

Training Elements of Human Subjects Research Coordination CTSA Research Coordinator Taskforce

Overview of the Regulatory Environment in Academic Health Centers

Introduction

Research on humans may be defined from many perspectives (e.g. social and behavioral research, clinical research, public health research, etc.). It is critical to remember that regardless of the type of study, it involves a human subject. Throughout this module, the term “human subjects research” will be used to consistently remind us of our commitment to respect and protect the rights and welfare of human subjects. Most of the module content is focused on human subjects research taking place in an Academic Health Center (AHC); however, the majority of content would be applicable in all research settings involving human subjects.

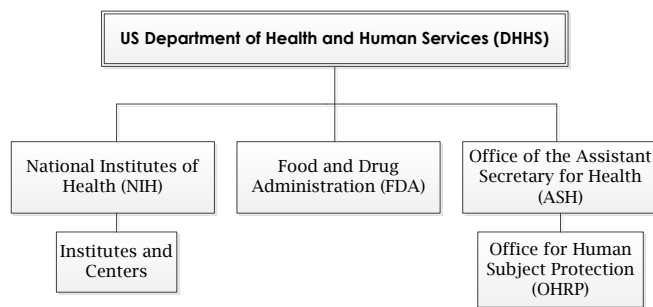
Regulations, Rules, and Research Oversight

Depending on the research study, there may be multiple levels of regulatory/compliance oversight, including federal and state laws regulations, policies and guidelines, funding agency policies and guidelines and institutional policies. It is important to understand all of the regulations and policies that guide your particular research study so that you can ensure that you have the appropriate procedures in place.

Government Regulations Pertaining to Human Subjects Research

Most human research studies taking place at Academic Health Centers (AHCs) are regulated by one or both of two government agencies: the Office for Human Research Protection (OHRP) and/or Food and Drug Administration (FDA). These agencies function under different sets of regulations that will be discussed later. The National Institutes of Health (NIH) provides support for human research through funding and provides guidance and policies on the conduct of human research.

The diagram below has been extracted from the Department of Health and Human Services (DHHS) Organizational chart. The full organizational chart can be located at <http://www.hhs.gov/about/orgchart/>.



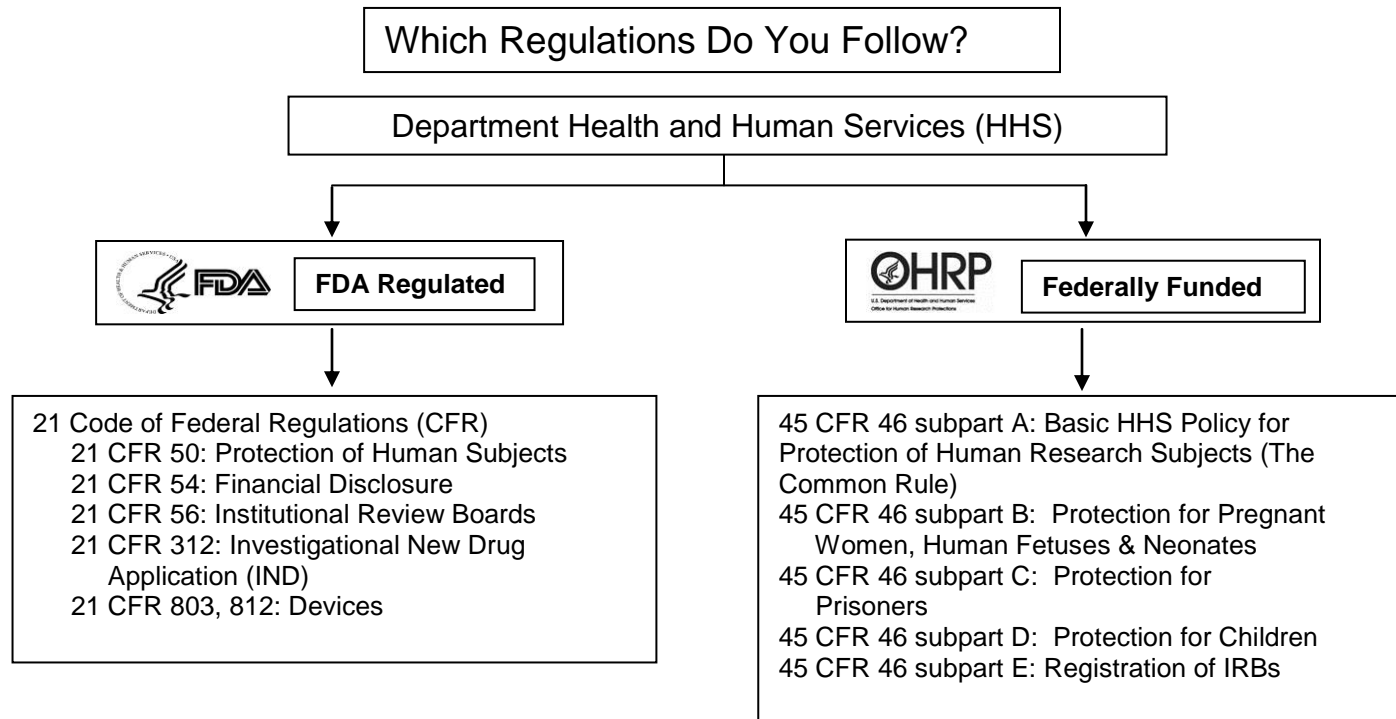
1. National Institutes of Health (NIH): NIH is located in the DHHS. In addition to the NIH conducting its own research studies, the NIH provides federal funding for thousands of researchers in universities and research institutions through its institutes and centers (e.g. National Cancer Institute). It is important to note that the NIH is primarily a funding agency, not a regulatory body. Studies funded through NIH are regulated under 45 CFR 46 (The Common Rule).
2. Food and Drug Administration (FDA): FDA is also located in the DHHS. Relative to human subjects research, FDA is the regulatory body responsible for the regulation and oversight of human subjects research studies that involve investigational products (e.g. drugs, biologics and devices). Studies conducted under FDA must adhere to Title 21. There are several Parts under Title 21 that will be discussed later in this module.
3. Office for Human Research Protections (OHRP) is the federal office that generates regulations for human subjects research- Institutional policy may dictate how and when OHRP regulations are followed, therefore it is

