THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

Good Clinical Practice (GCP)

A review of best practices for conducting research

GW IRB Days
September 15-17, 2015

Overview

- Definition of GCPs
- Research team review
- Research activities

What are GCPs?

- Good Clinical (research) Practices;
- Regulations and ethical codes;
- Designed to accomplish 2 goals:
  1. Protect the rights and welfare of human research subjects.
  2. Ensure quality and integrity of the data obtained from research.

GCPs

Regulations

- 21CFR111- Electronic Records
- 21CFR50- Protection of Human Subjects (FDA)
- 21CFR54- Financial Disclosure
- 21CFR56- Institutional Review Boards
- 21CFR312- Investigational New Drug Application
- 21CFR812- Investigational Device Exemption
- 45CFR46- Protection of Human Subjects (OHRP)
- International Conference on Harmonisation

Ethical Codes

- Nuremberg Code
- Declaration of Helsinki
- Belmont Report
- National Research Act
- National Bioethics Advisory Committee

A Shared Responsibility

Who is the Research Team?

- Principal Investigator;
- Sub-Investigator;
- Study coordinators;
- Support staff (regulatory personnel, lab techs, others)

Team Responsibilities

- Recruitment;
- Informed consent;
- Data collection and management;
- Specimen management;
- Required reporting;
- Test article management;
- Quality assurance

Research Activities

Protocol Compliance

Recruitment

Consent

Data collection and management

Specimen management

Required reporting

“Protocol Compliance” means…

- Accurate data recording
- Meeting data timelines
- Resolution of queries
- Prompt adverse event reporting
- Good record keeping
- Working with auditors and monitors
- Meeting recruitment targets
- Ensuring study is in compliance with Irb approvals and GW policies and procedures

Recruitment

- Ethical goals:
  - Minimize the risks
  - Maximize the benefits
  - Protect vulnerable subjects
  - Enhance scientific validity

Recruitment- Target Population

- Patient or community based?
- Are they currently available (inpatient)?
- How to they get information?

Recruitment- Advertising

- Requires IRB approval prior to distribution;
- Anything the potential subject will hear/see/read;
- Databases such as list-servs;
- Facebook, Twitter, or other social media;
- Print ads such as Express;
- Radio ads;
- Community outreach including physician offices and clinics;
- Others?

Recruitment- Inclusion and Exclusion

- Use checklists;
- Maintain a screening log;
- Train all research team members who may recruit;
- Use separate screening protocol as necessary for large scale/multiple studies.

Consent

- Informed consent means:
- Subject has legal capacity to give consent;
- Given with free power of choice, without intervention of any element of force, fraud, deceit, duress, over-reaching, or other form of coercion, and;
- Has sufficient knowledge and comprehension of the subject matter and the elements involved to make an informed decision.

Consent

- *TAPC*
  - **T**ime to read the consent;
  - **A**sk questions and receive explanations;
  - **P**rior to study related procedures;
  - **C**opy of the signed form is provided to the subject**.
    - **Although not required by 45CFR46, always good practice. Additionally, it is good practice to have investigator or designee sign consent.

Consent

- Ensure person obtaining consent has been trained and designated to do so;
- Document consent process at beginning of participation and continued consent for each study visit;
- Consent at each study visit may be verbal affirmation and does not require additional signatures.

When is Re-consenting Needed?

- When new information becomes available that may impact the risks and voluntariness of research;
- When subject enrolled as minor and has reached age of majority;
- If LAR provided initial consent but subject is not able to provide own consent;
- At any of these stages the subject may refuse to re-consent and withdraw from the study.

Documenting Informed Consent

- Who obtained consent?
- Was amount of time sufficient?
- Were all questions addressed?
- Did subject receive all materials necessary to make informed decision?
- Was any COI disclosed?
- Was subject provided with copy of consent?

Documenting Informed Consent

- Example:
- Consent version 8/30/2015 was reviewed with subject by team member ABC. Process took approximately 20 minutes to complete with questions about study procedures, risks, benefits, and schedule reviewed thoroughly. Subject had few questions but was instructed to contact research team member ABC if any future questions or concerns arose. Copy of signed, dated document and study brochure with schedule was provided to subject. *ABC 8/30/2015*

Common Issues with Consent

Problems

- Presentation of materials may vary from person to person;
- Document may be too complicated;
- Subject may hesitate to ask questions;
- Verifying comprehension may be difficult.

Solutions

- Develop script for team members and train all consistently. Use other materials such as video presentation;
- Revise document to ease reading;
- Ensure no person of influence performs consent. Provide a list of FAQs;
- Use standard consent comprehension quiz to assess understanding.

Common Consent Violations

- Wrong or expired version;
- Not dated by subject or LAR;
- Date of person obtaining consent does not match subject/LAR date;
- Person obtaining consent did not sign;
- No copy provided;
- Not documented in progress note;
- Missing pages;
- Lost consent.

