Good Clinical Practice (GCP)

Monica Unger, BA, CCRA, CCRC

QA/QI Research Compliance Administrator

Topics reviewed

- Defining Good Clinical Practice
- Standard Practice vs. Research
- Institutional Review Board(IRB)/ Independent Ethics Committee (IEC) Responsibilities
- Investigators Responsibilities
- Sponsor Responsibilities
- Clinical Trial Protocol
- Investigator's Brochure
- Essential Documents
- Storage of Essential Documents
- GPC Guidance Docs & Additional Resources

What is Good Clinical Practice

- An international ethical and scientific quality standard for
  - Designing trials
  - Conducting trials
  - Recording trials
  - Reporting trials

  that involve the participation of human subjects. They were derived from the International Conference on Harmonization (ICH).
- Main Objective of ICH GCP's is to provide a unified standard for the
  - European Union(EU)
  - Japan
  - United States (US)

Standard Practice vs. Research

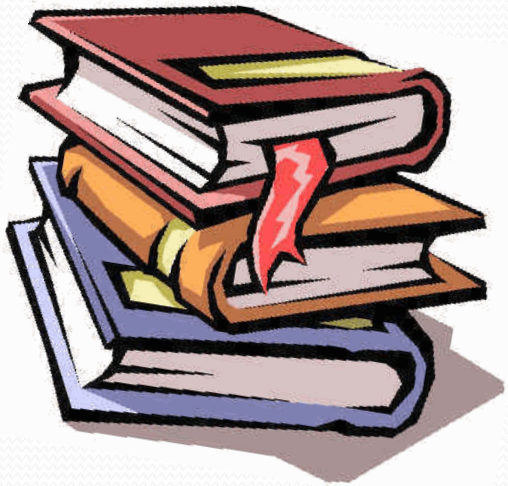
Defining the boundaries

Standard Practice

- Interventions designed to promote the well being of an individual patient or client
- Has a reasonable expectation of success
- Provides diagnosis, preventative treatment, or therapy

Research

- Tests a hypothesis
- Provides conclusions
- Develops or contributes to generalizable knowledge
- Described in a formal protocol with objectives and procedures to reach the objective



IRB / IEC Responsibilities

- Research study must be approved prior to recruiting subjects. This includes ALL documents ie. ICF's, Protocol, Recruitment material, IB, Subject Questionnaires.
- Report adverse events (AE's) and deviations.
- IRB is required to maintain study records as well for at least 3 years
- IRB should consist of at least 5 members
  - 1 Non-scientific; 1 Independent of institution/study site

Investigator Responsibilities

Investigator Responsibilities

- Qualified by education, training and experience
  - To be documented by up to date CV (most sponsored trials require a revised CV every 2 years with signature/date)
- Maintain an **up-to-date** list of qualified personnel who they(PI) delegated study responsibilities
  - This should be one ***ongoing*** list or log in order to review past and present study team members
- Allow monitoring and auditing by the sponsor & regulatory authorities
- Compliance with GCP's
- Adequate resources: Sufficient time, Appropriate amount of qualified staff, Facilities & Recruitment

Investigator Responsibilities cont.

- **Medical Care**
  - A qualified MD(or dentist) is responsible for trial-related medical decisions including assessments of AE's, lab values and concomitant medications for intercurrent illnesses.
    - PI/Sub-I should mark whether an abnormal lab value is clinically significant (**CS**) or Not (**NCS**) and acknowledge labs by signing and dating
  - While the subject is not required to give a reason for withdrawing a reasonable effort to should be made, while respecting their rights
    - If the subject is a lost to follow – a min. of 3 documented attempts + certified letter should be sent

Investigator Responsibilities cont.

- **Communication with the IRB**
  - Dated and written approval prior to start of study
  - Provide initial and any updated copies of the Investigator Brochure (IB)
  - Provide all documents subject to review (ICF, IB, Questionnaires, Recruitment material, Medical release forms, Amendments, and any changes to the above

Investigator Responsibilities cont.

- **Compliance with the Protocol**
  - Sign off on the protocol and not implement deviations
  - If deviations occur, document and report to appropriate authorities (including IRB – HRPP policy 713)
    - Recommend creating NTF to clarify any deviation in subject chart.

Investigator Responsibilities cont.

- **Investigational Product (IP)**
  - Accountability, Storage, Use, and Maintenance of records of IP delivery, use by subject, product returned to sponsor and unused IP
    - IP Log should include dates, Quantities, serial #'s, Expiration dates and any unique codes

Investigator Responsibilities cont.

