Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

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IRB Director

The PI & FS are Ultimately Responsible for All Aspects of Research

- Development of scientific investigation
- Implementation of study methods
- Supervision of all staff and procedures
- Collection, analysis and security of data
- Protection of rights and welfare of participants
- Adherence to federal guidelines, state and local laws
- Adherence to IRB and institutional policies and procedures
- Adherence to Good Clinical Practice guidelines

Additional Responsibilities of UVM Faculty Sponsors

- Provides active mentorship to the student during the conduct of the research
- Shares responsibility with the student/trainee researcher for the ethical conduct of the research
- Institutionally accountable for the study, ultimately responsible

General Responsibilities of Principal Investigators

Obtaining and documenting informed consent of subjects or subjects' legally authorized representatives prior to the subjects' participation in the research, unless these requirements have been waived by the IRB (45 CFR 46.116; 45 CFR 46.117);

Obtaining prior approval from the IRB for any modifications of the previously approved research, including modifications to the informed consent process and document, except those necessary to eliminate apparent immediate hazards to subjects (45 CFR 46.103(b)(4)); and

Ensuring progress reports and requests for continuing review are submitted to the IRB in accordance with the policies, procedures, and actions of the IRB as referenced in the institution's OHRP-approved Federal wide assurance (45 CFR 46.103(b)(4), 45 CFR 46.109(e), 45 CFR 46.115(a)(1)).

Additional Regulatory Requirements

Providing to the IRB prompt reports of any unanticipated problems involving risks to subjects or others 45 CFR 46.103(b)(5);

Providing to the IRB prompt reports of serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB (45 CFR 46.103(b)(5)); and

Keeping certain records as required by the HHS regulations for at least three years after completion of the study (45 CFR 46.115(b)).

ClinicalTrials.gov

The FDA requires registration for clinical trials defined as:

- For any trials of drugs and biologics: controlled clinical investigations, other than Phase I investigations, of a product subject to FDA regulation.
- For trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.

The ICMJE (International Committee of Medical Journal Editors) definition of a clinical trial includes:

- Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

The NIH defines a clinical trial as:

- A prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (drugs, treatments, devices, or new ways of using known drugs, treatments, or devices)

