Good Clinical Practices (GCP)
For Clinical Researchers
Part 2
(Videotaped 10/16/2014)
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GCP in Practice

- Investigator Responsibilities
  - Quality Assurance
  - Delegated Activities
  - Safety Reporting
  - Informed Consent
  - Documentation
Overview of Good Clinical Practices (GCP)
Historical Context
Historical Context – The Need for GCPs

• Each nation sets rules on safety, quality, and efficacy of pharmaceutical products
• International requirements lacked standardization
• Costs to comply with multi-national regulations were prohibitive
• Increased research and development costs translated to increased consumer healthcare costs
International Conference on Harmonization (ICH)

- European Community was first to create common regulations for drug development
- At a World Health Organization Conference, the U.S., the European Union, and Japan made plans that led to the creation of the International Conference on Harmonization (ICH)

“It is our common duty to take initiatives to move towards a world citizenship in health which supersedes [sic] national boundaries.”

Mr. Claude Evin, Minister of Health, France
Approval of Guidance on Good Clinical Practice

- The ICH began meeting in a biannual conference in 1991
- In May 1996, the Consolidated Guidance on Good Clinical Practice was finalized
- All three government members, (Japan, the European Union, and the U.S.), eventually approved this document
- The U.S. published the guidance in the Federal Register on May 9, 1997
“Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects. Compliance with GCP assures that the rights, safety, and well-being of trial subjects are protected and that the clinical trial data are credible.”

ICH-GCP:1.24

Note: GCP standards are NOT statutes or regulations and do not have the force of law. Rather, they are generally accepted, international best practices for conducting clinical trials and device studies.
Why is GCP Important?

• Sets minimum quality standards for the conduct of clinical research

• Compliance with GCP
  o Ensures that the rights, safety, and well-being of study participants are protected
  o Ensures the integrity of the data submitted for approval

  ➔ Sets standards for a system of mutual accountability among sponsors, regulatory authorities, investigators, and IRBs
Good Clinical Practices Components

- Food and Drug Administration (FDA) regulations and guidance documents
- International Conference on Harmonization (ICH) guidelines
- State and local laws
- Medical Standard of Care
- Medical Ethics
Shared Responsibilities

Responsibility for following GCPs is shared among the following:

- Institutional Review Board (IRB)
- Investigator
- Sponsor
- Monitor
The Guiding Principles of GCP
The Thirteen Principles (#1 & 2)

1. Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s). (Sponsor monitoring – including Investigator-Sponsor studies)

2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks. (IRB Review)
3. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society. (IRB Review)

4. The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial. (Sponsor – pre-trial background, including Investigator-Sponsors)

5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol. (Sponsor, including Investigator-Sponsors)
6. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB) approval. (Investigator Responsibility)

7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist. (Investigator Responsibility)
The Thirteen Principles (#8 & 9)

8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s). (Investigator Responsibility)

9. Freely given informed consent should be obtained from every subject prior to clinical trial participation. (Investigator Responsibility)
10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification. (Investigator Responsibility)

11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s). (Investigator Responsibility)
12. Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol. (Sponsor and Investigator Responsibility)

13. Systems with procedures that assure the quality of every aspect of the trial should be implemented. (Investigator Responsibility)
Non-Clinical Research
(Good Research Practices)
It is important to remember that the human subject protection requirements in the DHHS regulations are essentially the same as the FDA regulations and include research that is not clinical. Good research practices include compliance with:

- Informed Consent Process
- Documentation of Informed Consent
- Data and Safety Monitoring
- Privacy
- Confidentiality
FDA Regulatory Requirements for GCP
Clinical Investigator/Site (21 CFR 312 and 812):

- Conduct the study according to the signed agreement, the investigational plan and applicable FDA regulations
- Protect the rights, safety, and welfare of subjects under the investigator’s care
- Control investigational product
- Dispose of/return investigational product
- Ensure that an IRB that complies with its requirements (21 CFR 56) will be responsible for initial and continuing review and approval
Clinical Investigator/Site (21 CFR 312 and 812):

- Obtain Informed Consent per 21 CFR 50 prior to study participation
- Submit Reports (progress, safety, final, financial disclosure)
- Maintain accurate, complete, and current records relating to the investigator’s participation in an investigation
- Retain records and make them available for review
Clinical Investigator/Site (21 CFR 54, PHS Regulations & SUNY-B P&Ps):