recommended to consult with the study's Institutional Review Board (IRB) for guidance on what federal regulations apply to a specific project.

Most government agencies have the legal authority to develop and enforce their own regulations and rules that are specific to the agency's focus and mission (e.g. Department of Health and Human Services, Food and Drug Administration, Veteran's Administration). These agency-specific regulations and rules are announced in the daily Federal Register (FR) and published (codified) in an annual update to the Code of Federal Regulations (CFR). The CFR has 50 titles representing broad areas subject to Federal regulation. Each title is further divided into parts that cover specific regulatory areas, for example, 21 CFR 56 is shorthand for Title 21 CFR Part 56.

In 1974 the Department of Health, Education and Welfare (later to become the DHHS) published regulations for the protection of human research subjects, Title 45 CFR Part 46: Federal Policy for the Protection of Human Subjects. This regulation became known as The Common Rule as in 1991 when an additional 14 federal departments and agencies incorporated the policy into their own CFR (now the total number is 17). OHRP human subjects protection regulations fall under 45 CFR 46. FDA functions under Title 21 and incorporated 45 CFR 46 into the following FDA regulations: 21 CFR 50 (Protection of Human Subjects) and 21 CFR 56 (Institutional Review Boards).

When conducting human subjects research it is important to know how the study is funded and the regulations to which the study must comply.



If a study is federally funded (e.g. NIH, Department of Defense) and involves an FDA-regulated investigational product, then the regulations applicable to FDA and the federal funding agency apply.

There are organizations that provide funding for human subjects research but do not fall under FDA or OHRP regulations (e.g. foundations) because the research does not involve an investigational product and is not federally funded. Most of these organizations default to requiring adherence to 45 CFR 46. If such a study is carried out at an AHC, compliance with 45 CFR 46 may be required, consult with the study's IRB for guidance.

