UVM IRB Quality Assurance Monitoring Program

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Educational Session Goals

1. Purpose & Scope of Monitoring Program
2. Common QA Findings
3. Best Practice Examples
4. What the IRB will Review during the visit
5. PI QA Review Response
6. Quality Assurance Resources

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UVM IRB Quality Assurance Monitoring Program

Purpose: to be proactive in ensuring our institution is compliant with local UVM/UVMHN research requirements and federal regulations

Selection: The QA program covers a sampling of all IRB approved studies, both medical and behavioral, non-exempt and ceded studies.

Priority will be given to, but not limited to, the following:

- Investigator-initiated studies
- Studies where the investigator is new or inexperienced;
- Studies not regularly monitored by other entities such as federally and internally funded studies;
- Studies reviewed and approved by an external IRB
- Studies involving vulnerable populations

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Scope of the IRB QA Program

1. Enhancing the protection of human research participants

2. Improving the quality and data integrity derived from research studies

3. Serves as a training & educational opportunity for research teams as they conduct research.

Notification Process for an IRB Quality Assurance Visit

Prior to the QA review:

- Notification Email: The PI and the primary study contact will receive an email indicating that the study has been selected for QA monitoring
- The email will contain the date and time of the review, as well as instructions on what documents to provide to the QA team prior to and at the time of the meeting and what types of access should be granted to the QA team (i.e. EPIC, study EDC, REDCap, Sharepoint folder)

The day of the QA review:

- Introductory Meeting: The QA team will meet with the PI and designee(s) before the QA review (hear about the study, answer questions)
- QA Review: The QA team will review the study materials (regulatory binder, consent, eligibility checklists, training logs etc.)
- Exit Interview: The QA team will meet with the PI and designee(s) to provide an overview of the review and briefly discuss findings and action items requiring follow-up, if applicable

The QA Reviews Focus on (but are not limited to)

- Regulatory Binder and Essential Documents
- IRB approved protocol and study procedures were followed (all original source documents, such as completed surveys, lab reports, etc. will be reviewed)
- Informed Consent and Consent Process Documentation for each participant
- Eligibility Criteria are met and source documentation is available for each participant
- Research Data Management & Security Plan is being followed
- UVM IRB policies and procedures are being followed, including Reportable New Information
- EPIC research subject registration requirements are being followed (if applicable)

What the IRB Will Review

•All applicable sections in the protocol Regulatory Binder

•Current IRB approved protocol and all previously approved versions;

•Current IRB approved informed consent documents and all previously approved versions;

•All original signed informed consent documents;

•All continuing review IRB submissions;

•All IRB regulatory documents including, investigator's brochure, FDA 1572, etc. (if applicable);

•All modifications to the protocol, consent, study personnel and corresponding approvals;

•If applicable to the study, all FDA required documentation and correspondence;

•If applicable to the study, all sponsor required documentation and correspondence;

•All study correspondence with the IRB, coordinating centers, participants etc.;

•Documentation of all unanticipated problems involving risks to participants and others as well as IRB notification of such;

•Documentation of all study deviations ;

•Data Safety Monitoring Board (DSMB) reports as well as IRB notification of such;

•Investigator and research staff training logs if applicable; and

•Other applicable study logs (i.e. screening log, enrollment log, consent log, etc.).

•The signed informed consent documents, inclusive of, when applicable, parental consents, LAR consent documents, assents and HIPAA authorizations;

•Documentation of informed consent;

•Inclusion and exclusion criteria documentation;

•Source documentation and data collection forms; and

•EPIC research subject registration requirements are being followed (if applicable)

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External IRB Studies

UVM may conduct quality assurance monitoring in addition to, or in cooperation with, the External IRB

- The same notification, review, report, and PI response processes are followed
- The External IRB is notified of the QA visit in accordance with the Reliance Agreement

UVM will review:

- All relevant versions of External IRB-approved protocol and consent
  - These are not required to be maintained in Click. They will be requested in advance of the visit.
  - UVM will ensure the required local consent/HIPAA language is being used
- Regulatory determinations made by the External IRB (i.e. approval memos)
  - This may require access to the External IRB or Lead Site's regulatory submission platform
- The terms of the Reliance Agreement are being followed
- The study team is adhering to the policies and procedures of the External IRB

Common Consent QA Review Findings

- The wrong version of the consent form was used (or non-IRB stamped version)
- Person obtaining consent not approved on the Study Team page in UVMClick
- Pre-signing and dating of consent forms by PI/designee
- The consent form was not signed or dated by the study participant and/or PI/designee
- The consent was signed by PI, but the consent process was documented by designee
- Participant consent was obtained via a Non-IRB approved method (e.g., verbally over the phone)
- Additional consent form checkboxes are not completed, or initials are missing
- Non-IRB approved version uploaded to electronic consent platform
- Consent process documentation not completed or completed after consent signatures
- Not maintaining original, fully executed consent.

