# Clinical Trials Guidebook

**Purpose**

Clinical trials are the leading catalyst for advancing science and medicine. Emory is a leader in sound ethical research that will benefit local, national, and international communities. Compliance with federal regulations, federal guidance, state and local laws, and ethical principles is essential for ensuring protection for human participants participating in clinical trials and high quality, reliable research data. Clinical trials must be managed in an organized way where data can be verified for accuracy. Federal agencies such as the United States Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) have issued guidance to assist researchers. Although compliance with federal guidance is not required by federal agencies, guidance is usually an agency's interpretation of the best way to meet the regulations.

Good Clinical Practice (GCP) is an international quality standard that is provided by the International Conference on Harmonization (ICH). The ICH brings together regulatory authorities and pharmaceutical industries from around the world to discuss scientific and technical aspects of drug registration and approval. While some countries have adopted GCP as regulation, the FDA has adopted it as guidance. Emory has not formally adopted all organizational components of GCP; however, GCP is much of an Industry standard and some pharmaceutical or device companies require compliance with GCP in clinical trials conducted at Emory. Sponsors may require GCP standards as outlined in the clinical trial agreement, clinical protocol, or other written sponsor materials.

The FDA GCP guidance incorporates the best practices for meeting the requirements of the federal regulations and will help the Investigator optimize compliance with the regulations. **The purpose of this Clinical Trials Guidebook is to pull together some of the requirements of federal regulations, federal guidance, state and local laws, and Emory policies and translate them into practical instructions that are applicable to clinical trials at Emory.**

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## 1 Study Start Up

### Materials

The sponsor of the trial will provide the relevant study materials to the Emory investigator (e.g., the investigator's brochure, protocol, financial disclosure statements, and clinical trial agreement). When the trial is investigator-initiated, the Emory investigator will need to obtain the written information on the drug/device and is responsible for the development of the written protocol and informed consent forms.

The investigator must develop the informed consent form by using the Informed Consent Template on the Emory IRB website. This template contains required language and the IRB stamp placeholder. If the sponsor provides the investigator with a sample informed consent form, the investigator will need to incorporate the required Emory language and IRB stamp placeholder from the IRB Informed Consent Template.

### Required Approvals at Emory

There may be multiple approvals required for your clinical trial. Please see Appendix 1 at the end of this guidebook to determine which committee approvals are necessary for your clinical trial.

### Study Start Up Checklist

☐ 1. Obtain study material from sponsor; if investigator-initiated, obtain written material on the drug/device and develop the written protocol and informed consent form utilizing the templates on the Emory IRB website (https://www.irb.emory.edu/forms/protocol-templates.html and https://www.irb.emory.edu/forms/consent/index.html)
***Note!*** *If the sponsor requires you to sign a confidentiality disclosure agreement (CDA) prior to sending you the study material, submit the CDA to the Office of Sponsored Programs for approval before signing it.*

☐ 2. Identify study personnel

☐ 3. Decide which Emory approvals you need to obtain (see CTAC Guidebook Appendix 1) and complete applications

- ☐ IRB submission via eIRB for Emory IRB
  - Visit Emory IRB's Getting Started Webpage (https://www.irb.emory.edu/guidance/getting-started/study-submission.html)
  - If you plan for Emory IRB to serve as the IRB of record for a multisite study or Emory to rely on another institution's IRB or commercial IRB, visit the Emory IRB Collaborative Research page (https://www.irb.emory.edu/guidance/research-types/collaborative.html)

- ☐ OCR submission via Clinical Research eForm (https://ocr.emory.edu/resources/systems/ocr-cr-eform-app.html) for studies with billable items and services from Emory Healthcare or Grady
- ☐ OSP submission via EPEX for federal and foundation grants
- ☐ OTT submission for industry-sponsored research (https://ott.emory.edu/resources/forms.html)
- ☐ ORIC submission for sponsor-investigator studies
- ☐ COI submission via eDisclose (https://ediscloseemory.huronresearchsuite.com/)
- ☐ Radiation safety, if applicable
- ☐ Biosafety, if applicable
- ☐ IDS submission, if applicable. If studies are already routed through OCR, OCR will initiate the contact to IDS.
- ☐ Emory Healthcare Office of Quality Checklist
- ☐ Clinical Research Key Points Summary
- ☐ Request for Sensitive Study Status Worksheet, if applicable
- ☐ Grady Office of Grant Administration. Seek financial clearance for all studies using Grady as a site.
- ☐ clinicatrials.gov

***Note!*** *If changes to protocol or other study materials occur during IRB submission and before approval, submit the revised documentation to OCR and OSP as well to eliminate delay to approval.*

☐ 4. After IRB approval seek the following approvals, if applicable

- ☐ GROC (Grady Research Oversight Committee)
- ☐ VA R&D (Veterans Affairs Research Development Committee)
- ☐ Emory St. Joseph's or Johns Creek approval
- ☐ Children's Healthcare of Atlanta IRB Authorization Acknowledgement Form