What is "GCP"

A phrase one hears frequently in the human subjects research environment is the necessity of conducting a study according to "Good Clinical Practice (GCP)". Per International Conference on Harmonization (ICH) E6, [Good Clinical](#)

Practice is defined as an "...ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects". The key concepts of GCP in fact began with FDA regulations, and GCP became an international standard through the ICH. The ICH, formed in 1990 through collaboration among the EU, Japan and the United States, evolved (through its ICH Global Cooperation Group) to respond to the increasingly global face of drug development, so that the benefits of international harmonisation for better global health can be realised worldwide. ICH's mission is to achieve greater harmonisation to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner." (<http://www.ich.org/>). As new ICH guidelines have been developed through the years, FDA has adopted them as guidance rather than codify them as regulation, stating ICH Guidelines are already addressed in FDA regulations as it would be a duplication of efforts to codify ICH Guidelines. But, there are some differences between ICH Guidelines and FDA regulations that FDA has acknowledged. Therefore, in human subjects research in the US, ICH Guidelines are considered *guidelines*, not regulation unless required through institutional policy, sponsor Standard Operating Procedures (SOPs), or the study protocol.

There are four-topics in ICH guidelines. Efficacy is one of the topics and within Efficacy there are several guidelines. The 6th is known as Good Clinical Practice, or E6 GCP. So, under ICH, E6 GCP is defined as:

"...an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety and well-being of trial subjects are protected..."

ICH E6 GCP is organized by 13 principles under the following seven categories:

Ethics	Data Quality and Integrity
Protocol and Science	Investigational Products
Responsibilities	Quality Control/Quality Assurance
Informed Consent	

A Broader Context of GCP

Some researchers may assume that ICH GCP really only applies to industry drug/device studies that will eventually be seeking (or hope to seek) regulatory approval to market the drug or device. However, though all of ICH GCP would not apply to every study, ICH GCP does present a standard for the conduct of human subjects research. This is especially important, considering that the Common Rule provides much detail on IRB operations and consent, but very little on the roles and responsibilities of the investigator and/or sponsor and the actual conduct of the research by the study team.

Consider the quote from World Health Organization's (WHO) Handbook for Good Clinical Practice, 2002: "To the extent possible, the principles of GCP should generally apply to all clinical research involving human subjects, and not just research involving pharmaceutical or other medical products." Included here are:

- "studies of a physiological, biochemical, or pathological process, whether physical, chemical, or psychological – in healthy subjects or in patients;
- controlled studies of diagnostic, preventive or therapeutic measures, designed to demonstrate a specific generalizable response to these measures against a background of individual biological variation
- studies designed to determine the consequences for individuals and communities of specific preventive or therapeutic measures"

Summary

When conducting human subjects research, the applicable regulations, policy and guidelines at national, state, and local (institutional) levels must be followed. Sometimes the regulations are quite broad and do not address specific situations with which the researcher may be confronted. To assist with the interpretation of regulations, agencies issue policies to address or clarify research issues. FDA issues guidance(s) that represent FDA's current thinking on a particular subject. Although these guidance(s) are not regulations, they provide approaches that would be acceptable to FDA.

Version 5/31/12 (minor revision 11/29/12)

Regardless of how GCP is defined, a fundamental concept is to understand that the best practice in the conduct of human subjects research is one of compliance with regulatory requirements and application of professional standards that result in sound and ethical research design, integrity of the data, and most importantly, protection of the rights and welfare of the human subjects involved in research studies.

In addition to following the general principles of GCP, study coordinators should have a solid foundation of the history and ethics of human subjects research and should be trained to understand and follow all regulations and guidance(s) governing their particular human research protocols. A detailed list of these regulations is provided here.

Human Subjects Research Regulatory Requirements:

- Historical & Ethical Background of Research
 - The Belmont Report
 - The Nuremburg Code
 - The Declaration of Helsinki
- Good Clinical Practices
 - ICH E6
 - Sponsor responsibilities – 21 CFR 312 & 812
 - Investigator
 - Responsibilities – 21 CFR 312 & 812 (IND & IDE)
 - FDA information sheets
 - Financial Disclosure – 21 CFR 54
 - Drug/Device quality standards
 - Drugs – 21 CFR 210 & 211
 - Biologics – 21 CFR 600 & 606
 - Tissue – 21 CFR 1271
 - Devices – 21 CFR 820
 - Protocol standards & requirements
 - Standards – 21 CFR 312 & 812
 - IRB review requirements – 21 CFR 56
 - Subject related issues
 - Informed Consent – 21 CFR 50
 - Medical care – 21 CFR 312
 - Protection of human subjects 21 CFR 50; 45 CFR 46
 - Documentation
 - Essential documents & source documents – 21 CFR 312 & 812
 - Electronic records & signatures – 21 CFR 11
 - Safety reporting
 - To IRB – 21 CFR 56 & 812
 - To Sponsor – 21 CFR 312 & 812
 - To FDA – 21 CFR 312, 812, & 803
 - To manufacturer – 21 CFR 803
 - Monitoring (Quality Assurance & Quality Control) – 21 CFR 312 & 812