Potential Legal Consequences if PI's fail to Register or Submit Results

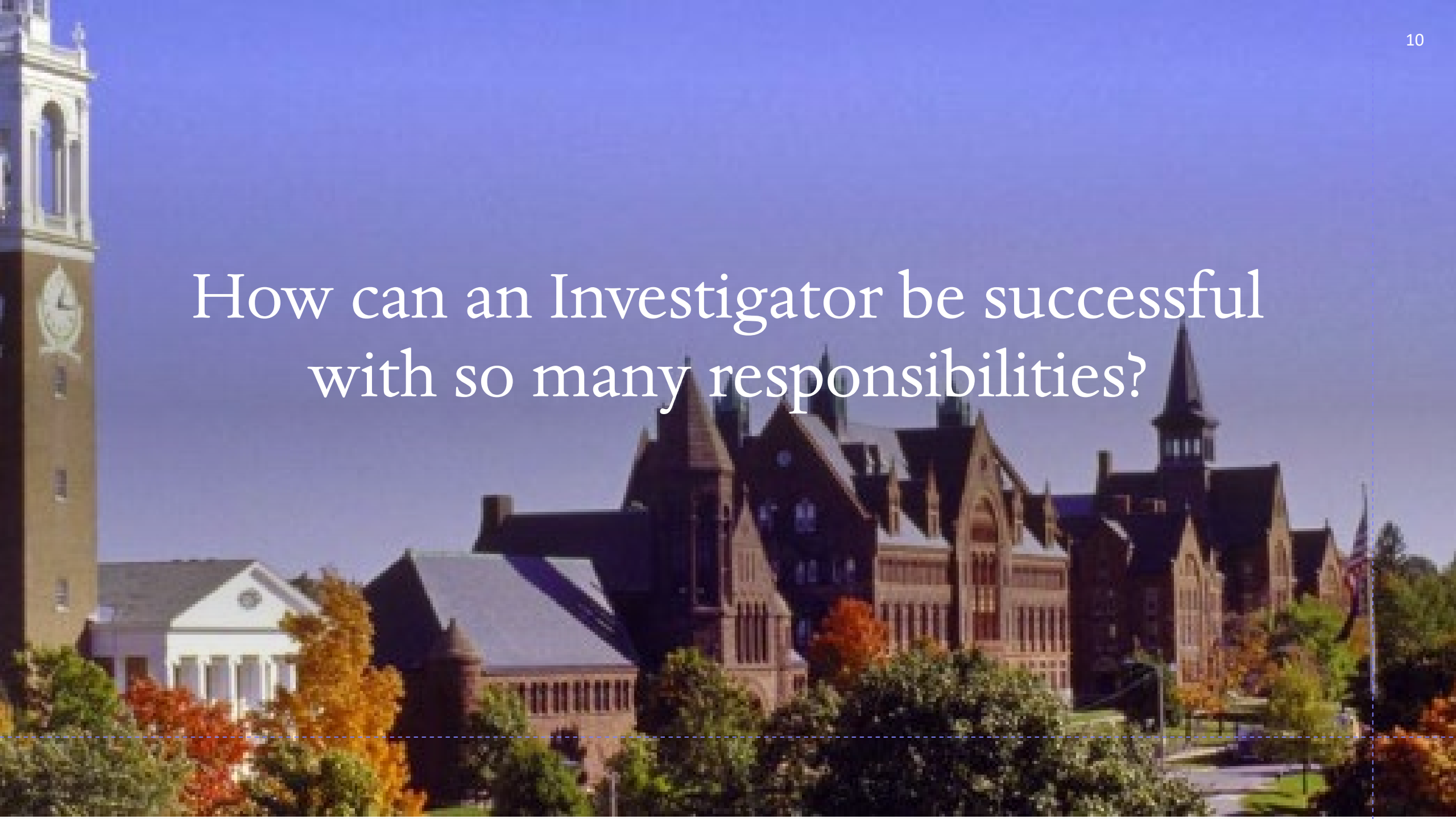
Civil monetary penalties against responsible parties who fail to comply with registration and/or results submission requirements.

Withholding of remaining or future federal grant funds from a grantee for failure to submit clinical trial registration and results information.

On July 22, 2022, the revised federal policies for ClinicalTrials.gov took effect, including new penalties for non-compliance. The financial penalty is significant ($13,237 per day of non-compliance), and existing and future NIH funding may be impacted.

Common Mistakes in PI/FS Supervision

- Poor training of staff
- Insufficient investigator involvement
- Poor communication with staff
- Inappropriate or lack of delegation of authority
- Lack of directed course of action for remediation



How can an Investigator be successful with so many responsibilities?

Considerations for PI's Planning to Conduct Human Subjects Research

Time: Does the investigator have adequate time to devote to study oversight and the work that he/she must perform?

Other Obligations: anticipated personal, financial, or professional obligations that might interfere with meeting the study commitments? New studies should not jeopardize ongoing protocols.

Funding: Is there adequate funding (budget appropriate), sufficient personnel and space for study procedures available to conduct the study?

Study Procedures: Does the research team have the ability and training needed to perform all required study procedures?

Are **facilities and equipment** adequate to perform the study?

Delegation of Authority Log

The study team may include but is not limited to the following members:

Sub-Investigator or Co-Investigator

Clinical Research Coordinator

Research Nurse

Other Research Staff as appropriate

FDA and Good Clinical Practice Guidelines call for investigators to ”maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.”

In delegating duties, the PI will ensure that those delegated will uphold their duties within the scope they are delegated.