• Disclosure of Conflicts of Interest that affect the design, conduct, reporting, and analysis of the research (Disclose to Sponsor and SUNY-B)
  o Compensation or equity interest of $5,000 or more
  o 5% or greater ownership interest
  o Executive position with sponsoring agency
  o Intellectual property interests
  o Compensation or equity interest of any amount that could be affected by the outcome of the research
Clinical Investigator/Site: Statement of Investigator Form

FDA 1572

By signing the Form 1572 (contract), the Investigator agrees to:

- Personally conduct or supervise the study in accordance with the approved, relevant, current protocol
- Inform subjects (including controls) that drugs are investigational
- Meet the requirements of obtaining Informed Consent (21 CFR 50)
- Report Adverse Events to the IRB and Sponsor
- Maintain adequate and accurate records (available for inspection)
By signing the Form 1572 (contract), the Investigator agrees to:

- Read and understand the information (including potential risks and side effects) in the investigator’s brochure
- Ensure all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations in meeting the above requirements
- Ensure that an IRB that complies with FDA requirements (21 CFR 56) will be responsible for initial and continuing review and approval
- Promptly report to the IRB all changes in research activity and all unanticipated problems related to the study
By signing the Form 1572 (contract), the Investigator agrees to:

- Comply with all other requirements regarding obligations of clinical investigators and all other pertinent requirements in 21 CFR 312
- Not change the research without IRB approval except where necessary to eliminate immediate hazards to subjects
- Signature signifying agreement to follow all of these requirements

“(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)”
GCP in Practice
Investigator Responsibilities in a Nutshell

**Follow** Approved Protocol
- Responsible for research team’s adherence as well

**Protect** Human Subjects
- Ensure informed consent

**Control** Investigational Product

**Document** Study Progress
- Submit appropriate reports
- Retain records (adequate case histories)
Investigator Responsibilities – Quality Assurance

GCP principles require investigators to ensure the following:

- Participants receive adequate medical care
- Primary care physicians are notified of patient involvement
- Protocol deviations are documented and reported to IRB and sponsor
- Randomization and blinding procedures are followed
- Records and reports are accurate, complete, legible and timely
- Safety reporting is timely and as complete as possible
- Proper study termination and suspension activities are performed to manage the care of trial subjects and to inform the regulatory authorities
Delegate study-related activities only to qualified study team personnel

Determine site personnel are qualified by ensuring:

- Qualified by education, training and experience in the field being researched
- Maintains appropriate licensure for study-related duties that require a licensed professional
- Familiar with the investigational product and its proper use
- Document that responsibilities are delegated only to qualified personnel
Investigator Responsibilities – Adequate Resources

Investigators must ensure the following resources exist prior to starting a research study:

- Sufficient access to the patient population being studied
- Sufficient time to properly conduct and complete the study
- Adequate number of qualified personnel
- Adequate facilities and equipment
- Personnel trained on protocol, investigational product, and assigned duties and functions
Investigator Responsibilities – Medical Care

Medical Care of Subjects:

- Medical decisions should be made by a qualified physician who is an investigator or sub-investigator for the study
- Adverse events and other medical issues should be managed adequately
- Subject’s Primary Care Physician should be notified of participation, with subject’s approval
- Withdrawn subjects should be assessed
Investigator Responsibilities – IRB Review

Interaction with IRB:

- Written and dated approval should be obtained for the protocol, informed consent form, advertisements, subject literature and amendments prior to being implemented.
- All documents to be reviewed should be provided in a timely manner and updated as necessary throughout the trial.
Protocol Compliance:

- The investigator should formally agree to comply with the approved protocol and confirm this by signing the protocol.
- The investigator should not deviate from the protocol without prior knowledge and agreement from the sponsor and the IRB.
- The investigator should not implement protocol amendments prior to review and approval by the IRB.
Protocols that are greater than minimal risk require a data and safety monitoring plan (even if they do not require a DSMB).

