method, formula
Electronic CRF

- Commercially available software
- Used to design CRF and maintain data
- Data exported in Microsoft Access format
- Fully CFR21 Part 11 compliant
- Audit trail reports available upon request
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Data Management

- Verification of data entered
- Validation of formula
- Data transfer
- Record retention and archiving
• Core Lab Film Tracking Program
  - Microsoft Access database
  - Each step in workflow is scanned
  - Full query and reporting functionality
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Quality Assurance
Core Lab Quality Assurance Program

- QA Program is outlined in the lab Quality Policy Manual
- Reviewed annually
Internal Auditing Procedures

- Procedures outlined in the Quality Policy Manual
- Each study is audited annually
  - Documentation
- Action Plan is developed for corrective and preventive actions (CAPA)
- Final report is sent to Core Lab Manager and Core Lab Directors
- Deficiencies addressed at weekly department meetings
Training and Continuing Medical Education
Staff Training

- Outlined in the Quality Policy Manual
- Completed by Core Lab Manager
- Covers all computers, Measurement & Analysis systems
- Requires Inter-observer Variability Studies
- Ongoing training requirements annually
Close out of trial

Data cleaning, analysis
Transfer to sponsor
Data interpretation
Results dissemination
Regulatory submission support
THANK YOU.