Strategies to Enhance Effectiveness in Nuclear Medicine Research

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Research Program Manager
Objectives

- Project Development & Project Management Stages
- Imaging Management Plan
- Feasibility
- Regulatory Considerations
- Communicating with sponsors/investigators
- Data Acquisition and Data Collection
- Record Keeping
Project Timeline

- Project development phase
- Project conduct phase
  - Patient Accrual
  - Study Execution
  - Data Collection/QA
- Data analysis/publication phase
Project Management (PM) Stages

(PMI) defines PM as "the application of knowledge, skills, tools and techniques to a broad range of activities in order to meet the requirements of a particular project."
Project Management Phases

- Project Conception and Initiation
- Project Definition And Planning
- Project Launch Or Execution
- Project Performance And Control
- Project Close
Project Conception and Initiation

- Before you begin, think of where you want to be at the end of the project?
- What is the scope of the project?
- What is the budget?
- Who is principally responsible?
- Break the complex project into smaller, measureable parts (tasks, content areas)
Project Conception and Initiation

- In Clinical Research, regulatory and reporting requirements drive timelines, structure activities
- Consult Protocol, Investigator’s Brochure
- Goals: Develop mechanisms to reach milestones and evaluate effectiveness, performance
Project Conception and Initiation

- Imaging Management Plan
  - Indication and Usage
  - Image Display and Interpretation
- Drug interactions
- Drug Request Forms/Cancellation
- Dose Dispensing Log
- Image Acquisition Form
- Camera QA Log
Dose Request Form

- Date: Protocol; Site #; Subject ID
- Product: Amount Requested (mCi):
- Requested Date of Imaging Session:
- Clinical Contact/Imaging Site Contact: Name/Email
- Imaging Site Location
- RAM license #: Amendment; Authorized User Name
- Comments/ Details for Sponsor:
- Preparer Signature and date
Dose Request Receipt

- Dose Request Receipt
- Sponsor Address, Telephone Number, Fax Number
- Dosage Amount (mCi)
- Date DRF Received
- Imaging Site
- Injection Date
- Injection Time
Dose Request Receipt

- Clinical Site Contact Name
- Imaging Site Contact Name
- Protocol Number/Identifier
- Clinical Site #
- Subject #
- Product Name
- Dose Delivery Address
- Contact information about receipt
Dose Request Receipt

- RAM License Info
  - Address of License holder
- Special Delivery Notes:
- Licensee
- License #: Amendment
- Expiration Date:
- Status:
- Authorized User
- Approval Status
Data Receipt/Review Form

- Institution Name
- Site Number
- Subject Number
- Baseline Time point
- List of Data types sent
- Comments
Project Definition And Planning

- Capacity Building: assess organizational structures, culture, motivation and capacity to meet objectives
- Identify institutional limitations, obstacles, competing objectives, and potential barriers to project implementation
- How much space staff time and effort and space and resources will be involved?
Research Responsibilities

- Different from routine CNMT duties
- Supported effort to achieve study objectives
- Responsibilities defined in the Delegation of Authority and Signature Log
- Conduct clinical research in accordance with Good Clinical Practice (GCP) for the protection of human subjects
- Obtain good quality data
Research Responsibilities

- Develop or comply with protocol
- Participate in enrollment, Informed Consent
Quality Control & Drug Accountability

- Scanning Phantoms
- Drug accountability (QC from manufacturer)
- Shipment/receipt of drug or device or investigational product
- Image Acquisition & documentation
- Ensure proper storage, handling and dispensing of data and investigational products
Activities: List all activities in the plan
Dynamic process: many concurrent activities occur simultaneously
Is it parallel or sequential?
Sequential: X must occur before Y occurs
Sequential activities: stoppers and stallers
Project Definition And Planning

- Processes & Procedures to accomplish specific aims
- How to overcome limitations and barriers
- Feasibility to achieve objectives
- Personnel qualifications, expertise
- Overcoming problems
- Troubleshooting, Risk assessment
Project Definition And Planning

- Organize the work flow
- Staff Development: build new teams or integrate staff into existing groups
- Start-up phase: mission & acquisition
- Scope and authority defined clearly
- Clear role and function in the project
- Allow adequate time for hiring, training
Project Definition And Planning

- Code of Federal Regulations (CFR)
  - Administrative law in the US from the FDA
  - Regulations & rules on clinical trials & research
    - 10 CFR § 33.11 Types of specific licenses of broad scope.