This plan should outline how you will monitor:

- Individual subject safety
- The conduct of the research
- The data collected

The plan should also tell us:

- Who will review the data
- What data will be reviewed
- When and how often the data will be reviewed
Informed Consent

- Documented approval of consent document by IRB
- Revisions to consent document approved by IRB and subjects notified of changes when appropriate
- No subject should be coerced or unduly influenced to participate or continue to participate in a research trial
- No exculpatory language that causes the subject or the subject's legally authorized representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence
Informed Consent

- Investigator, or designee, should fully inform the subject, or the subject's legally authorized representative, of all pertinent aspects of the trial
- Written informed consent form, should be understandable to the subject or the subject's legally authorized representative
- Provide the subject, or the subject's legally authorized representative, ample time and opportunity to decide whether or not to participate in the trial
Informed Consent

- Written informed consent form should be signed and personally dated by the subject, or by the subject's legally authorized representative, and by the person who conducted the informed consent discussion.

- If a subject, or legally authorized representative is unable to read, an impartial witness should be present during the informed consent discussion, and sign and personally date the consent form attesting that the information in the consent form was accurately explained to, and apparently understood by, the subject or the subject's legally authorized representative.
Informed Consent – Required Elements

- Trial involves research
- Purpose of trial
- Treatment with probability
- Procedures (+ invasive)
- Subject responsibilities
- Experimental aspects
- Risks/inconveniences
- Expected benefits
- Alternatives
- Compensation for injury

- Prorated payment
- Expenses
- Voluntary, free to withdraw
- Direct access to records
- Confidentiality
- New information timely
- Contact person
- Reasons for termination
- Duration
- Number of subjects
Informed Consent

- Subject, or subject's legally authorized representative should receive a copy of the signed and dated written informed consent form.

- Subjects who can only be enrolled in a trial with the consent of a legally authorized representative should be informed about the trial to the extent compatible with the subject’s understanding and, if capable, the subject should assent, sign and personally date the written informed consent.
Informed Consent

- Trials with no anticipated therapeutic benefit should be conducted only on subjects who personally give consent and who sign and date the written informed consent form (with specific exceptions)
  - Objectives of the trial cannot be met by involvement of only subjects who can give informed consent personally
  - The foreseeable risks to the subjects are low
  - Negative impact on the subject’s well-being is minimized and low
  - The trial is not prohibited by law
  - Approval of the IRB is expressly sought on the inclusion of such subjects
When prior consent of the subject is not possible, the consent of the subject's legally authorized representative, if present, should be requested. When prior consent is not available, enrollment of the subject should require measures described in the protocol, with documented approval by the IRB, to protect the rights, safety, and wellbeing of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally authorized representative should be informed about the trial as soon as possible and consent to continue.
Documentation Requirements

- Accurate, complete, legible, and timeliness of data reported to sponsor in the CRFs and in all required reports
- CRF data should be consistent with the source documents or discrepancies should be explained
- Corrections to CRF should be dated, initialed, and explained, and should not obscure the original entry
- Maintain trial documents as specified in Essential Documents for the Conduct of a Clinical Trial
Documentation Requirements

• Essential documents should be retained until at least 2 years after the last approval of a marketing application and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since formal discontinuation of clinical development of the investigational product.

• Financial aspects of the trial should be documented in an agreement between sponsor and investigator/institution.

• Upon request of monitor, auditor, IRB, or regulatory authority, investigator should make available for direct access all requested trial-related records.
Special Considerations for Investigator-Initiated Research

- Sponsor
- Monitor

GCP Audit Readiness

- GCP Oversight and Enforcement

Preventing Non-Compliance with GCP

- Consequences of Non-compliance

Available Resources
Good Clinical Practices (GCP)  
For Clinical Researchers  
Part II-B  
(Videotaped 10/16/2014)
Special Considerations for Investigator-Initiated Research
ICH-GCP Definition of “Sponsor-Investigator”

- “An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.”

FDA Definition of “Sponsor-Investigator”

- “An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.”
Securing FDA approval for the use of an investigation new drug (IND):

- The sponsor of the investigation is responsible for submitting an IND for the drug to FDA (21 CFR 312)
- FDA will notify the sponsor in writing of the date it receives the IND. The IND goes into effect:
  - 30 days following FDA’s receipt of the IND, unless FDA notifies the sponsor that the investigation described in the IND are subject to a clinical hold, or
  - Upon earlier notification by the FDA of the IND
Exceptions to the requirement for FDA approval for the use of an investigation new drug (IND):

- When the proposed use of the drug meets one of the exemption from an IND criteria in FDA regulations (21 CFR 312.2(b))
  - This exemption from an IND must be granted by the IRB as part of their review of the study.