Common QA Review Findings

Eligibility

- Inclusion/exclusion criteria not documented (no corresponding source documents)
- Eligibility checklist not attributable to verifying and completing key personnel
- Study participant ineligible for the study

Missing Essential Documents in the Regulatory Binder (if applicable)

- Original documentation not retained (e.g., documents shredded after scanning)
- Deviation Log
- Documentation of Protocol and DMSP Training
- Screening/Enrollment Log
- Delegation of Duties Log
- Minutes of safety meetings/DSMB/training meetings
- CVs (signed and dated), and Licenses
- Communications and approvals from External IRB or Lead Site

Protocol Compliance

- Ensure your study has documentation that the IRB approved protocol and processes (consent process, recruitment plan, study visits, data security and management plan, etc.) were followed.
- Any deviation from the approved protocol is a protocol deviation and should be appropriately recorded and/or reported to the IRB.

"If it isn't documented, it didn't happen"

Study Participant Files

- Should be maintained so an independent person, with no knowledge of the study, can review each participant file and follow the entire study participation course without any input from the study team.
- Documentation starts with the consenting process and eligibility determination, and follows through each study visit and study communication.

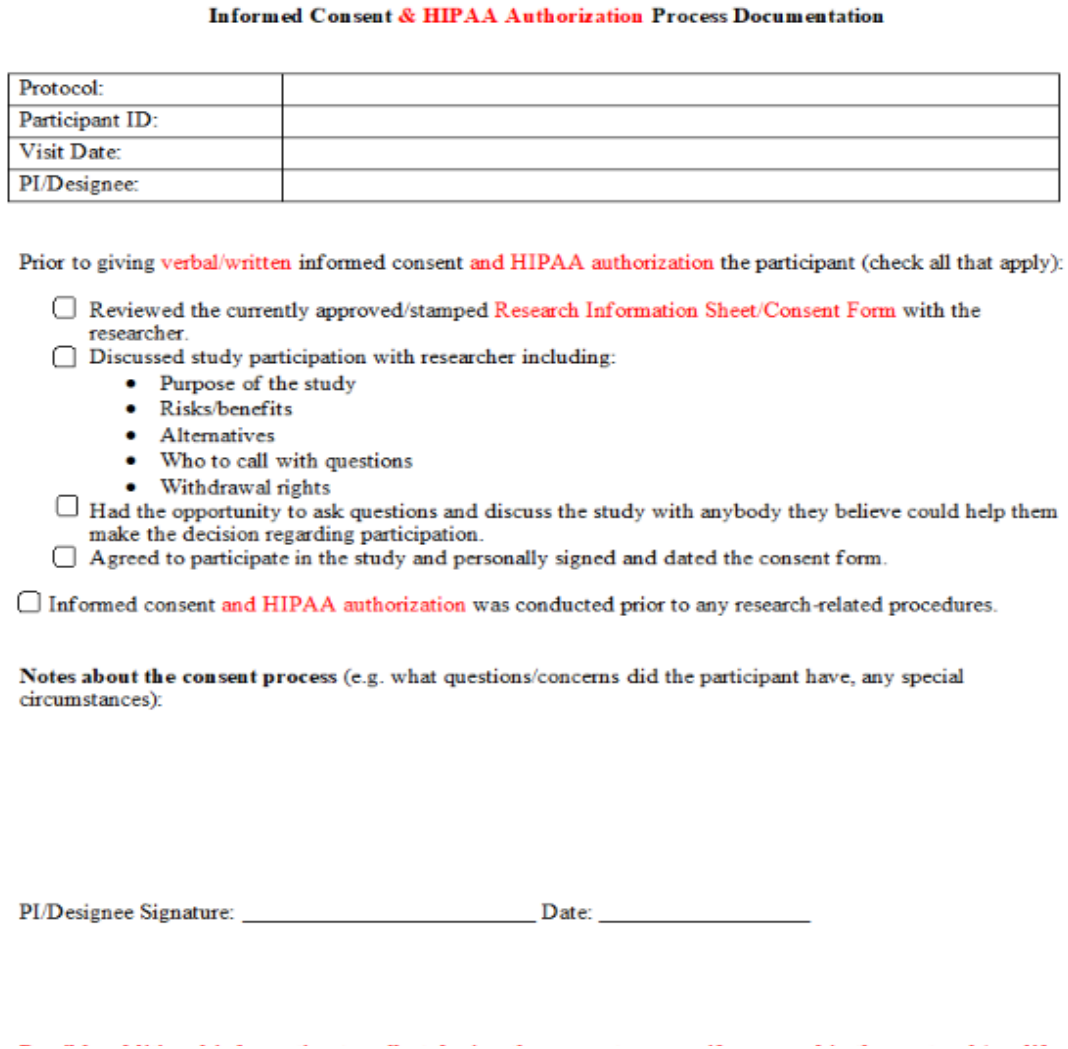
The Consent Process and Documentation

Consenting according to the IRB approved process:

- Appropriately delegated and trained member of the study's IRB approved key personnel

Consent Process Documentation:

- Two different templates can be found in the IRB Forms Library under Consent Process Documentation
- A separate form should be used if participants are reconsented
- Alternatively, consent process may be documented in EPIC



Informed Consent & HIPAA Authorization Process Documentation

Protocol:	
Participant ID:	
Visit Date:	
PI/Designee:	

Prior to giving verbal/written informed consent and HIPAA authorization the participant (check all that apply):

- ☐ Reviewed the currently approved/stamped Research Information Sheet/Consent Form with the researcher.
- ☐ Discussed study participation with researcher including:
  - Purpose of the study
  - Risks/benefits
  - Alternatives
  - Who to call with questions
  - Withdrawal rights
- ☐ Had the opportunity to ask questions and discuss the study with anybody they believe could help them make the decision regarding participation.
- ☐ Agreed to participate in the study and personally signed and dated the consent form.

☐ Informed consent and HIPAA authorization was conducted prior to any research-related procedures.

Notes about the consent process (e.g. what questions/concerns did the participant have, any special circumstances):

PI/Designee Signature: _____ Date: _____

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How Can Researchers Document the Consent Process?

Example of a note to the research file in EHR documenting the informed consent process:

03/30/2024 @ 3:30pm: Mrs. Jones was seen in GI clinic today. After reviewing her labs, she was found to meet all eligibility criteria for STUDY0000xxxx, Title. Reviewed the consent form; specifically explained the purpose of the study, risks and benefits, expected duration of participation, the number of visits per year, weekly diaries, confidentiality, right to withdraw at any time and emergency contact information. She was given time to review the consent form and asked questions prior to signing.

All questions were answered.

Mrs. Jones signed/dated the consent form and was given a copy for her records. She will begin research procedures on 04/05/2024. -Judith Smith, MD

Consent Process - Example

the investigator's professional judgment or actions in the performance of the study (e.g. the design, conduct, oversight, evaluation or reporting of the results of the study). Please discuss with the Investigator any questions you may have about this.

Contact Information
You may contact Dr. Smith the Investigator in charge of this study, at 802-656-5040 for more information about this study. If you have any questions about your rights as a participant in a research project or for more information on how to proceed should you believe that you have been injured as a result of your participation in this study you should contact the Director of the Research Protections Office at the University of Vermont at 802-656-5040.

Statement of Consent
You have been given and have read or have had read to you a summary of this research study. Should you have any further questions about the research, you may contact the person conducting the study at the address and telephone number given below. Your participation is voluntary, and you may refuse to participate or withdraw at any time without penalty or prejudice to your present and/or future care.

You agree to participate in this study, and you understand that you will receive a copy of this form.

Signature of Participant — Date: 9-16-2024

Allison Roberts
Name of Participant Printed

Signature of Principal Investigator or Designee — Date: 9-23-2024

John Smith
Name of Principal Investigator or Designee Printed

Name of Principal Investigator: Dr. J. Smith
Address: 1 South Prospect St, Burlington, VT 05401
Telephone Number: 802-656-5040

Informed Consent & HIPAA Authorization Process Documentation

Protocol:	STUDY00003333
Participant ID:	#0036
Visit Date:	Sept 16, 2024
PI/Designee:	John Smith

Prior to giving verbal/written informed consent and HIPAA authorization the participant (check all that apply):

- [x] Reviewed the currently approved/stamped Consent Form with the researcher.
- [x] Discussed study participation with researcher including:
  - Purpose of the study
  - Risks/benefits
  - Alternatives
  - Who to call with questions
  - Withdrawal rights
- [x] Had the opportunity to ask questions and discuss the study with anybody they believe could help them make the decision regarding participation.
- [x] Agreed to participate in the study and personally signed and dated the consent form.
- [x] Informed consent and HIPAA authorization was conducted prior to any research-related procedures.

Notes about the consent process (e.g. what questions/concerns did the participant have, any special circumstances):

PI had consent discussion with Participant by phone on 9-16-24. Answered all questions/concerns. Participant returned signed consent in addressed envelope to PI via US postal service. Received 9-23-24

