



Documentation:
Principle Investigator Oversight/Source Documentation

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Background

- ~2000 research studies involving human subjects ongoing at U or R
- U of R bears responsibility for compliance with DHHS and FDA regulations for all research activities that involve human subjects, includes funded and non-funded research, minimal risk and greater than minimal risk research.
- Federal Wide Assurance (FWA) contract with federal government that our institution agrees to apply the federal regulations and be guided by the principles of the Belmont report.


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Background

- FWA is only required for federally sponsored research
- U of R voluntarily chooses to extent the procedures and protections to all research conducted at the institution
- The RSRB review system is a requirement set forth in the assurance.
- All research conducted at the University is expected to follow Good Clinical (Research) Practices which really are the federal regulations.

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How can an assessment be made that an investigator has adequate oversight of a study?



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Documentation

Documentation

“All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) **that describe or record the methods, conduct/and or results, of a trial, the factors affecting a trial, and the actions taken.**”

International Conference on Harmonization (ICH) Guideline for Good Clinical Practice, Published in the Federal Register May 9, 1997




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A Research Study Tells a Story


Prologue	Study Initiation
Plot	Protocol
Characters	Subjects/Patients
Ending	Study Closeout
Epilogue	Tie up loose ends



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Your documentation tells the study of what happened during the study. So if a sponsor monitor/auditor, agency auditor, or an internal quality improvement team member comes to your site they can easily follow who did what, when, how and why.

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study team
Principle Investigator ^ (PI) Oversight

The PI is personally responsible for the conduct/oversight of the research project including the actions of personnel under his/her supervision.


- Delegation
- Training/Study Procedures
- Protocol Adherence and Oversight Throughout the Course of the Study
- Responsibilities Upon Completion of the Study

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Delegation

The PI can delegate responsibility to various members of the research team

- Co/sub-investigators
- Clinical Research Coordinators (CRC)
- Research Nurses
- Students, Grad Students, Research Assistants

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Delegation

- The PI can delegate study specific-tasks, but the level of responsibility must coincide with the education/training/experiences/capabilities of the team member.
- The responsibilities delegated should be documented.

Delegation/Documentation

Complete a Delegation of Authority form describing each team member's role in the research project:

- Name, Position or Title, Signature, Initials
- Dates of service on study (From: To:)
- What roles are assigned, e.g., make eligibility decisions, History/Physical Exams, obtain informed consent, administer questionnaires/surveys, review medical test results, evaluate adverse events
- Required Training /Dates
- PI sign-off on the form

SIGNATURE, TRAINING & DELEGATED RESPONSIBILITIES LOG

Investigator _____ Project _____ IRB # _____

NAME (print or type)	TITLE OR POSITION	Task* Codes	Signature	INITIALS	TRAINING DATE	DATES for work on study
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:
						From: To:

* = Make eligibility/determination decisions E = Evaluate adverse events (cases/serious) I = Pharmacology
 B = Obtain informed consent ** P = History & Physical Exam
 C = Label and dispense study drug G = Scheduling Study Visits
 D = Make data entries and corrections M = Maintain drug accountability records

**Note: If the protocol involves a drug, device or surgical procedure, the MD/Investigator must participate in the consent process and signed the consent document.

I confirm that this log accurately reflects the signatures, training and delegation of responsibilities during the research study.
 Principal Investigator _____ Date _____

Version 2/10/09

FDA has identified study tasks that have been delegated to individuals lacking appropriate qualifications in these specific areas:

- Screening evaluations, including obtaining medical histories and assessment of inclusion exclusion criteria
- Physical examinations
- Evaluation of adverse events
- Assessments of primary endpoints
- Obtaining informed consent

Training/Study Procedures

- The PI should insure that all persons assisting with the trial are adequately informed about the protocol, any investigational products, and their trial related duties and functions.
- The PI should ensure that adequate training be provided for all staff participating in the conduct of the study for any special training required, e.g., interview/testing techniques, device use, diary completion.