Delegation of Authority Log

The University of Vermont
LARNER COLLEGE OF MEDICINE

Delegation of Authority Log

IRB Number: **Principal Investigator:**
Study Title:

The purpose of this form is to serve as the 'Delegation of Authority Log' and assure that the individuals performing study related tasks/procedures are appropriately trained and authorized by the Investigator to perform the task/procedure. This form should be completed prior to the initiation of any study-related tasks/procedures. The original form should be maintained at your site in the study regulatory/study binder. This form should be updated during the course of the study as needed.

Printed Name	Title	Responsibilities*	Signature	Initials	Start Date	PI Initials/Date	Stop Date

***Use code numbers provided below.**

Principal Investigator: _____ _____ _____
(Sign at study closure) **Printed Name** **Signature** **Date**

Responsibilities: (examples below, tailor to your specific protocol)		
1 – Informed Consent Discussion	5 – Study Drug Accountability	
2 – Informed Consent Signature	6 – Study Drug Dispensing	
3 – Eligibility Confirmation	7 – Case Report Form Completion	
4 – Physical Exam	8 – Regulatory Documents	

Types of duties that can be delegated

Obtaining informed consent from study participants

Preparing or dispensing investigational drugs or devices

Conducting clinical exams to evaluate response to the investigational drug

Collecting vital signs or documenting medical history

Assessing adverse events

Assessing eligibility criteria

Maintaining regulatory documents

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National Center for Complementary and Integrative Health

Tool Summary Sheet

Tool:	Delegation of Authority Log
Purpose:	To record all study staff members' significant study-related duties
Audience/User:	Principal investigators (PIs), study coordinators, other site staff, clinical monitor
Details:	This log should provide a comprehensive list of study staff members and the duties that have been delegated to them by the PI. It is required for both observational and interventional clinical research studies.
Best Practice Recommendations:	• List the names of study staff members and record the responsibilities that have been assigned to them using the boxes under the responsibilities header. • Revise the Responsibilities Header as needed to reflect study-specific needs, such as signing CRFs and reviewing/signing laboratory reports. • Each study staff member listed should initial and sign to indicate understanding of the responsibilities assigned. • The site PI should initial and date each line of the form as entries are recorded. The PI's signature at the bottom of each form is required at the conclusion of the study. • Update the log as needed following any change in site study personnel. • Number each page and maintain this log in the Essential Documents Binder, behind the Delegation of Authority Log tab. (Synonyms for this binder include Investigator Binder, Regulatory Binder, Investigator Site File [ISF], and Study File.) • Store pages in reverse chronological order, with the newest pages of the log placed at the front of the section. • At the conclusion of the study, identify the final page of the log by checking the box in the footer. • Remove this Tool Summary Sheet before use of the log.

Tool Revision History:

Version		
Number	**Date**	**Summary of Revisions Made:**
1.0	20Apr2012	First approved version
2.0	24Apr2013	Added Tool Summary Sheet

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Delegation of Authority Log

STUDY NAME

Site Number: ____________________

The purpose of this form is to: a) serve as the Delegation of Authority Log and b) ensure that the individuals performing study-related tasks/procedures are appropriately trained and authorized by the investigator to perform the tasks/procedures. This form should be completed prior to the initiation of any study-related tasks/procedures. The original form should be maintained at your site in the study regulatory/study binder. This form should be updated during the course of the study as needed.

Please Print	Obtain Informed Consent	Source Document Completion	Case Report Form (CRF) Completion	Assess Inclusion and Exclusion Criteria	Physical Examination	Medical History	Medication History / Concomitant Medication	Collect Vital Signs	Review Vital Signs and Labs for Clinical Significance	Laboratory Specimen Collection/Shipping	AE Inquiry and Reporting	AE/SAE Interpretation (severity/relationship to IP)	Administration of Investigational Product (IP)	IP Accountability	Regulatory Document Maintenance	Administrative	
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:
NAME:	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	OTHER (specify):
STUDY ROLE:	SIGNATURE:														INITIALS:		DATES OF STUDY INVOLVEMENT:

I certify that the above individuals are appropriately trained, have read the Protocol and pertinent sections of 21CFR 50 and 56 and ICH GCPs, and are authorized to perform the above study-related tasks/procedures. Although I have delegated significant trial-related duties, as the principal investigator, I still maintain full responsibility for this trial.