Coordinators should be aware of their research setting, study funding and study type(s) for which they coordinate:

- Research Settings
 - University-based/Academic Health Center (medicine, dental, education)
 - Community-based (local agencies, private medical practices, networks)
- Types of Study Funding
 - NIH
 - Industry
 - Foundation
 - Private

- Cross-Agency
- Institution Supported (department support)
- Study Types:
 - Drug
 - Investigational New Drug (IND)
 - Phases of studies (Principal Investigator-initiated, IND submission)
 - Device
 - Investigational Device Exemption (IDE)
 - Principal Investigator-initiated: IDE submission
 - IDE: classification, SR, NSR, Exempt, compassionate/expanded access
 - Pre-market Notification 510K
 - Pre-Market Approval (PMA)
 - Humanitarian Use Device (HUD)
 - Humanitarian Device Exemption (HDE)
 - Non-Drug/Non-Device
 - Behavioral/Social Science

Core / Essential Training Requirements for Protocol Management

These core/essential elements do not stand alone. Institutional, job specific and department requirements are other core components.

- Pre-Study Start-Up Processes:

These processes refer to the pre-enrollment phase of a study and may differ depending upon study funding source (Industry, NIH, Principal Investigator (PI)-initiated, internally funded). The study site needs to determine if it has the necessary resources and capabilities to carry out the proposed protocol (Ex. Industry sponsored studies often have a representative who visits the study site to determine resources and site initiation). Also, the study team must review the study's protocol for feasibility including assessing the science, ethical elements, available resources, and financial resources. If all parties are in agreement to initiate the study, specific institutional processes must be followed such as those listed below.

- Confidentiality Disclosure Agreement (CDA)
- Conflict of Interest / Risk Management Plan
- Financial Disclosure
- Study Contract / Clinical Trial Agreement (CTA)
- Protocol review and feasibility assessment
- Budget review, if applicable
- IRB Submission with inclusive documents (Ex. IND/IDE letter from FDA)
 - (see listing in "Essential Documents/Regulatory Binder" below)
- Informed consent:
 - Consent/Assent Research Participants
 - Adults
 - Pediatric
 - Legally Authorized Representatives, use of
 - Other vulnerable populations
 - Informed Consent Process
 - IRB approved study members who obtain consent
 - Read/ Discuss/ Health Insurance Portability and Accountability Act (HIPAA) / Personal Health Information (PHI) / Assess comprehension
 - Signature/ date/ initial/ copy distribution
 - Documentation in chart (research chart and/or medical record)
- Final check or a check to see if you are "Good to Go" to meet all institutional requirements for study start up (often tied with in IRB release of approval).
- Site assessment and initiation (if applicable)

- Essential Documents / Regulatory Binder:

As per the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guideline 4.9.4, a key responsibility of an investigator is to maintain certain trial-related documents so that it is possible to evaluate the ethical and procedural conduct of a trial and the quality of the data produced. These “Essential Documents,” including both study-related documents (such as the approved protocol and amendments) and participant-specific documents (such as completed Case Report Forms, source documentation and signed consent forms which are further discussed in the Documentation section on page 8) are specified in the ICH Guideline (Good Clinical Practice E6, section 8, Essential Documents for the Conduct of a Clinical Trial) of <http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html> . The term “Regulatory Binder” refers to the place where regulatory documentation related to your study is stored and updated. This place is not necessarily one location or even one “binder” and can consist of the following:

- FDA forms/communications
 - Statement of Investigators 1572
- Institutional Review Board (IRB)
 - Submitted Forms
 - Communications/safety reports/Protocol Deviation Reporting (IRB, Sponsor, FDA)
 - Approvals
 - Protocol
 - Amendments
 - Consents
 - Continuing Reviews
 - Federal Wide Assurance (FWA) document
 - IRB membership roster
 - Sign-off forms of various institutional entities (could be filed w/ financial documents)
- Curricula vitae/resumes
- Medical license copies
- Laboratory Certificate & reference values
- Processes & Tracking Logs:
 - Study staff training log (protocol specific)
 - Delegation/roles/responsibility of research team members log
 - Signature log
 - Adverse Event/Unexpected Events log
 - Screening log
 - Consent log
 - Enrollment log
 - Withdrawal/Termination log
 - Subject Compensation log (is filed separately with the financial records)
 - Investigational Agent log
 - PI/Other Entity monitoring signed log (ex. sponsor monitoring log)
- Correspondence (important decision making documents)
 - Sponsor communications
 - Monitoring visit reports