Training/Study Procedures/Documentation

The PI conducts a pre-study meeting with the study team to include:

- Providing a copy of the complete protocol and consent form(s)
- Review the consent process including the documentation of consent
- Review case report forms/data collection tools; when and how to use and how to make corrections
- Review randomization plan: drug, device accountability and storage
- Review screening and enrollment logs
- Review method for capturing, reviewing and reporting Adverse Events or unanticipated problems involving risks to subjects or others (UPIRISO)
- Prepare minutes of the meeting, who was present, what was discussed
- File the minutes in the study file

Protocol Adherence and Oversight Throughout the Course of the Study

The PI must maintain an effective working relationship with all team members to ensure they perform procedures as the protocol requires. Responsibilities to include:

- Maintain current IRB approval of the protocol, informed consent documents, and evaluation tools (surveys, questionnaires, advertisements)
- Submit IRB required continuing review reports
- Ensure any modifications to the protocol/consent form are submitted to the IRB for review and approval prior to their implementation
- Ensure that if any additional staff added to the study has obtained a Human Subject Protection number, an amendment with the name(s) of the additional staff has been submitted to the IRB, and the amendment approved before their involvement in the study

Protocol Adherence and Oversight Throughout the Course of the Study

- Ensure only the current IRB approved consent form containing the watermark stamp with the RSRB expiration date, printed out on department letterhead, is used
- Ensure that informed consent is obtained from all subjects, a copy is provided to the subject, and the original signed consent document is retained in the study records
- Ensure all study procedures are conducted per the IRB approved protocol.
- Review subject files for any protocol variations or deviations. Document any findings in the subjects study file and contact the IRB for guidance and instruction.
- Prepare a corrective actions plan(s) to avoid recurrence and place in study file
- Ensure that adequate, current, and accurate records of research data, subject outcomes, unanticipated and adverse events are maintained to permit an ongoing assessment of the risks and benefits of study participation

Protocol Adherence and Oversight Throughout the Course of the Study

- Review investigational product accountability on a regular basis. Compliance to study investigational product should be conducted at each subject study visit and deviations noted. If concomitant medication is provided, these records should be reviewed as well.
- Ensure conduct of Data Study Monitoring Plans (DSMP)/Data Study Monitoring Board (DSMB) meetings as required by the IRB approved protocol. Maintain minutes of meetings
- Maintain records of all communications with the sponsor and IRB (i.e., emails, letters, monitoring visits and log of telephone conversations)
- Periodically review the study file to ensure all required documents have been filed.

Protocol Adherence and Oversight Throughout the Course of the Study/Documentation

The PI holds regularly scheduled meetings through out the course of the study with the study team to discuss the progress of the study and study related issues.

- Prepare minutes of the meetings, who was present, what was discussed.

- File the minutes in the study file

Protocol Adherence and Oversight Throughout the Course of the Study/Documentation

Narrative notes should be generated for the subject’s study file to document:

- how the subject is tolerating the study procedures,
- any telephone calls or unscheduled contacts with the subjects,
- missed visits missed procedures/blood work or protocol deviations*, and
- adverse events or any unanticipated problems

**Note: Narrative notes to subjects’ study records or to the study file is acceptable. They do not take the place of corrective action plans to avoid recurrence of deviations from the approved protocol.*

PI Responsibilities Upon Completion of the Study

- Ensure all documentation is complete. Provide note to file explaining any omissions

- Complete final investigational product accountability and return or destroy per the sponsor’s requirements

- Prepare and submit a final study report per the sponsor’s requirements

PI Responsibilities Upon Completion of the Study

- Prepare and submit the IRB required final report
- Retain and store subject records per requirements of sponsor. If requirements unknown, contact the sponsor
- For non-sponsored research, check with the Office of Research and Project Administration (ORPA) for University document retention policy

Source Documentation

- Adequate and complete source documents are critical to any research study
- Source documents are required to confirm the subjects are adequately protected, the validity of the trial conduct, and the integrity of the data collected
- Source documents not only confirm the subjects are protected, they also serve as a source to protect the PI and his/her research staff

Source Documents

- Source documents are the original documents, data and records containing the first recording of information used as research data
- The purpose of source documents is to document the existence of the subject and substantiate the integrity of the data collected to include original documents related to the trail, to medical treatment and history of the subject

Source Documents

- In regulatory terms, the source documents along with case report forms, comprise what FDA regulations refer to as “case histories.”
- “an investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual ...in the investigation.”