PI/Designee Signature: J Smith Date: 9-23-2024

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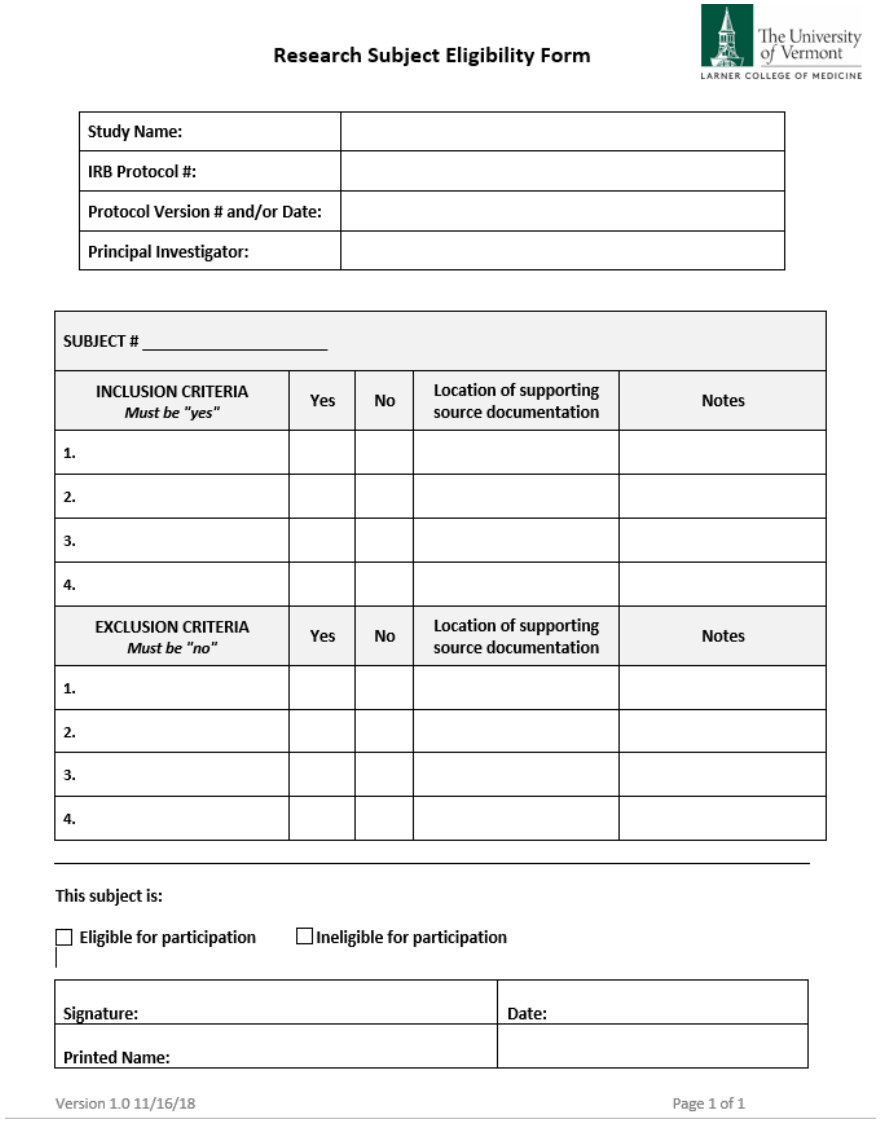
What Special Circumstances Require *More* Documentation

- ✓ Minor participant
- ✓ Legally Authorized Representative
- ✓ Participant physically unable to sign consent (i.e., bandaged hands, tremor, stroke)
- ✓ Participant not able to read a consent form (i.e., illiteracy, vision-impairment)
- ✓ Cognitively impaired
- ✓ Ward of the state
- ✓ Non-English speaking consent process
- ✓ Use of non-legal birth name
- ✓ Screen failure

Eligibility must be documented and confirmed for each research participant

The IRB recommends developing an inclusion/exclusion checklist to document all criteria were met.

- Ensure delegated key personnel sign and date the checklist
- A template can be found on the Commons website



Research Subject Eligibility Form

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Study Name:	
IRB Protocol #:	
Protocol Version # and/or Date:	
Principal Investigator:	

SUBJECT # _____

INCLUSION CRITERIA *Must be "yes"*	Yes	No	Location of supporting source documentation	Notes
1.				
2.				
3.				
4.				
EXCLUSION CRITERIA *Must be "no"*	**Yes**	**No**	**Location of supporting source documentation**	**Notes**
1.				
2.				
3.				
4.				

This subject is:

☐ Eligible for participation ☐ Ineligible for participation

Signature:	Date:
Printed Name:	

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Collection, Management, and Storage of Research Data

Source Documents:

All information in **original** records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.