KEY CONSIDERATION: You may need to keep a note-to-file to describe the location of any electronic documents locations – consult with your PI and sponsor.

- Adherence to IRB approved protocol:

Studies conducted under an IRB approved protocol must adhere to that protocol. This means the research team cannot do any procedures, visits, or interactions that are not in the IRB approved protocol, but they must also do what is specified in the protocol. If changes in research are necessary for the conduct of the study a modification must be submitted to and approved by the IRB prior to implementing the change. The exception to this may occur when a change is necessary to eliminate apparent immediate hazards to participant(s). Failure to conduct the

study according to the IRB approved protocol puts the study into noncompliance and this must be reported to the IRB. Following your IRB approved protocol consists of the following:

- Recruitment Plan
- Informed Consent Process
- Inclusion/Exclusion Study Eligibility Criteria
- Randomization
- Procedures & Study Interventions
- PI / Medical oversight
- Unblinding procedures
- Data & Safety Monitoring Plan

- Interactions with:

Conducting a research study involves interactions between the: research team, clinical team(s), sponsor, governmental and institutional representatives, and research participants. As a member of the study team, coordinators need to become acquainted with roles and responsibilities of each to aid in appropriately addressing issues that arise. Continually building upon these relationships listed below will foster positive outcomes and help ensure research integrity.

- Clinical care providers/staff (if applicable)
- IRB & other regulatory agencies (FDA)
- Research participants/subjects (and their families, if applicable)
- Principal investigators
- Research Administrative Office (grants, finances, contracts, etc.)
- Sponsor / monitor (monitor visits, audits)
- Study team
- Clinical Research Center/Unit Staff
- Hospital Ancillaries Services/ (Billing, radiology, laboratory, etc.)
- Research Pharmacy
- Subject Advocacy Groups

- Recruitment & Retention:

Recruitment

Recruitment is a process to identify and communicate with potential study participants. It is key for the research team to appropriately develop and implement an effective recruitment strategy to successfully meet projected enrollment. Knowledge of regulations, GCP and institutional policies prior to implementation of the recruitment process is essential.

- Subject recruitment strategy – Understanding and adherence to:
 - IRB approval process
 - Institutional policies
 - Budget and billing review
 - HIPAA policies (i.e. pre-authorization, chart review)
- Identification of sources to recruit (i.e. radio, newspaper, etc.)
- Confidentiality strategies
 - Certificate of Confidentiality
 - Data protection plans (accessibility and data sharing/computing)
 - Social Security numbers and other Protected Health Information
- Understanding participant's health care support systems within research activities: provider(s), caregiver, family, Legally Authorized Representative.

Retention

Retention of enrolled participants is critical to the success of every human research study. Building a solid relationship between the research team and the human research subject will help to ensure good communication and follow through for the duration of the protocol.

- Communication strategies
 - Development of informational packets (i.e. diaries, business cards etc.)
 - Human research subject appreciation (i.e. Special event cards, thank you notes)
- Communication with human research subject's health care support systems (i.e. provider(s), caregiver, family, legally authorized representative) – following institutional policies.
- Compensation / Payment to participant
 - IRB review of strategy and the informed consent language
 - Ensure funding is adequate
 - Institutional/Department payment process (Internal Revenue Service form 1099)
- Facilitation of scheduled/unscheduled study visits
 - Prescreening and screening visit(s)
 - Human research subject enrollment/randomization
 - In-study visits
 - Discharge procedures
 - Adverse Event unscheduled visits (and applicable follow-up visits)
 - Human research subject withdrawal process

- Documentation:

Documentation is the recording of all activities relating to the conduct of a research study and serves to substantiate the integrity of trial data, confirm observations that are recorded and verify the existence of participants. More specifically, it is the collection of a human research subject's complete record of participation in a study. Whether written notes in a medical chart, completion of source/protocol work sheets, the entering of information in an electronic medical record, the collating of human research subject's electronic communications (e-mail) or the logging of telephone calls, documenting these research activities is of utmost importance. This documentation serves as a way to verify activities, ensure data integrity, allow the research team to review the events of the study and provide critical information for any auditor who may monitor. Every step from initial screening to last contact with a human research subject must be verifiable. Consult with your institution's documentation experts (i.e. medical records department, human subject protection office) and follow regulations associated with providing adequate documentation:

- 21 CFR 312 <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?fr=312.62>
- 21 CFR 812 <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=812.140> 21 CFR 11 (electronic records) <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?cfrpart=11>
- Hospital/Academic Health Center policy
 - *Source Documents* - The initial, first location where the recording of data occurs is called source documentation or source data. The recording of source data by the originator or recorder (physician, coordinator, specialist, and human research subject) may be on paper or use electronic means (e-record) that are accessed by current and later users and retained as per regulations.

KEY CONSIDERATION: Regarding your study's Essential Documentation *Regulatory* binder please refer to page 6.

- *Case Report Forms (CRFs)* are a printed or an electronic data collection tool used in *human* research studies to *record* protocol required information for each research participant. Because CRFs collect relevant data in a specific format, their use helps facilitate the standardization of data collection by the study team(s). Unless otherwise stated in the protocol, all data must be collected on each CRF. Only data to be analyzed should appear on a CRF. Data reported onto CRFs are derived from source documents and thus need to be consistent with source documents

(any discrepancies should be explained). The CRFs should not be used as an original source document(s) unless indicated in the protocol. CRFs may be monitored by sponsors or other regulatory entities.

- Basics
 - Accessibility –
 - Restricted access by specific personnel
 - Security
 - Location (storage for study chart, medical records, case report forms)
 - Short term storage during study
 - Long term storage upon study completion
- Components of Study Chart (source documents)
 - Orders
 - Signed Informed Consent Forms
 - Laboratory results
 - Progress notes
 - Communications, written or electronic, with human research subject and study-affiliated clinicians
 - Assessment forms
 - Certified Copies of source documents (if applicable)
- Case Report Forms (CRFs)
 - Completion
 - Corrections
 - Query resolution process
 - Electronic Data Capture, Part 11 compliance and data sharing/exporting 21 CFR 11 & Database and data entry

- Safety Monitoring Process:

Monitoring the safety of the human research subjects and the integrity of the clinical research data is the responsibility of a number of people including the sponsor, the Principal Investigator (PI), members of the study team, an independent/non-independent entity (Safety/Medical Monitor, Safety Monitoring Committee or Data & Safety Monitoring Board) or a combination of these.

Under 21 CFR 56.111 subpart C (a) and 45 CFR 46.111(a)(6), when appropriate, an IRB reviewing the study must determine if the research plan includes adequate provision to ensure the safety of human research subjects. Protocols include a description of how safety will be ensured by ongoing review of the accumulating data.

- In general, any human research study that is considered greater than minimal risk would require a *Data and Safety Monitoring Plan* (DSMP), which details how the PI plans to oversee the safety and welfare of the human research subjects and the validity of the data. DSMPs are developed based on the potential risks, complexity, size and nature of the study. As per NIH guidelines (<http://www.nlm.nih.gov/ep/dsm.html>) a DSMP typically includes plans for:
 - Monitoring the progress of trial and the safety of human research subjects (who is monitoring, what is monitored and at what frequency).
 - Description of the mechanism for reporting adverse events (AEs)/unanticipated problems (UPs) to the IRB, FDA and NIH. (What gets reported to whom and in what timeframe) <http://www.hhs.gov/ohrp/policy/advevtguid.html#Q1> (Also see pages 10-11 for additional links.)
 - Plans for assuring data accuracy and protocol compliance.

KEY CONSIDERATION: Individual IRBs may have specific reporting requirements.

It is important for research coordinators to understand that monitoring to ensure the safety of the human research subjects also includes ensuring the performance, collection and verification of adequate, accurate research data. Ultimately it is the sponsor's and/or the PI's responsibility that the collected data are accurate.