Investigator Signature: ____________________ **Date:** ____________________

Appropriate Delegation of Study-Related Tasks

The investigator should ensure staff:

Are qualified by education, training, and experience to perform the delegated task

In some cases, state licensing or hospital certification may be required. Sometimes a protocol may specify the qualifications of the individuals who are to perform certain protocol-required tasks.

Schedule time to review reports, decisions and documentation verifying actions taken for those duties

Make recurring meetings at the beginning of the study to review the study tasks

Are the delegation of protocol related tasks still current?

Tasks change over the life of the protocol, delegate new tasks as the study reaches new milestones

Are the staff delegated carrying out the duties appropriately?

Trust but verify

Inappropriate delegation of authority

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Delegation of Authority Log

IRB Number: STUDY 1234 **Principal Investigator:** John Smith, MD
Study Title: Randomized trial of a new osteoarthritis drug

The purpose of this form is to serve as the 'Delegation of Authority Log' and assure that the individuals performing study related tasks/procedures are appropriately trained and authorized by the Investigator to perform the task/procedure. This form should be completed prior to the initiation of any study-related tasks/procedures. The original form should be maintained at your site in the study regulatory/study binder. This form should be updated during the course of the study as needed.

Printed Name	Title	Responsibilities*	Signature	Initials	Start Date	PI Initials/Date	Stop Date
Mary Jones	Research nurse	1, 2, 3, 9			5/1/2024		
Kevin Kennedy	Data coordinator	7, 8, 6			5/1/2024		
Chris Lobel	4th year medical student	1, 2, 3			6/1/2024		8/25/2024
John Smith	Rheumatologist, PI	1 - 9			5/1/2024		

*Use code numbers provided below.

Principal Investigator: _____ _____ _____
(Sign at study closure) **Printed Name** **Signature** **Date**

Responsibilities: (examples below, tailor to your specific protocol)		
1 – Informed Consent Discussion	5 – Study Drug Accountability	9 – Assessing SAE's and UAP's
2 – Informed Consent Signature	6 – Study Drug Dispensing	
3 – Eligibility Confirmation	7 – Case Report Form Completion	
4 – Physical Exam	8 – Regulatory Documents	

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John Smith	Rheumatologist, PI	1 - 9			5/1/2024		

***Use code numbers provided below.**

Train the research team

- The investigator should ensure staff:
- Have read the protocol
- Have an adequate understanding of the specific details of the protocol and attributes of the investigational product needed to perform their assigned tasks
- Are aware of regulatory requirements and acceptable standards for the conduct of clinical trials and the protection of human subjects
- Are competent to perform or have been trained to perform the tasks they are delegated
- Are informed of any pertinent changes during the conduct of the trial and receive additional training as appropriate
- Document the trainings!!!!!!

Documenting Training

- ✓ Record minutes of meetings
- ✓ Print certificates of online completion for webinars, training modules etc.
- ✓ Use a training log - date of training, who was the trainer, topic, and trainee name and role
- ✓ Ensure the training log matches the tasks delegated on the DOA

TRAINING LOG Template *(Training Topic Specific)*

Training Log Template (Training Topic Specific)

Principal Investigator (PI): *add PI*	**Protocol Number:** *add protocol number,*
Training Topic: *(e.g. Protocol, Manual of Procedures, re-training on consenting procedures, include version number and date of the respective document covered during training.)*	
Date of Training: *add Date of Training (DD/MMM/YYYY)*	**Training Delivery Method:** *add training delivery method (Classroom/ Conference Call/ Face-to-Face, Virtual)*
Trainer Name and Role: *add trainer name and role*	**Trainer Signature and Date:** *add trainer signature and date*