- International Conference on Harmonisation (ICH)
  - Guidelines and requirements for EU, Japan, US
  - Not binding laws in US, guidelines from the
Standard Operating Procedures

- Introduction/purpose
- Scope
- Background/considerations/definitions
- Regulations/guidelines
- Procedure
- Description of activity and person responsible
- Step-by-step procedures
- Related procedures
- Regulatory Information
- Signatures: Evidence of training
Project Definition And Planning

- Research Team and Staff: Qualified personnel to carry out study conduct study
  - Approval by the IRB, Sponsor
  - 1572 FDA form for investigators and key staff
- Delegation of Authority Logs on file
  - Clear and designated responsibilities
- Curriculum Vitae (CVs) on file
- Medical Licenses/ Nuclear Medicine certifications on file, Authorized users, designated staff
About The Collaborative Institutional Training Initiative (CITI)

The Collaborative Institutional Training Initiative (CITI) was founded in March 2000 as a collaboration between the University of Miami and the Fred Hutchinson Cancer Research Center to develop a web based training program in human research subjects protections. In response to the June 2000 education policy announcement, the collaboration was expanded to include content experts from 10 institutions who provided the content for the first 12 biomedical modules. In addition to the “Basic” content, the CITI model provides the opportunity for institutions to post additional instructional materials specific to their institution. The first version of the CITI Course in The Protection of Human Research Subjects, hosted at the University of Miami, was rolled out to the participants on September 3, 2000. In December 2000, the CITI Course site was made available to institutions by subscription.

In Spring 2004, the CITI Program was migrated to a new software platform developed by the VA by Mike Fallon, DVM, Ph.D., and Stephanie Manuel, MSME. In January 2007, with the help of Dr. Fallon and Ms. Manuel a software upgrade was implemented to permit the program to broaden its scope and to expand the courses offered to our participating institutions and organizations around the world.

The CITI Program, co-founded by Karen Hansen and Paul Braunschweiger Ph.D., is now in its 7th iteration and includes:

- Basic Courses in the Protection of Human Research Subjects:
  - Biomedical Focus
  - Social and Behavioral Focus
  - Refresher Courses
- Good Clinical Practice Course
- Health Information Privacy and Security Course (HIPSA)
- Laboratory Animal Welfare Courses for Investigators and IACUC Members
- Responsible Conduct of Research (RCR)

A multi-language site, targeting international researchers was made available at [http://www.cititraining.org](http://www.cititraining.org) in Fall 2004. This multi-language capability has been added to the current CITI platform. A Spanish and Portuguese language site will be added in November 2007.

As of October 2007, the CITI Program is used by over 830 participating institutions and facilities from around the world. Over 600,000 people have registered and completed a CITI course. The CITI Program could not remain dynamic and responsive to the needs of our participants without the unselfish efforts of the CITI Developers Group. The Group meets semi-annually to review the courses, make editorial changes and to develop new initiatives for the CITI Program. The Co-founders are provided guidance and advice from the CITI Executive Advisor Committee chaired by Ernest Prentice Ph.D.

Inquires about the CITI Program should be directed to the CITI Office at the University of Miami at 305-243-7970 or by email to citisupport@med.miami.edu

Offering On Line – No Cost
Basic GCP and Research Protection Courses
Through CITI Program
1572: To be completed by the Investigator of the clinical trial

Sent directly to the sponsor *not* the FDA

Provides information to the sponsor and assurance that he/she will comply with FDA regulations

Includes information on the investigator’s qualifications
  - E.g. Curriculum Vitae (CVs)

Information about the clinical site and facilities

Information about the IRB of the investigative site
  - 21 CFR 312.53
Project Definition And Planning

- Project Development: Study design, rationale, Phase
- Dose, schedule
- Characteristics of the Population
- Feasibility of Projected Accrual
- Investigator Brochure, Risks
- Clinical Trials.gov registry
Feasibility Strategies: (ROTC)

- Assess Feasibility to Overcome Barriers
  - Rajadhyakska (2010)
- 4 components (ROTC):
  - Regulatory
  - Operational
  - Technical
  - Clinical
Regulatory

- Managing protocol timelines
- Fulfill regulatory requirements: sponsor, local, institutional
- Amendments
- Evaluating safety considerations: DSMP, DSMB, Medical Monitors
Operational

- Develop plans to assess study performance
- Identify competing studies: location, investigator interest, available subjects
- Consult registries: Clinical trials.gov
- Develop Media & tools to maintain interest
Technical

- Development and usage of Case Report Forms or eCRF’s,
- Randomization tools
- Clinical supplies drug/device shipment
- Data Use Agreements
- Information Technology interface
Clinical

- Standard of care vs. research
  - Billing issues
  - Procedures covered by research funding/grant
- Studying the desired population, disease stage
- Managing the number of subjects
- Risk vs. Retention
- Competition for subjects in multisite trials
- Define, convey inclusion/exclusion criteria
Project Launch or Execution

- Conduct the study according to the approved protocol
- Personally conduct or supervise the study
- Oversee informed consent, enrollment procedures
- Review and evaluate the evidence relating to the safety and effectiveness of the drug or device

21 CFR 312.50-312.70 and 812
Project Launch or Execution

- **Interface with Sponsor/Investigator:** Adequate procedures and forms for regular communications with the study sponsor.