Data Collection and Management

- Data collection and management pertains to all of the following:
  - Source documents and essential documents
  - Case report forms (CRFs) including electronic data capture (EDCs; EDFs; e-CRFs)
  - Research record

Source Documents and Essential Documents

Source

- Patient records
- Consent form
- CRFs
- Lab reports
- Physician notes
- IRB approval
- Patient diaries

Essential

- Investigator brochures
- IRB modifications
- CV, CITI, other documents for team members
- Lab certifications
- Signed consent documents
- Screening log

Case Report Forms

- What is it?
  - A standardized form used to abstract study data from the source document and report it to the data management system;
  - Depending on the study, may be developed by sponsor or site
- When completing a CRF, remember:
  - Incorrect entries are lined through once, dated an initialed;
  - All entries are clear, accurate, legible, and complete;
  - All sections completed at the time of the study visit or as soon as results are available.

Research Record

- Separate from the medical record;
- Kept in a secure location under lock and key accessible only by authorized team members;
- Must be made available to monitors or auditors;
- Original medical record is considered the source document.

Specimen Management

- Protects the rights and safety of subjects;
- Ensures integrity of research data;
- Provides precise results suitable for clinical interpretation;
- Protects the public.

Specimen Management- Types of Specimens

- Blood
- Urine
- Sputum
- Saliva
- Stool
- Buccal swabs
- Cultures
- Nasal wash
- Biopsy materials
- Semen
- Vaginal secretions
- Cerebral spinal fluid
- Breast milk
- Fingernail clippings

Specimen Management- Common Issues

- SOPs
  - Timing
  - Temperature
  - Sterility
- Personal Protective Equipment
  - Gloves, eye protection, masks, gowns, hoods
- Equipment
  - Centrifuge, rocker, incubator

Specimen Collection Procedures

- Quality of specimen is critical to accuracy of results:
  - Containers
  - Labeling
  - Patient education (fasting, etc.)
  - Preservation
  - Transportation

Required Reporting

- PI is responsible for informing IRB, sponsor, and other agencies of any unanticipated events involving risks to subjects or others that are serious, unexpected, and research related;
- ***Unexpected***: specificity and severity are not accurately reflected in the informed consent document, Investigator's brochure, or package insert.
- ***Unanticipated***: unforeseeable at the time of its occurrence.
- ***Related***: if in the opinion of the PI, it was more likely than no to be caused by the research procedures.

Required Reporting- Unanticipated

- Unforeseeable;
- Related to study, procedures, or subjects;
- Not limited to physical harms;
- Can include breaches of confidentiality or emotional harms (such as the emotional distress that could be triggered by questions about traumatic life events);
- Some unanticipated problems involve social or economic harm instead of the physical or psychological harm associated with adverse events;
- Unanticipated problems that do not involve adverse events but must be reported are listed under the HHS regulations at 45 CFR 46.103(a) and 46.103(b) (5).

Unanticipated Causing Risks to Subjects or Others

- Death
- Life-threatening experience
- Prolonged hospitalization
- Persistent or significant disability ort incapacity
- Congenital anomaly or birth defect

Other Unanticipated Events

- Unresolved subject complaints
- Breaches of privacy/confidentiality
- Unauthorized use or disclosure of protected health information (PHI)
- Loss of study records
- Disappearance of study drug
- Research staff misconduct affecting the research
- Incarceration of a subject
- Injury sustained by research staff relating to the study
- Higher than expected volume of subject drop-out rates
- Higher than expected volume of adverse events
- Higher than expected volume of protocol deviations
- Suspension of principal investigator's medical license
- Complaint from a subject involving an unanticipated risk that cannot be resolved by the research staff
- Others??

Protocol Deviations

- Study visit outside of window, if in the opinion of the investigator, it does not affect the safety or welfare of the subject or others, the rights or participants or other or the integrity of the study design. (eg. usually within a week or in long windows, within 2 weeks);
- Failure to report a withdraw of a subject in adequate time;
- Use of expired recruitment materials.

Protocol Violations

- Failure to obtain informed consent
- Informed consent obtained after the initiation of study procedures
- Omitting study procedure(s) required by approved protocol
- Performing a study procedure that is not outlined in the IRB-approved protocol
- Failure to report a Serious Adverse Event
- Drug dispensing/dosing error
- Failure to securely control the study product
- Enrolling participants outside of inclusion criteria
- Failure to follow a Safety Monitoring plan
- Study visit outside of window, only if in the opinion of the investigator, if affects the safety or welfare of the subject or others, the rights of subjects or other or the integrity of the study design. (eg. subject is on study drug and PK values are vital to data collection and subject safety)
- Use of an unapproved consent form

Reporting Requirements

- Use Promptly Reportable New Information Form (HRP-204);
- File GW Policy HRP-801: Prompt Reporting Requirements for reference;
- Modify study and consent as needed/requested;
- Any events not considered promptly reportable should be reported at annual review.

Reporting Requirements- Deviation Log

Date of Event	Description of Event	Corrective Action	Preventive Action
08/30/2015	Subject ABC123 did not present for study visit #4. Re-scheduled but outside visit window.	Visit #4 a follow-up interview only. No increase in risk to subject.	Schedule visits for ABC123 closer to beginning of visit window to allow for re-scheduling.

Thanks to…

Part of information for this presentation taken from:

University of Maryland Baltimore

Clinical Research Coordinator Training

How to Assemble a Regulatory Binder