Trainee´s Name	Trainee´s Role	Trainee´s Signature and Date
Add Trainee Name	*Add Trainee Role*	*Add Trainee Signature and Date*
Add Trainee Name	*Add Trainee Role*	*Add Trainee Signature and Date*
Delete/add rows as needed		

Standard Operating Procedures

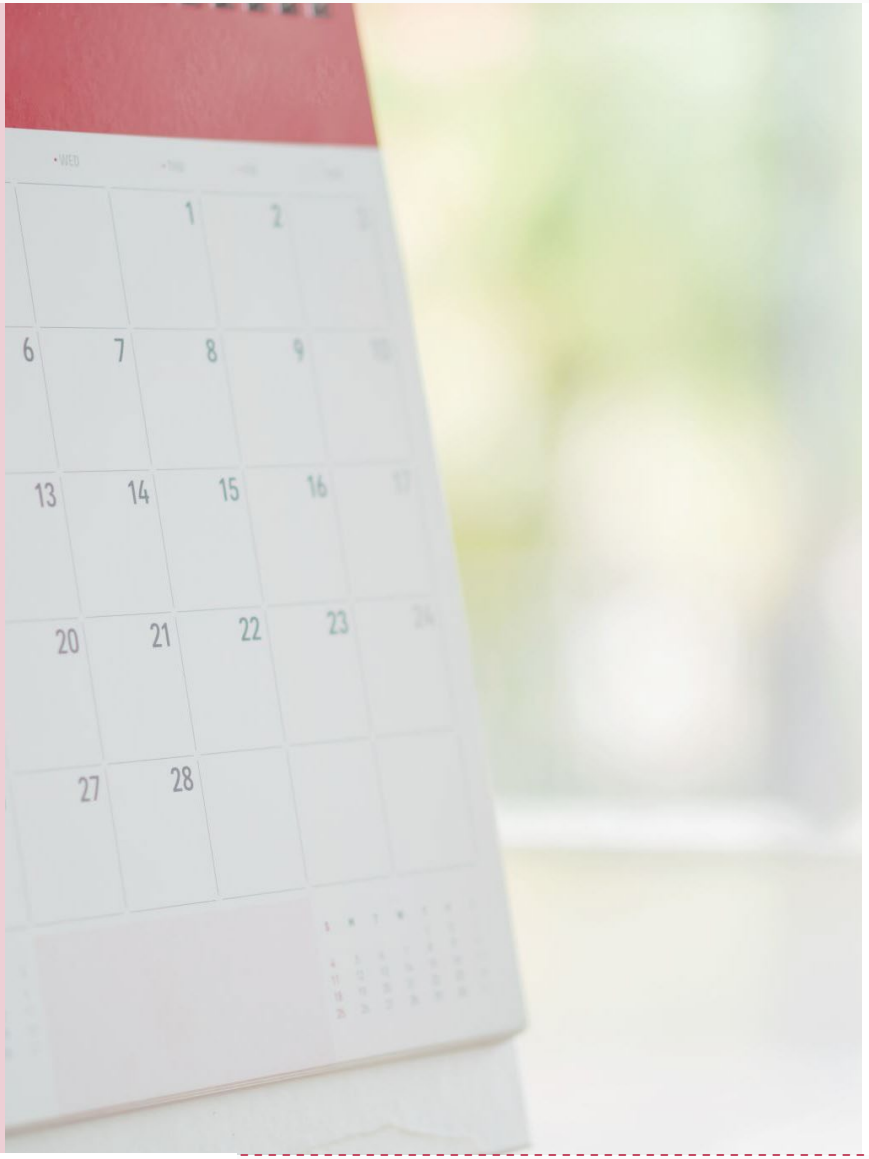
(ensures protocol compliance)

Written procedures, with detailed instructions to record routine daily operations, processes and practices followed within a research protocol.

The research team has uniformed guidance on a particular research procedure, identifying the responsible person for the procure, simple steps to carry out the procedure and contingencies if the SOP can not be followed.

Common SOP's in research: AE reporting, completion of case report forms, training, determining eligibility etc.