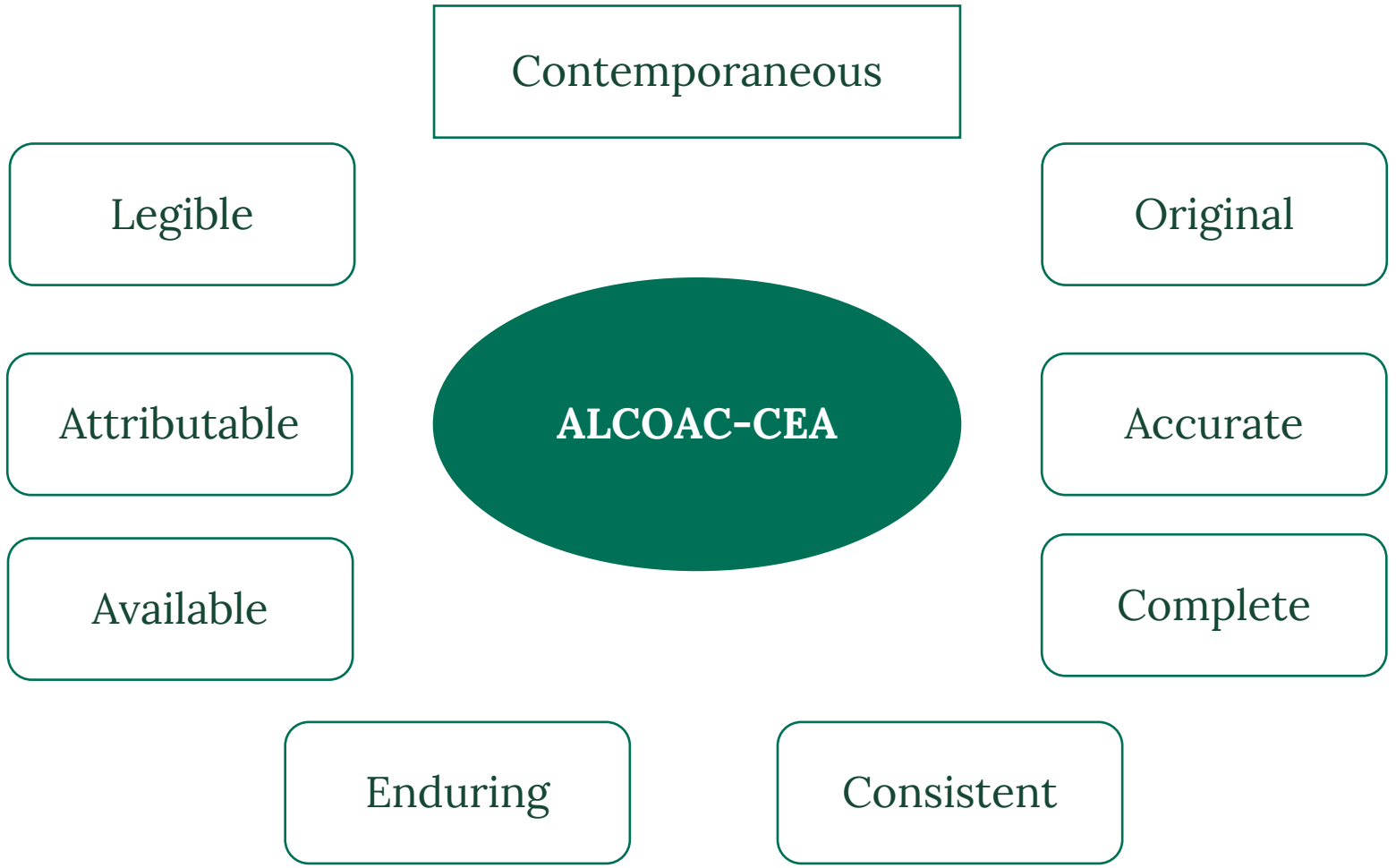
Note: All source material must be signed and dated by the person who documented the information (this includes electronic signatures)

Case Report Forms (CRFs):

A printed, optical, or electronic document designed to record all the protocol required information to be reported to the sponsor on each participant.

CRFs can be paper or electronic, for example: REDCap, RAVE, Excel

ALCOAC-CEA Principles



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ALCOAC-CEA Examples

Error	Do's	Don'ts
• Correction needed on the original source document or a case report form	• Cross out wrong information with a single line and initial and date the correction	• Scribble over the mistake • Use white out • Write over the original data to correct it • Destroy the originals
• Missing data located at a later date	• Incorporate the data into the research record with the current date and a Note to the file	• Ignore the missing data • Backdate or predate the information
• Eligibility checklist not attributable	• Fully sign and date (delegated/qualified study personnel) • Ensure all signatures are identifiable	• Not signed • Create source documents without signature lines

Essential Documents in a Regulatory Research Binder

- Federal and state regulations, institutional policy, and good clinical research practices require investigators to maintain essential documents related to human subject's research.
- These documents should be maintained so that an independent person, with no knowledge of the study, can review the regulatory binder (and participant files) and follow the life cycle of the study without input from the study team.
- If there are any gaps or errors, a note to file should be generated to explain the inconsistency.
- Documents may be maintained on paper or electronically

Regulatory Research Binder – Essential Documents

1. **Protocol**
2. **IRB Documents (both UVM and External IRB, if applicable)**
3. **Consent and HIPAA Authorization Forms**
4. **Consent Process Documentation**
5. **Key Personnel**
6. Correspondence with Reporting Agencies (FDA, NIH, DOD/OHRP, etc.)
7. Sponsor correspondence
8. Monitoring/DSMB reports
9. Product Information, progress reports and safety notices
10. Laboratory Documentation/ training and sample shipping
11. Drug/Device/Equipment Accountability
12. **Data Collection (CRF's)**
13. **Study Logs (Delegation, Training, Deviation, Compensation)**

Regulatory Binder – Delegation of Authority & Responsibilities Log

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Delegation of Authority Log

IRB Number: STUDY00001234 **Principal Investigator:** Dr. John Smith
Study Title: Blood Collection Study

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
John Smith	PI	1,2,3,4,5,6,7,8	JS	JS	8/1/23	JS 8/1/23	
Jane Doe	Sub-I	1,2,3,4,7	Jane Doe	JD	8/1/23	JS 8/1/23	
Mary Brown	Coordinator	1,2,7,8	Mary Brown	MB	9/15/23	JS 9/15/23	

*Use code numbers provided below.