- **Informed Consent & Process**
  - Most recent and approved ICF by the IRB
  - No coercion or unduly influence to participate or continue to participate
  - No language to waive legal rights
  - Subject or Legally Authorized Representative (LAR) to be fully informed of all aspects of the trial
  - ICF to be written in lay language (*6-8th grade reading level*)
  - Ample time to review and ask questions should be given

Investigator Responsibilities cont.

Informed Consent & Process Cont.

- Should be ***personally signed and dated*** by the **subject** or LAR and/ or witness.
- Should be ***personally signed and dated*** by **person obtaining consent** and/or **investigator**
- Subjects to be given a copy of the informed consent !
- For revised ICF's during the study – a copy of the signed/dated of the ICF to be given

Investigator Responsibilities cont.

- **Records & Reports**
  - Accuracy, Completeness, Legibility & Timeliness of data reporting
  - Source Documentation and CRF's should be consistent
  - Corrections to CRF to be initialed/ dated & explained
    - *ie. No AEs since last visit - Late entry MU 05/01/2013*
  - Maintain / Retain study documents (min. 2yrs on site)
    - Including all financial aspects noted in contract
  - Make all study related documents available to monitors, auditors, IRB or other regulatory authorities

Investigator Responsibilities cont.

Records & Reports Cont.

- **Progress Reports** (including Final reports & suspension/termination of a trial)
  - Submit written summary of trial status to the IRB
  - Promptly provide written reports to sponsor, IRB and other regulatory authorities

- **Safety Reporting**
  - **SAEs** should be reported immediately (most 24hrs)
  - **AEs** should be reported according to sponsor guidelines
  - Report deaths and any additional information to the sponsor and IRB

Sponsor Responsibilities

Sponsor Responsibilities

- Quality Assurance & Quality Control
- Contract Research Organization (CRO)
- Medical Expertise
- Trial Design
- Trial Management, Data Handling, Recordkeeping, & Independent Data Monitoring Committee
- Investigator Selection

Sponsor Responsibilities cont.

- Allocation of Duties & Functions
- Compensation to Subjects & Investigators
- Financing
- Notification/Submission to Regulatory Authorities
- Confirmation of Review by IRB

Sponsor Responsibilities cont.

- Information on Investigational Products
- Manufacturing, Packaging, Labeling, & Coding Investigational Products
- Supplying & Handling Investigational Products
- Record Access

Sponsor Responsibilities cont.

- Safety Information
- Adverse Drug Reaction Reporting
- Monitoring
- Auditing
- Noncompliance
- Premature Termination or Suspension of a Trial
- Clinical Trial/Study Reports
- Multicenter Trials

Clinical Trial Protocol

- General Information
- Background Information
- Trial Objectives & Purpose
- Trial Design
- Selection & Withdrawal of Participants
- Treatment of Subjects
- Assessment of Efficacy
- Assessment of Safety

Clinical Trial Protocol cont.

- Statistics
- Direct Access to Source Data
- QA & QC
- Ethics
- Data Handling & Recordkeeping
- Financing & Insurance
- Publication Policy
- Supplements

Investigator's Brochure

- Defined as a compilation of the clinical and nonclinical data on the investigational product(s) that are relevant to the study of the product(s) in human subjects.
  - Includes info on animal studies
  - Includes info on past human studies

Essential Documents for the Conduct of a Clinical Trial

- **Preclinical trial commencement**
  - IB, Protocol, ICF, Recruitment material, Financial documents, signed agreements between parties, CV's, Lab ranges/ manual, IP Logs/ decoding procedures
- **During clinical conduct of trial**
  - Monitoring reports, screening/enrollment log, IP accountability
- **After completion or termination of trial**
  - Documentation of IP destruction, Close-out report, Final report to IRB, Clinical study report

Storage of Essential Documents

- **USF IRB Rule:** 5 years from the date of study closure
- **OHRP Rule:** 3 years following study completion
- **NIH Rule:** 3 years from date of submission of final expenditure report
- **FDA Rule:** 2 options
  - 2 years following marketing of the drug or,
  - 2 years after IND application is withdrawn if drug was not marketed
- **Sponsor Rule:** refer to study protocol

Storage of Essential Documents cont.

- HIPAA Authorizations must be kept for 6 years
- Follow rule that gives the time limit that is **longest**

Where to find GCP Guidance?

- Guidance Documents can be found on the FDA website
  - http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/default.htm

- ICH E6- Good Clinical Practice: Consolidated Guidance
  - http://www.fda.gov/downloads/Drugs/Guidances/ucm073122.pdf

Additional Resources

- http://www.fda.gov/cder/guidance/959fnl.pdf
- http://www.clinicaltrials.gov/
- http://www.fda.gov/oc/ohrt/irbs/websites.html
- http://ohrp.osophs.dhhs.gov/

Questions?

Thank You!