See HRP-306 – Worksheet: Drugs
Securing FDA approval for the use of an \textit{investigational device exemption} (IDE):

- The sponsor is responsible for submitting an application to FDA (21 CFR 812)
- The sponsor shall not begin an investigation for which FDA's approval of an application is required until FDA has approved the application
Exceptions to the requirement for FDA approval for the use of an investigation device exemption (IDE):

- When the proposed use of the device is deemed approved by meeting one of the abbreviated IDE categories in FDA regulations (21 CFR 812 2(b))
  - This abbreviated IDE must be granted by the IRB as part of their review of the study along with a Non-significant Risk (NSR) determination.

- When the proposed use of the device meets one of the exemption criteria in FDA regulations (21 CFR 812 2(c))
  - This exemption from an IDE must be granted by the IRB as part of their review of the study.

See HRP-307 – Worksheet: Devices
Medical Expertise

- Sponsor should designate appropriately qualified medical personnel who will be readily available to advise on trial-related medical questions or problems

Trial Design

- Sponsor should utilize qualified individuals (e.g., biostatisticians, clinical pharmacologists, and physicians) as appropriate, throughout all stages of the trial process
Sponsor – Investigator (Sponsor Responsibilities)

Quality Assurance and Quality Control

• Ensure trials are conducted and data are generated, documented (recorded), and reported in compliance with the protocol

• Ensure direct access to all trial-related sites, source data/documents, and reports for the purpose of monitoring and auditing

Contract Research Organization (CRO)

• A sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO (specified in writing), but the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor

• trial-related duties and functions not specifically transferred to and assumed by a CRO are retained by the sponsor
Sponsor – Investigator (Sponsor Responsibilities)

Trial Management, Data Handling, Recordkeeping, and Independent Data Monitoring Committee

• Sponsor should utilize appropriately qualified individuals to supervise the overall conduct of the trial
• Sponsor may consider establishing an independent data monitoring committee (IDMC) to assess the progress of a clinical trial, including the safety data and the critical efficacy endpoints at intervals
• When using electronic trial data systems:
  o Ensure system meets requirements for completeness, accuracy, reliability, and consistent intended performance
  o Maintain SOPs for using these systems
  o Maintain an audit trail, data trail, edit trail
  o Prevent unauthorized access to the data
  o Maintain list of the individuals who are authorized to make data changes
Trial Management, Data Handling, Recordkeeping, and Independent Data Monitoring Committee (Cont.)

- When using electronic trial data systems: (Cont.)
  - Maintain adequate backup of the data
  - Safeguard the blinding, if any (e.g., maintain the blinding during data entry and processing)

- It should always be possible to compare the original data and observations with the processed data

- Sponsor should use an unambiguous subject identification code that allows identification of all the data reported for each subject

- Sponsor, should retain all of the sponsor-specific essential documents pertaining to the trial in conformance with the applicable regulatory requirements

- If sponsor discontinues clinical development of an investigational product, sponsor should maintain all documents for at least 2 years after formal discontinuation or in conformance with applicable regulatory requirements
Trial Management, Data Handling, Recordkeeping, and Independent Data Monitoring Committee (Cont.)

- If sponsor discontinues clinical development of an investigational product, the sponsor should notify all the trial investigators/institutions and all the appropriate regulatory authorities.
- Transfer of ownership of the data should be reported to the appropriate authorities.
- Sponsor documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product.
- Sponsor should inform the investigator(s)/institution(s) in writing of the need for record retention and should notify the investigator(s)/institution(s) in writing when the trial-related records are no longer needed.
Investigator Selection

- Sponsor is responsible for selecting the investigator(s)/institution(s) qualified by training and experience with adequate resources to properly conduct the trial.
- Sponsor should provide the investigator(s)/institution(s) with the protocol and an up-to-date Investigator's Brochure, and should provide sufficient time for the investigator/institution to review the protocol.
- Sponsor should obtain the investigator's/institution's agreement:
  - To conduct the trial in compliance with GCP, with the applicable regulatory requirements.
  - To comply with procedures for data recording/reporting: and
  - To permit monitoring, auditing, and inspection.
  - To retain the essential documents that should be in the investigator/institution files until the sponsor informs the investigator/institution these documents are no longer needed.
- Sponsor and the investigator/institution should sign the protocol, or an alternative document, to confirm this agreement.
Sponsor – Investigator (Sponsor Responsibilities)