Principal Investigator: (Sign at study closure) John Smith (Printed Name) | JS (Signature) | 8/1/23 (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	

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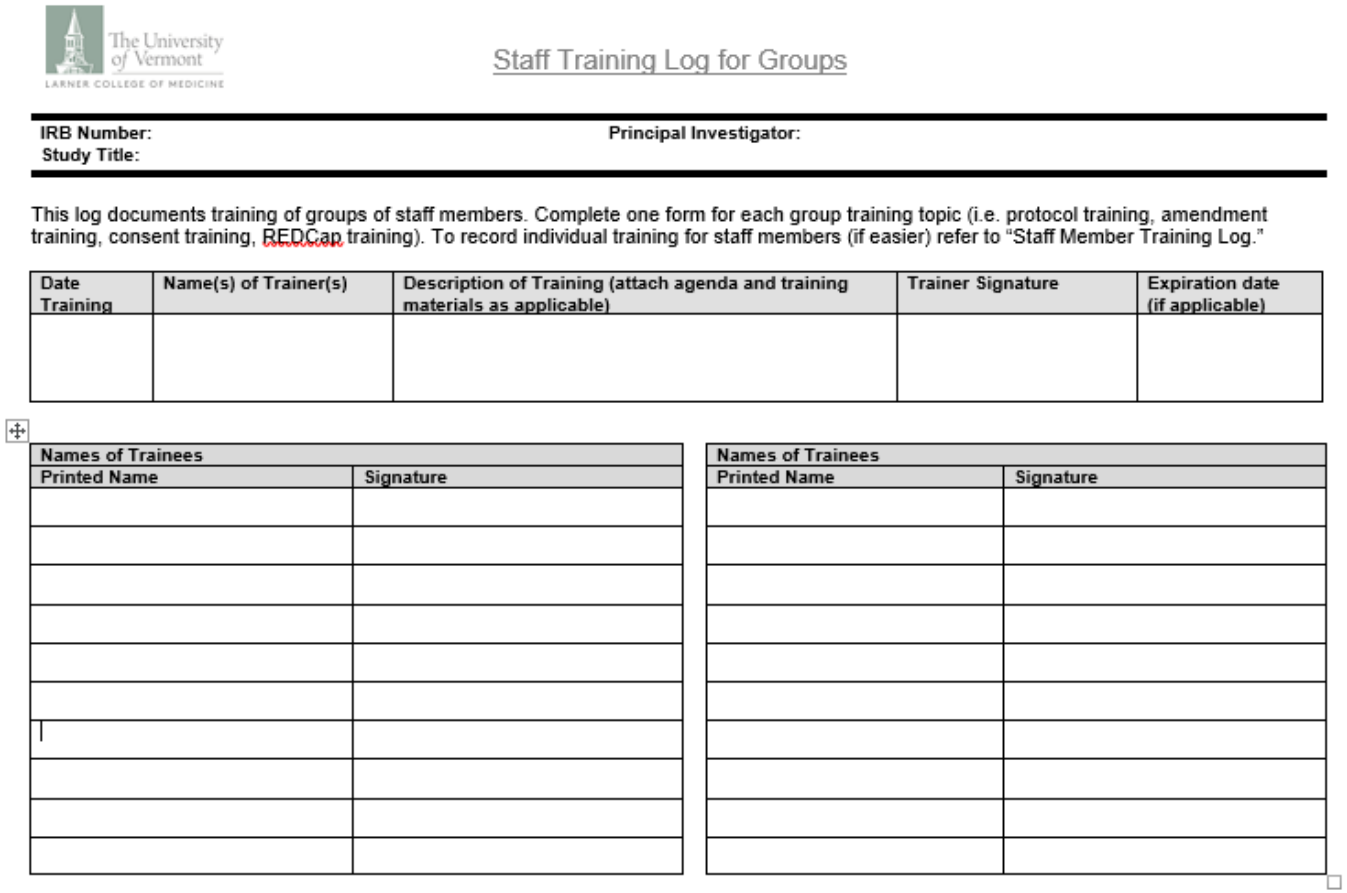
A template can be found on Commons

Regulatory Binder – Training

- Key Personnel Training Log
- Initial Protocol
- DMSP
- Protocol/Study modification
- Study specific procedure (EKG, blood draws, vitals etc.)

A template can be found on Commons



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Staff Training Log for Groups

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

This log documents training of groups of staff members. Complete one form for each group training topic (i.e. protocol training, amendment training, consent training, REDCap training). To record individual training for staff members (if easier) refer to "Staff Member Training Log."