☐ 5. Ensure proper institutional credentialing and training of study personnel (see CTAC Guidebook Chapter 2)

☐ 6. Document study-specific protocol, reporting, and EDC training for each study team member

☐ 7. Complete the Form FDA 1572 (drug studies) or Investigator Agreement (device studies), if applicable

☐ 8. Develop or complete the Delegation of Authority (DOA) log with specific study tasks delegated from the PI

**When to Apply to the Departments Listed Above**

For the quickest time to approval, researchers may apply to multiple departments simultaneously. Apply to the following offices as soon as the required materials become available:

| | |
|---|---|
| COI: | Complete eDisclose after you submit the eIRB application |
| IRB: | Submit eIRB application when the following become available: written protocol, draft informed consent form, drug/device information, and recruitment materials. |
| OCR: | Email materials to OCR when the following become available: written protocol, draft informed consent form, contract, and draft budget. |
| OSP: | For federal and/or foundation grants, submit proposal in Emory Proposal Express (EPEX) when the grant is available. |
| OTT: | For industry-sponsored research, submit when contract becomes available |

**References**

*Emory IRB Policies and Procedures (https://www.irb.emory.edu/guidance/index.html); Emory University Policies and Procedure; HIPAA Security Policy; FDA Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs: Frequently Asked Questions—Statement of Investigator (Form FDA 1572)*

## 2 Emory Training Requirements

**Required Training and/or Certification for Researchers at Emory**

*Choose the training below that is appropriate for your clinical trial. All applicable requirements must be met prior to starting the research. See Emory Training Tracking Sheet in Appendix 2 of this Guidebook.*

New Hire Checklist (https://www.ocr.emory.edu/resources/training/courses.html)

**Training**

1. Clinical Research Orientation for new Emory hires, rehires, and those new to a clinical research coordinator, nurse or project manager role (https://www.ocr.emory.edu/resources/training/courses.html)

2. CITI Certification, Biomedical Focus and Good Clinical Practice modules (www.citiprogram.org)

    a. Create an account and affiliate yourself with Emory, CHOA, or VA

    b. Obtain prior to IRB initial submission

    c. Biomedical must be maintained every 3 years

3. Basic Life Support with Cardiopulmonary Resuscitation (CPR) for Emory University Research Staff who need it for credentialing (https://www.ocr.emory.edu/resources/training/courses.html)

4. Bloodborne Pathogens for Research for researchers handling or anticipate exposure to human cells, cell lines, blood, tissues, cell cultures, Hepatitis B, Hepatitis C, or HIV. (https://www.ehso.emory.edu/guidance/programs/research-safety.html

5. Research Compliance and Regulatory Affairs HIPAA Security and Research training (http://compliance.emory.edu/hipaa/HIPAA-training.html)

6. Responsible Conduct of Research (RCR), for some study teams conducting NIH or NSF-funded clinical trials that are required by the contract to obtain RCR training (https://rcra.emory.edu/oric/responsible-conduct.html)

7. International Air Transportation Association (IATA) training, for study team members who will package or ship "dangerous goods." Dangerous goods are articles or substances which are capable of posing a risk to health, safety, property or the environment (e.g., infectious substances, diagnostic specimens, genetically modified microorganisms and dry ice). www.ehso.emory.edu

8. VA Research Training, for study teams using the Atlanta VA Medical Center as a site. Information on training requirements can be found on the Atlanta Research and Education Foundation website at www.atlaref.org

9. Documented study-specific training (e.g., protocol, sponsor's requirements) for each study

a. Sponsors may provide a training log, or you can use this template

**Optional Training at Emory**

1. Certification of Research Administration at Emory http://www.osp.emory.edu/trainingtools/certification/index.html
2. eIRB training (http://www.irb.emory.edu/eirb/index.html)
3. Emory Research A to Z (ERAZ) (http://ora.emory.edu/eraz/index.html )
4. Oncore, Emory's Clinical Trials Management System (CTMS) (https://www.ocr.emory.edu/resources/training/courses.html )
5. EPEX training (https://hr.emory.edu/eu/learning/index.html). Click on ELMS log in tab on front page.). After completing the on-line or in-person class, request access to EPEX by completing the EPEX Access form on the OSP website.
6. Export Control (https://rcra.emory.edu/oric/index.html)
7. Office for Clinical Research's Research Matters https://ocr.emory.edu/resources/training/research-matters.html)
8. 6-week, small group training series with CTAC of topics of your choice (request to ctcompliance@emory.edu)
9. Emory IRB webinars (https://www.irb.emory.edu/resources/training/webinars.html)

**References**

*Emory IRB Policies and Procedures, Emory University Policies and Procedures, and HIPAA Security Policy*

## 3 Essential Documentation

Clinical trial documents are referred to as "essential documents" in GCP. These documents demonstrate the compliance of the investigator, sponsor and monitor with the standards of GCP and with other applicable regulatory requirements. Essential documents should be organized in a paper or electronic binder, commonly referred to as a regulatory binder, with tabs dividing each category. Essential documents should be gathered at the time of study initiation and maintained until the study is complete. Original and all updated versions of the documentation must be maintained.