The study coordinator may assist with the following activities:

- Host monitoring visits
- Conduct monitoring activities, if applicable
- With PI, review monitoring reports with study team
- Below are process items to review when training on the DSMP:
 - Adherence to the Data & Safety Monitoring Plan
 - PI/Other Entity Monitoring Process (reports and logs filed in Regulatory Binder)
 - Critical Documents to Review
 - Adverse Event (AE) / Unanticipated Problems (UP) Identification
 - Assessment of Study Volunteer
 - Responsibility of Principal Investigator (PI) (assessment, review, tracking)
 - Responsibility of study team
 - Responsibility of the sponsor
 - Requirements per Protocol
 - Expected versus Unexpected
 - Serious AE versus non-serious AE
 - Reporting to IRB, Sponsor, Other
 - Suspected Adverse Reaction (SAR) / Serious Unexpected Suspected Adverse Reaction
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.32>

KEY CONSIDERATION: Safety monitoring document Information is often stored in the Regulatory Binder.

- Numerous resources are available to provide to the research coordinator when instructing on the concept of clinical research monitoring, including:
 - Guidance documents from OHRP
 - Guidance documents from FDA in regards to DSMPs, DSMBs (Data and Safety Monitoring Boards), and Reporting of AEs and Unanticipated Problems
 - Refer to the links below for a more complete list of resources
 - FDA and OHRP Regulations and ICH GCP:
45 CFR 46
21 CFR 312.32 *IND Safety reports*
21 CFR 812.50 (b) (1) *Unanticipated device effects reports*
ICH GCP 4.11 *Safety reporting*
ICH GCP 4.13 *Final reports*
ICH GCP 5.17 *Adverse Drug Reaction Reports*
ICH GCP 8.3.16, 8.3.17, 8.3.18 *Essential documents, AE reporting*
Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans. (Final rule; Federal Register /Vol. 75, No. 188 /Wednesday, September 29, 2010 /Rules and Regulations) http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2010_register&docid=fr29se10-3.pdf
 - FDA and OHRP Guidance and NIH Policies on Data and Safety Monitoring

OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, Jan. 15, 2007
<http://www.hhs.gov/ohrp/policy/advevntguid.html>

NIH Policy for Data and Safety Monitoring, June 10, 1998
<http://grants.nih.gov/grants/guide/notice-files/not98-084.html>

NIH Guidance on Reporting Adverse Events to Institutional Review Boards for NIH-Support Multicenter Clinical Trials, June 11, 1999 <http://grants1.nih.gov/grants/guide/notice-files/not99-107.html>

Further Guidance on Data and Safety Monitoring for Phase I and Phase II Trials, June 5, 2000
<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>

FDA Guidance for Clinical Trial Sponsors Establishment and Operation of Clinical Trial Data Monitoring Committees, March, 2006,
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127073.pdf>

FDA Draft Guidance for Industry Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring, August, 2011
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM269919.pdf>

FDA Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting to IRBs - Improving Human Subject Protection, Jan, 2009
<http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf>

FDA Draft Guidance for Industry and Investigators Safety Reporting Requirements for INDs and BA/BE Studies, September 2010
<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM227351.pdf>

US National Library of Medicine & other resource links: <http://www.nlm.nih.gov/ep/dsm.html>

FDA guidance documents which are updated periodically are available on the FDA web site at <http://www.fda.gov/RegulatoryInformation/Guidances/default.htm>

- **Study Closure Process:**

Study close-out refers to the post-study portion of research activities. Close-out cannot fully occur until the items bulleted below are satisfied. Close-out processes noted below include activities with the sponsor, IRB and other applicable regulatory agencies and may or may not produce publication.

- Data clarification completion (may involve sponsor)
- Investigational agent accountability (disposition), if applicable
- Final visit by sponsor, if applicable
- Data analysis, if applicable
- Final IRB notification
- Financial close-out
- Update www.clinicaltrials.gov, if applicable
- Research participant notification, if applicable
- File storage (record retention regulations must be followed)

- **Tools/Resources Available:**

- Glossaries
 - Research terminology
 - Acronyms
- Websites:
 - Federal & local regulations
 - Internal: policies, forms, templates, networking

Institutional Requirements:

Academic Health Institutions establish their own specific requirements, procedures and resources for conducting human subjects research. Research coordinators must be trained to requirements and may also benefit from becoming familiar with other related topics. Common principles are listed below. It is recommended to check with your institution to determine what training requirements are necessary for those in the role of research coordinator.