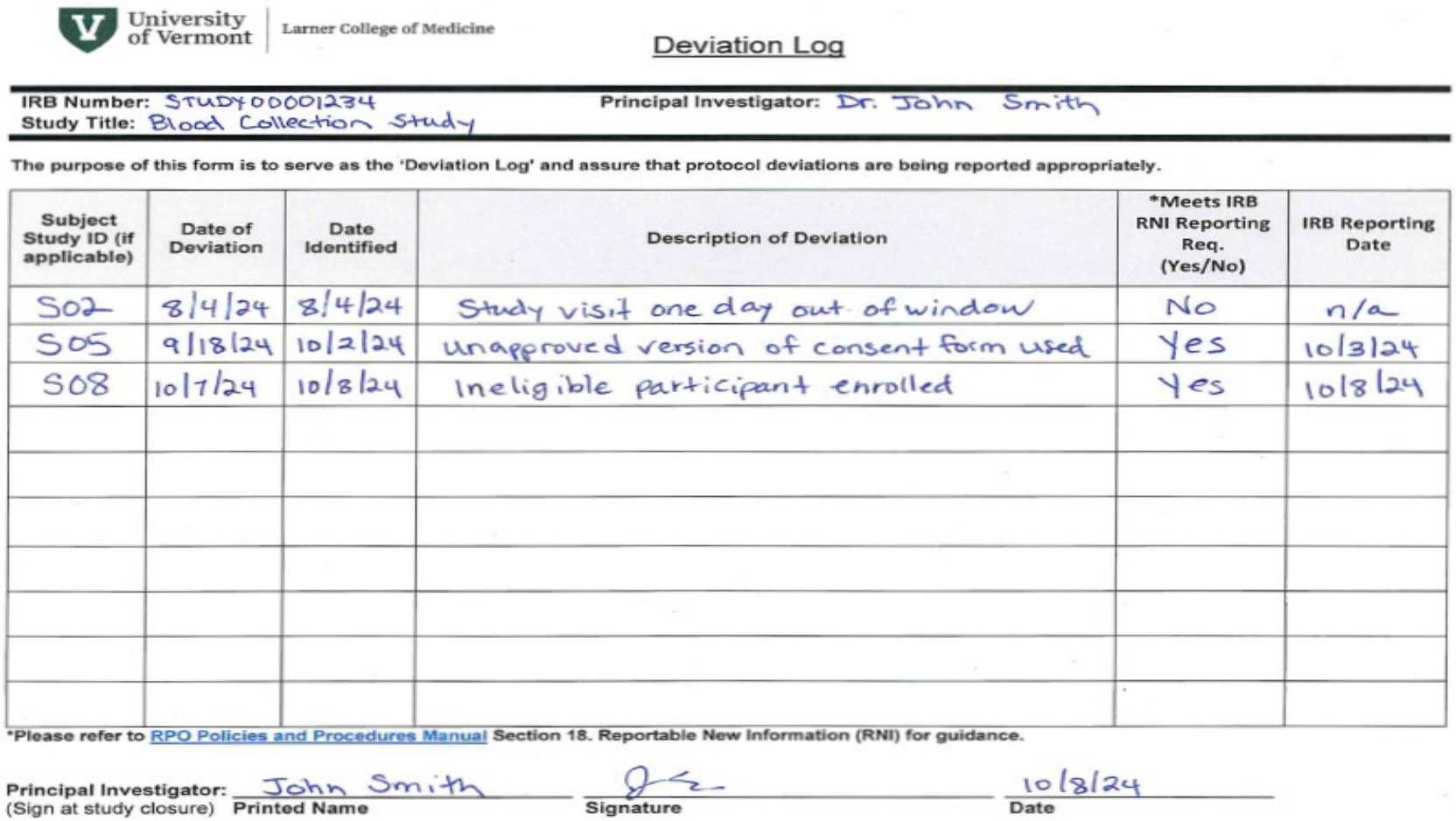
Date Training	Name(s) of Trainer(s)	Description of Training (attach agenda and training materials as applicable)	Trainer Signature	Expiration date (if applicable)

Names of Trainees	
Printed Name	Signature

Names of Trainees	
Printed Name	Signature

Regulatory Binder – Deviation Log

- All protocol deviations must be recorded
- Reporting requirements may differ between the UVM IRB and the External IRB
- Templates for both logs can be found on Commons



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Deviation Log

IRB Number: STUDY00001234 Principal Investigator: Dr. John Smith
Study Title: Blood Collection Study

The purpose of this form is to serve as the 'Deviation Log' and assure that protocol deviations are being reported appropriately.

Subject Study ID (if applicable)	Date of Deviation	Date Identified	Description of Deviation	*Meets IRB RNI Reporting Req. (Yes/No)	IRB Reporting Date
S02	8/4/24	8/4/24	Study visit one day out of window	No	n/a
S05	9/18/24	10/2/24	Unapproved version of consent form used	Yes	10/3/24
S08	10/7/24	10/8/24	Ineligible participant enrolled	Yes	10/8/24

*Please refer to RPO Policies and Procedures Manual Section 18. Reportable New Information (RNI) for guidance.