Routine Meetings with Staff



- Work closely with the research team throughout the research period
- Conduct regularly scheduled meetings with the study team to review research activities, discuss enrollment and safety and compliance issues, and other research-related topics
  - Determine milestones for the protocol and schedule meetings when the protocol is to enter a new phase (i.e., recruitment, change in procedures, closure to enrollment)
  - Has research staff been on vacation? Update team with current progress
- Capture meeting minutes and file them in the regulatory file

Ongoing Review of Research Data

Schedule time to review data during the course of the study.

Do not wait until the study is done enrolling and all research related interventions are complete.

1

Review data captured in questionnaires, assay reports, chart reviews, etc. to confirm the data is complete and captured/generated per protocol

2

Review eligibility documentation, are you enrolling your target population?

Does you study data reflect accurate inclusion/exclusion criteria?

3

Schedule time as needed with the designated research team member(s) to review data reports.

Follow-up on any discrepancies during the study

Keep the IRB up to date

Submitting required documentation to the IRB in a timely manner:

- Continuing Reviews
- Reportable New Information Reports
- Protocol Modifications

Review of *any changes* to previously approved research protocol is required by federal regulation [45 CFR 46.103(b)(4)] and is an essential element of the continuing review of research involving human subjects.

recruitment methods, consent form changes, treatment changes, modifications to the protocol, additions in study sites, investigators, or key personnel.

How does a PI protect the Rights, Safety, and Welfare of Study Subjects under their care during a clinical trial?

- Providing reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention
- Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, when specialized care is needed)
- Adhering to the protocol so that study subjects are not exposed to unreasonable risks
- 21 CFR 312.60 and 812.100

Failure to adhere to inclusion/exclusion criteria that are specifically intended to exclude subjects for whom the study drug or device poses unreasonable risks (e.g., enrolling a subject with decreased renal function in a trial in which decreased function is exclusionary because the drug may be nephrotoxic) may be considered failure to protect the rights, safety, and welfare of the enrolled subject.

***The PI is** responsible for ensuring all eligibility criteria is met or delegating this task to a study team member that has been trained by the PI to determine eligibility.*

Failure to perform safety assessments intended to detect drug toxicity within protocol-specified time frames (e.g., CBC blood draw for an oncology therapy that causes neutropenia) may be considered failure to protect the rights, safety, and welfare of the enrolled subject.

PI's are responsible for reviewing study procedures throughout the life of the protocol to reduce deviations and ensure the participants are not subjected to undue risk

Protocol Deviations that Present Unreasonable Risks

There are occasions when a failure to comply with the protocol may be considered a failure to protect the rights, safety, and welfare of subjects because the non-compliance exposes subjects to unreasonable risks.

Failure to adhere to inclusion/exclusion criteria that are specifically intended to exclude subjects for whom the study drug or device poses unreasonable risks (e.g., enrolling a subject with decreased renal function in a trial in which decreased function is exclusionary because the drug may be nephrotoxic) may be considered failure to protect the rights, safety, and welfare of the enrolled subject.

Failure to perform safety assessments intended to detect drug toxicity within protocol-specified time frames (e.g., CBC for an oncology therapy that causes neutropenia) may be considered failure to protect the rights, safety, and welfare of the enrolled subject.

Investigators can minimize such risks by adhering to the study protocol.

Federal & Local Regulations Outlining Responsibilities of Investigators

- DHHS: Office of Human Research Protections (OHRP): Investigator Responsibilities FAQs
- FDA: Statement of the Investigator Form FDA 1572 FAQ
- FDA: Guidance: Investigator Responsibilities - Protecting the Rights, Safety and Welfare of Study Subjects
- FDA: 21 CFR 312, Subpart D: General Responsibilities of Sponsors and Investigators: Drugs
- FDA: 21 CFR 812, Subpart E: Responsibilities of Investigators: Devices
- NIH Investigator Manual: Roles and Responsibilities of the Principal Investigator
- UVM IRB: Section 5.1 Responsibilities of Principal Investigators

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