- Human Resources
- Coordinator Education & Networking opportunities
- Internal Policies Governing Research:
 - Electronic system access
 - Medical records Ex. reviewing and obtaining, disclosure
 - Human Subject Protection Ex. CITI training, NIH
 - HIPAA
 - Internal research policies
 - Travel
 - Educational benefits
 - Research staff roles
 - Monitor visits
 - Facility layout/tour
 - Shadowing
 - Information Technologies
- Overview of Research Requirements: Historical & Ethical Background and Good Clinical Practices - see page 1.

Job Specific Requirements:

Earlier in this training document, many items for which a coordinator should be familiar were listed. However, there are numerous other processes, skills and study management activities for which a coordinator may also be responsible. Items from the below list may be helpful in reviewing job specific requirements for coordinators.

- Institutional Processes
 - Clinical Trial Review / Sign-off steps
 - Departmental Review
 - Institutional Offices Review
 - Grants
 - Contracts
 - Conflict of Interests
 - Risk Assessment
 - IRB submission
 - Other Subcommittee reviews:
 - Pharmacy & Therapeutics
 - Medical Radiation Protection Committee
 - Surgical Pathology
- Essential Computer Skills
 - Microsoft Word
 - Microsoft Excel
 - Microsoft Access
- Protocol Management (study activities)
 - Pre-Study Start-Up Processes:
 - Site assessment and site initiation
 - Feasibility of protocol
 - Budgeting/billing

- Assessment/Development and negotiations
 - Development of in-study billing processes
- Financial disclosure
- Clinical study/trial agreements
 - Contracts
 - Indemnification
 - Intellectual property
 - Liability issues
- ClinicalTrials.gov management
- Informed Consent Development
 - Readability
 - Required elements
 - Available templates
 - Submission/approval & revision process
- Quality control checks
- Certificate of Confidentiality
- Institutional Review Board Process:
 - Submission
 - Study approval maintenance: events reporting processes, progress reports, amendments, closure.
- Recruitment methods and approval processes
 - Advertisements
 - Print
 - Radio
 - Online:
 - Websites/blogs/surveys: (i.e. ResearchMatch.org, You-Tube)
 - Social networking: Twitter, Facebook, Linked-in
 - Outreach Strategies
 - Metrics, capturing
- Recruitment and Retention
 - Billing compliance and resolution
- Monitor Visits to Sites: to host or to conduct
 - Roles of: PI, research staff
 - Schedule: PI, coordinator, research team, space
 - Preparation: study files
 - Policy review
 - Pre/onsite/Post responsibilities and processes:
 - Meetings with monitor, PI and study team
 - Report review
 - Monitor tracking log
- Case Report Forms:
 - Development
- Quality assurance (site specific and institutional)
- Concomitant Medications Documentation:
 - Start/stop date
 - Dosing
 - Diagnoses, etc.
 - Other treatments
- Clinical supplies management
- Laboratory Samples:
 - Tubes
 - Processing
 - Specimen handling
 - Patient education
 - Laboratory certification & lab references
- Shipping Biohazard materials:
 - Vendors

- Waste handling
 - Labeling
 - Safety precautions
 - Required training
 - Study product accountability:
 - Inventory
 - Site specific: use of Investigational Research Pharmacies
 - Randomization process
 - Dispensing process and log
 - Labeling
 - Restricted access by personnel
 - Patient compliance
 - Unblinding
 - Destruction/return at study close-out
 - Monitoring
 - Proper storage
 - Voice systems
 - Interactions with:
 - Sponsors and Clinical Research Associates (monitors)
 - Contract Research Organizations;
 - Mentor assigned to new coordinator, if applicable
- Audits: preparing for and/or facilitating audits
 - External
 - FDA
 - NIH
 - Sponsor
 - Internal
 - Institution
 - Self-Audit
 - Compliance/Noncompliance/Protocol Deviations
 - Fraud/Misconduct
 - Corrective and Preventive Action (CAPA)

Departmental Specific Requirements

As part of a department within an institution, coordinators might be given direction on the following items:

- Working Schedule (hours in office/clinic)
- Tour of research areas
- Mentor assigned to new coordinator, if applicable
- Time Management: Allocation of time for specific projects/processes
- Competency assessment using tools
- Standard Operating Procedures: Departmental and/or study specific