Source Documents

- “ Case histories include the case report forms and supporting data, including for example, signed and dated consent forms, any medical records, for example progress notes of the physician, the individual’s hospital chart(s) and nurses notes.”
- Clinical and office charts, lab reports, patient diaries, questionnaires, surveys, data recorded from automated instruments, diagnostic reports (x-rays, EKGs), surgical reports

What Inspectors (Auditors) Assess Regarding Human Subject’s Records During Clinical Investigator/Site Inspection*

- Describe investigator’s source documents in terms of organization, condition, completeness, an legibility
- Determine whether there is adequate documentation to ensure all subjects were alive and available for the duration of their stated participation in the study
- Determine whether the records contain:
 - Observations, information, and data on the condition of the subject at the time of entry into the study and throughout participation
 - Identification of key personnel involved in collecting and analyzing data at the site

* FDA December 2008 Compliance Program Guidance 7348.811

What Inspectors (Auditors) Assess Regarding Human Subject's Records During Clinical Investigator/Site Inspection

- Determine whether:
 - The study subjects met eligibility requirements (inclusion/exclusion)
 - Protocol specific clinical laboratory testing (including EKGs, X-rays) was documented by laboratory records
 - All adverse events/unanticipated problems were documented and appropriately reported
 - All concomitant therapies and/or inter-current illnesses were documented and reported
- Determine whether the clinical investigator reported/documentated all dropouts and reasons to the sponsor

Data Collection Tools as Source Documents

Tools can be developed and completed to address study activities and can serve as source documents

- screening logs
- eligibility criteria checklists
- enrollment logs
- subject sign-in logs
- individualized subject visit schedules with study procedures; e.g., blood draws, PFTs, questionnaires,
- investigational product dispensing, and returns


* All subject-specific source documents should be labeled with subject ID and the date and should be signed and dated by persons completing the document.

Regulatory Binder/Files

- All investigators must maintain regulatory binders/files that contain vital study documentation.
- The files should be organized in such a manner that they can be easily retrieved and documents located, e.g., use of tabs with titles.
- The regulatory file should contain at a minimum the following items:

Regulatory Binder/Files

- Protocol
- Informed consent(s)
- Amendments
- Investigators' CV's, PI and sub-investigators
- Copies of professional licenses
- Training certificates e.g., HSPP, EPRP, IATA (shipping of hazardous material), HIPAA

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Regulatory Binder/Files

- All IRB approvals (protocol, amendments, advertisements) and correspondences, (letters, emails, phone logs)
- Sponsor/granting agency correspondence

- Delegation of Authority log

- Case report forms/data collection forms

- Monitoring log/reports

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Regulatory Binder/Files

- Signed consent forms
- Subject screening logs
- Subject enrollment logs
- Subject identification code
- Adverse/unexpected event reports
- Minutes from staff meetings
- Final study report to IRB/sponsor

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Regulatory Binder/Files

If applicable to the study design, the following may also apply:

- Investigator’s brochure
- Package insert for concomitant medications
- Form FDA 1572 or Investigator’s Agreement for devices
- Drug accountability documentation
- Laboratory certification and range of normal laboratory values

Regulatory Binder/Files

Central Research Site File

- Acceptable to establish for documentation that pertains to all studies conducted at the site
- Cross-reference note should be placed in the specific study regulatory binder noting where these documents are located.

For example, the central research site file may contain;

- Investigator/staff CVs/licenses training certificates
- Laboratory certifications and range of normal values
- Staff training records

QUESTIONS????

On Global email, in Directory

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