Principal Investigator: John Smith (Sign at study closure) Printed Name | Signature | 10/8/24 Date

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Quality Assurance Review Outcomes

Within 10 business days of the QA review the PI will receive a written report via email from the team detailing the findings and specific action items, if any, and determine one of the following outcomes:

- Acceptable; No further action required
- Acceptable; Additional action required by Investigator
- Further Committee review required

PI Response to the QA Report

The study team will be expected to respond to the IRB with corrective actions, protocol modifications and other clarifications.

Responses should be in a point-by-point response and may need to include a Corrective and Preventative Action Plan (CAPA) for specific action items in the QA report.

Elements of your CAPA, as applicable:

- Description/narrative of the problem
- Number of participants affected/harmed or potentially affected/harmed
- The root and contributing causes for each finding
- Include how root cause was determined
- Corrective actions and preventive actions taken or to be taken
- Include description of new or changed processes and/or SOPs
- Describe plan for training
- Describe plan for evaluating the effectiveness

Reference a past RPN Workshop "Developing Effective Corrective and Preventative Action Plans (CAPAs)"

Example QA Response

Action Item:

Subject 03 signed and dated the consent form the day before the PI signed and dated the consent form. The day the subject signed the consent form they participated in study procedures. Per the protocol, consenting will be conducted in person by the PI prior to the start of any study events (Deviation).

Response:

It was discovered that the PI wrote the wrong date on the consent form. This was confirmed by the subject's electronic medical record documentation of their clinic visit (see attached) which was on the same date the subject signed the consent form.

Corrective Action:

A Note to File was written describing this error and was signed by the PI and placed in the subject file with their consent form. In the future, all consent fields will be double checked by another member of the study team to ensure the consent form was properly executed.

Example - Note to File

Date:
IRB #:
PI:
To: Participant Files
From:
RE: Consent

The PI misdated the informed consent form for subject 03. It was confirmed with the PI that the informed consent process was conducted in person per the protocol and on the date that the subject signed the consent form. Subject 03 had a clinic visit on the same date that they signed consent, confirming they were present in person the day they signed consent (see attached documentation of clinic visit). This deviation has been reported to the IRB as an RNI.

PI Signature

Dated by the PI

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GENERAL INSTRUCTIONS – delete this box from the completed form

A Note-to-File should:

- Explain clearly the reason for the error/omission/discrepancy or process/policy it aims to address.
- Be generated on a case-by-case basis, or used to describe multiple of the same error/omission/discrepancy or process/policy.
- Include the protocol number and participant ID number(s) it refers to, as applicable.
- Be signed and dated by the individual who prepared it.
- Include any corrective action and/or follow-up action taken.
- Be filed with the regulatory document, participant file, or in the study binder tab to which it applies.

Red text represents instructions to you – to be deleted from the final version.

Note to File

Date:

IRB #:

PI:

To: Select one: Regulatory Files / Participant Files

From: Person preparing note

RE:

Description:

- Include information about an issue, cause of the issue, and corrective actions taken to prevent issue from occurring again
- Explain alternative location that files may be stored
- Clarify a policy or process

Signature

Date

Example - Response to Action Items

Subjects 2, 4, and 6 were found to have completed their final study questionnaire outside of the study protocol's approved timeline of 2 weeks after the final study visit. Please review all other subject files to check for, and note, any other study timeline deviations. Please provide a plan to increase compliance around this questionnaire.

- This deviation was noted on the study's deviation log.
- A thorough review of all other subject files (1-20) revealed that subjects 10 and 15 had also completed the final study questionnaire outside of the approved 2-week window. These deviations were also noted on the deviation log.
- Moving forward, subjects will be reminded to complete the final study questionnaire within the 2-week window and if they return the questionnaire outside of this window, the deviation will be noted on the deviation log in real time.
- We have amended the protocol (MOD#) to increase the window since there was no scientific reason for the 2-week timeframe.
- We have amended the protocol (MOD#) to allow for the questionnaire to be filled out electronically or verbally over the phone.

Example – PI Response to the IRB

QA Response, and all supporting documentation should be submitted to the UVM IRB as a single RNI and include:

- The original QA report
- Study Team point by point Response (Corrective and Preventive Action Plan)
- All protocol deviations outlined in the QA review, and any additional deviations discovered in your review of the remaining study participant charts (deviation log)
- Supporting corrected documents (e.g., Notes to File, updated logs)
- Communication with the External IRB about the findings (if applicable)
- If a study Modification (or Update Study Details) is required, this should be submitted concurrently in UVMClick.

The IRB via the safety subcommittee, may have additional action items following their review of the RNI.

Resources to Assist with Research Compliance

Research Protections Office

Melanie Locher
Director of IRB
Melanie.locher@uvm.edu

Jen Dulin
IRB Reliance Administrator (for External IRB studies)
Jen.Dulin@uvm.edu

Contact your IRB Regulatory Analyst

UVM IRB Policies and Procedures Manual

UVM IRB Quality Assurance Policy

Office of Clinical Trials Research

Kim Luebbers
Assistant Dean for Clinical Research (LCOM)
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Research Navigator
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OCTR Commons Site

UVM Health Network

Compliance and Privacy Department

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