Allocation of Duties and Functions

- Sponsor should define, establish, and allocate all trial-related duties and functions

Compensation to Subjects and Investigators

- Sponsor should provide insurance or indemnify investigator/institution against claims arising from the trial, except for claims that arise from malpractice and/or negligence
- Sponsor's policies and procedures should address the costs of treatment of trial subjects in the event of trial-related injuries in accordance with applicable regulatory requirement
- When trial subjects receive compensation, the method and manner of compensation should comply with applicable regulatory requirements
Sponsor – Investigator (Sponsor Responsibilities)

Financing
- Financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution

Notification/Submission to Regulatory Authority(ies)
- Sponsor should submit any required application(s) to the appropriate authority(ies) for review, acceptance, and/or permission (as required by the applicable regulatory requirement(s)) to begin the trial(s)

Confirmation of Review by IRB
- Sponsor should ensure that reviewing IRB is organized and operates according to GCP and applicable laws and regulations
- Documented IRB approval, current copy of protocol, written informed consent form(s) and any other written information to be provided to subjects
Information on Investigational Product(s)

- Sponsor should ensure that sufficient safety and efficacy data from nonclinical studies and/or clinical trials are available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied.

- Update the Investigator's Brochure as significant new information becomes available.

Manufacturing, Packaging, Labeling, and Coding Investigational Product(s)

- Ensure that the investigational product(s) (including active comparator(s) and placebo, if applicable) is characterized as appropriate to the stage of development of the product(s), is manufactured in accordance with any applicable GMP, and is coded and labeled in a manner that protects the blinding, if applicable. In addition, the labeling should comply with applicable regulatory requirement(s).
Manufacturing, Packaging, Labeling, and Coding

Investigational Product(s)

- Determine acceptable storage temperatures, storage conditions, storage times, reconstitution fluids and procedures, and devices for product infusion, if any, and inform all involved parties.
- Investigational product(s) should be packaged to prevent contamination and unacceptable deterioration during transport and storage.
- In blinded trials, the coding system for the investigational product(s) should include a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but does not permit undetectable breaks of the blinding.
- If significant formulation changes are made in the investigational product(s), the results of any additional studies of the formulated product(s) needed to assess whether these changes significantly alter the pharmacokinetic profile of the product should be available prior to the use of the new formulation in clinical trials.
Supplying and Handling Investigational Product(s)

- Sponsor is responsible for supplying the investigator(s)/institution(s) with the investigational product(s) after obtaining all required documentation (e.g., approval from IRB and regulatory authorities)
- Ensure written procedures include instructions for the handling and storage of investigational product(s), and address adequate and safe receipt, handling, storage, dispensing, retrieval of unused product from subjects, and return of unused investigational product(s) in compliance with the applicable regulatory requirements
- Sponsor should:
  - Ensure timely delivery of investigational product(s)
  - Maintain records that document shipment, receipt, disposition, return, and destruction of the investigational product(s)
  - Maintain a system for retrieving investigational products and documenting this retrieval
  - Maintain a system for the disposition of unused investigational product(s) and for the documentation of this disposition
Supplying and Handling Investigational Product(s)

- Sponsor should:
  - Take steps to ensure that the investigational product(s) are stable over the period of use.
  - Maintain sufficient quantities of the investigational product(s) used in the trials to reconfirm specifications, should this become necessary, and maintain records of batch sample analyses and characteristics. To the extent stability permits, samples should be retained either until the analyses of the trial data are complete or as required by the applicable regulatory requirement(s), whichever represents the longer retention period.