- **Regulatory**
  - IRB approvals and issues
  - Investigator/staff issues

- **Study Execution**
  - Adverse event reporting
  - Dosage scheduling orders /confirmations /cancellations
  - Data transmission/collection
Project Launch or Execution

- Informed Consent Conducted
- Vulnerable Subject Consideration
- Diabetes, glucose testing; Allergies
- Logging research patients
- Standard of Care vs. Research - (Billing Codes)
- Prescription for subject
- Managing Adverse Events
- Imaging Delays > Protocol Deviations
- Subject Attendance (No shows)
Project Launch or Execution

- Investigators conducting site initiation may not be trained in Nuclear Medicine
- Dose Scheduling
- Verifying dose data
- Labeling – residual calculated, if not – simple math
- Timelines logistics
- Synchronizing
- Data Integrity
- Reporting to sponsor – sterility testing
Project Launch or Execution

- Risk Management: plan for contingencies
- Established plans for attending to adverse events, allergic reactions, incidental findings
- Prepare for the Worst Case Scenario
- Report deviations to sponsor, investigator
- Protocol is meant to be revised; not to be achieved without amendments
Project Launch or Execution

- Data Collection, labeling, forms, formats to record data and source documentation
- Handwriting and legibility
- ALCOA
  - Attributable
  - Legible
  - Contemporaneous
  - Original
  - Accurate
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<tr>
<td>13:15 24 hr Clock</td>
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**Injection site:**
- Left Arm [ ]
- Right Arm [ ]
- Left Hand [ ]
- Right Hand [ ]

**Lot Number:**
104E 972AM 6723

**Total Dose Administered:**
0.5 ml

**Saline flush immediately after injection:**
- Yes [ ]
- No [ ]

**Date and time of saline flush:**
07 MAR 2014 (DD/MMM/YYYY)
13:16 24 hr Clock

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**Injection site:**
- Left Arm [ ]
- Right Arm [ ]
- Left Hand [ ]
- Right Hand [ ]

**Lot Number:**
120E 972AM 6723

**Total Dose Administered:**
5 ml

**Saline flush immediately after injection:**
- Yes [ ]
- No [ ]

**Date and time of saline flush:**
07 MAR 2014 (DD/MMM/YYYY)
1:17 24 hr Clock

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**PET SCAN (time post injection)**

**Date of PET Imaging:**
07 MAR 2014 (DD/MMM/YYYY)

**Scan Emission Start Time:**
14:10 24 hr Clock

**Scan Emission Stop Time:**
14:30 24 hr Clock

**Were there any deviations from the standard PET Imaging protocol?**
- Yes [ ]
- No [ ]

**Patient fall down**

**Did the subject complete the full PET Imaging scan?**
- Yes [ ]
- No [ ]

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**PET SCAN (time post injection)**

**Date of PET Imaging:**
07 MAR 2014 (DD/MMM/YYYY)

**Scan Emission Start Time:**
21:0 24 hr Clock

**Scan Emission Stop Time:**
22:0 24 hr Clock

**Were there any deviations from the standard PET Imaging protocol?**
- Yes [ ]
- No [ ]

**Patient fall down**

**Did the subject complete the full PET Imaging scan?**
- Yes [ ]
- No [ ]
Project Launch Or Execution

- Data Acquisition to ensure consistency: for example, documents or imaging data uploaded or sent on DICOM CD to sponsor, investigator (or subject)
- De-identified data sets
- Confirm that your raw data for all subjects is backed up, not deleted
Project Launch Or Execution

- Data Collection on Source Documents and Case Report Form (CRF)
- Standard or military time, Date conventions
- Subject numbering, initials or identifiers
- Labeling and data distribution
- Standard Document Naming Conventions
  - Consistent method for naming files and folders
  - Keep names short; use standard abbreviations
  - Develop a glossary (cheat sheet)
Project Performance and Control

- Quality Assurance: planned, systematic documented review of quality issues, QA conducted by an objective person.

- Quality Control: Conduct ongoing internal audits. ICH E6. 5.1 Sponsor QA and QC

- Before freezing data, resolve all monitoring issues, complete all queries before starting analysis.
Project Close

- Data Review & Analysis
- Consult with a statistician
- Efficacy, Statistical Analysis Plan includes endpoints, and Safety Data Analysis Plan
- Analysis takes time
- Know the appropriate analysis method
Project Close

- Records & Reports
- Retain 2 years after marketed application if no application, after last IND use (in Canada 25 yrs.)
- Notified FDA the study has been completed or discontinued
- Final report to the sponsor when study is completed
- Permit inspection of the study records and reports by the FDA, sponsor’s monitor, IRB

21 CFR 312.50-312.70
Project Close

- Publication
- Review Study Results and Outcomes
- Check and recheck data findings
- Consult with experts before submitting
- Conduct an internal peer review before sending the manuscript
- Read editors instructions
Summary

- Following project management phases can facilitate efficient study management
- Utilizing feasibility assessments can aid in sorting through the regulatory, operational, technical, and clinical aspects of a research project
- Communication with the sponsor and investigator can ensure the protection of human subjects and good quality data
Works Consulted

- For FDA Drug Guidance:

- FDA 1572 Form FAQ:

Works Consulted