Record Access

- Sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) provide direct access to source data/documents for trial-related monitoring, audits, IRB review, and regulatory inspection.
- Sponsor should verify that each subject has consented, in writing, to direct access to his/her original medical records for trial-related monitoring, audit, IRB review, and regulatory inspection.
Safety Information

- Sponsor is responsible for the ongoing safety evaluation of the investigational product(s)
- Sponsor should promptly notify all concerned investigator(s)/institution(s) and the regulatory authorities of findings that could affect adversely the safety of subjects, impact the conduct of the trial, or alter the IRBs approval to continue the trial

Adverse Drug Reaction Reporting

- Sponsor should expedite the reporting to all concerned investigator(s)/institutions(s), to the IRB, where required, and to the regulatory authorities of all adverse drug reactions that are both serious and unexpected
- Sponsor should submit to the regulatory authorities all safety updates and periodic reports, as required by applicable regulatory requirement(s)
Ensure that the trial is conducted and documented properly by carrying out the following activities:

• Verify the investigator has adequate qualifications and resources throughout the trial period, and that the staff and facilities, including laboratories and equipment, are adequate to safely and properly conduct the trial

• Verify, for the investigational product(s):
  o Storage times and conditions are acceptable, and that supplies are sufficient
  o Investigational product(s) are supplied only to subjects who are eligible to receive it and at the protocol specified dose(s)
Verify, for the investigational product(s) (Cont.):

- Subjects are provided with instruction on properly using, handling, storing, and returning the investigational product(s)
- Receipt, use, and return of the investigational product(s) at the trial sites are controlled and documented adequately
- Disposition of unused investigational product(s) at the trial sites complies with applicable regulatory requirement(s) and is in accordance with the sponsor’s authorized procedures
Sponsor – Investigator (Monitor Responsibilities)

- Verify that the investigator follows the approved protocol and all approved amendment(s), if any
- Verify that written informed consent was obtained before each subject's participation in the trial
- Ensure that the investigator receives the current Investigator's Brochure, all documents, and all trial supplies needed to conduct the trial properly
- Ensure that the investigator and the investigator's trial staff are adequately informed about the trial
Sponsor – Investigator (Monitor Responsibilities)

- Verify that the investigator and the investigator's trial staff are performing the specified trial functions, in accordance with the protocol and any other written agreement between the sponsor and the investigator/institution, and have not delegated these functions to unauthorized individuals.
- Verify that the investigator is enrolling only eligible subjects.
- Report the subject recruitment rate.
- Verify that source data/documents and other trial records are accurate, complete, kept up-to-date, and maintained.
Sponsor – Investigator (Monitor Responsibilities)

• Verify that the investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial

• Check the accuracy and completeness of CRF entries, source data/documents, and other trial-related records, specifically verifying that:
  
  o Data required by the protocol are reported accurately on the CRFs and consistent with the source data/documents
  
  o Dose and/or therapy modifications are well documented for each of the trial subjects
Sponsor – Investigator (Monitor Responsibilities)

- Check the accuracy and completeness of CRF entries, source data/documents, and other trial-related records, specifically verifying that (Cont.):
  - Adverse events, concomitant medications, and intercurrent illnesses are reported in accordance with the protocol on the CRFs
  - Visits that the subjects fail to make, tests that are not conducted, and examinations that are not performed are clearly reported as such on the CRFs
  - Withdrawals and dropouts of enrolled subjects from the trial are reported and explained on the CRFs
Sponsor – Investigator (Monitor Responsibilities)

- Ensure that appropriate corrections, additions, or deletions are made, dated, explained, and initialed by the investigator or by a member of the investigator's trial staff
- Determine whether all adverse events (AEs) are appropriately reported within the time periods required
- Communicate deviations from the protocol, SOPs, GCP, and the applicable regulatory requirements to the investigator and take appropriate action to prevent recurrence of the detected deviations
• Provide monitoring report to sponsor including significant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken, and/or actions recommended to secure compliance

• The review and follow-up of the monitoring report by the sponsor should be documented
Resources

HRP-103 – Investigator Manual
HRP-503 – Template Protocol
HRP-502 – Template Consent Document
Informed Consent SOPs
  • HRP-090 – SOP – Informed Consent Process
  • HRP-091 – SOP – Documentation of Informed Consent
HRP-430 – Checklist – Investigator Quality Improvement Assessment

FDA website http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm
ICH GCP E6 (available for download from FDA website)

DHHS http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html
Clients include:

• More than 95 of the top 100 research universities
• Nine of the top ten largest healthcare systems
  - ranked by Modern Healthcare
• Eight of the top ten largest Children’s hospitals
• Many of the premier academic medical centers