**Required Essential Documents**

*The list below does not include the additional regulatory documentation requirements for Sponsor-Investigator studies. Sponsor-Investigator checklists are available on the Research Compliance and Regulatory Affairs website (www.rcra.emory.edu).*

1. All versions of the investigator's brochures (drug trials) or device manuals (device trials) and updates
2. All versions of the protocol and sample case report forms or electronic data capture manual
3. All versions of information given to participants, such as
    a. Informed consent forms,
    b. HIPAA authorization forms,
    c. Questionnaires and diaries, and
    d. Recruitment and retention materials
4. Financial aspects of the trial, such as
    a. Emory University eDisclose summary,
    b. Sponsor conflict of interest (COI) forms or FDA Form 3455, and
    c. Clinical trial budget and prospective reimbursement analysis (PRA)
5. Signed agreement between involved parties, such as
    a. FDA Form 1572 (drug trials) or Investigator Agreement (device trials),
    b. Fully executed clinical trial agreement, and
    c. Contract research organization agreement
6. IRB applications and associated approval letters for initial approval, modifications, continuing reviews, and reportable new information

7. Curriculum vitae or other relevant documentation evidencing qualifications of study team
8. External laboratory contact information
9. Normal values/ranges for laboratory or medical procedures included in the protocol
10. Certification, accreditation, or other quality control mechanisms for all medical/laboratory/technical procedures/tests included in the protocol
11. Sample labels attached to investigational product packaging
12. Instructions for handling the investigational product and trial-related materials
13. Shipping records for investigational products and trial-related materials
14. Decoding procedures for blinded trials
15. Monitoring reports
16. Notification of sponsor to investigator of safety information
17. Participant enrollment log
18. Investigational product accountability log
19. Delegation of authority (DOA) log
20. Records of retained fluid/tissue
21. Training logs
22. Correspondence

**Electronic Regulatory Binders**

The use of electronic regulatory binders ("eReg") to store clinical trial essential documentation is becoming the norm as more teams move away from paper. The use of eReg allows study team members from multiple locations to access documents, investigators to electronically sign-off on documents, and the sharing of documents with sponsors and contract research organizations. Emory researchers can use Emory's One Drive and Emory's Microsoft Teams platforms to create study-specific eReg binders. Emory also allows the use of Complion, Veeva Vault, and Florence for eReg. More information on eReg platforms at Emory can be found here (https://it.emory.edu/security/protecting-data/software_for_research.html). Sponsors may also provide eReg from other vendors platforms.

Study teams with multiple studies may find it difficult to keep personnel-specific essential documentation (e.g., CVs, medical licenses, CITI certificates, and departmental training) updated for each regulatory binder. One option is to have central paper or electronic binders to maintain personnel-

specific documents with a note in each study-specific regulatory binder that references the location of the personnel-specific central binders.

The use of electronic DOA logs eliminates some of challenges of maintaining a paper log. Electronic DOA logs may include electronic signatures by the PI and study team members. Wet-ink signatures are required by GCP in the case of audit so that the auditor can verify signatures located on paper research records. Study teams utilizing electronic DOA logs can capture wet-ink signatures for each study team member by using a Signature Sheet (https://www.ctac.emory.edu/_includes/documents/sections/tools/signature_sheet.doc ). Signature Sheets can be maintained in the personnel-specific electronic binders.

**References**

*International Conference of Harmonization, Efficacy Guidelines, Good Clinical Practice*

## 4 Informed Consent Process

Federal regulations require investigators to obtain informed consent of the participant prior to research interventions. The informed consent form (ICF) must have IRB approval before implementing with participants. The best resource with updated informed consent templates and guidance is the Emory IRB Consent Toolkit (https://www.irb.emory.edu/forms/consent/index.html) and Emory IRB Consent Instructions and Guidance (https://www.irb.emory.edu/forms/consent/guidance.html) for alternative consent methods.

### Informed Consent Form

The Emory IRB provides many ICF templates on their websites that are specific to study sites (e.g., CHOA, Grady, and VA) and the type of research study. The IRB template has been written at an 8th grade reading level and provides the IRB stamping template at the header. Periodically review Emory IRB's informed consent form templates to stay up-to-date on the available templates.

Utilize the most current IRB-approved ICF within the approval and expiration dates on the IRB stamp. The best way to ensure that you have the most updated version is to print the ICF from eIRB, Documents tab. Resist the urge to print 20 copies for future use or saving to your computer desktop because doing so will increase the chance that you will use an outdated form.

The IRB-approved and stamped version of the ICF must not be altered by the participant or research team. Study teams may provide a copy of the ICF to the participant to make notes during the informed consent discussion.

### Informed Consent Discussion

The researcher must conduct the informed consent discussion in a language that is understood by the participant. Additionally, the informed consent form must be in a language that the participant can read.

The investigator, or his/her designee as documented on the delegation of authority log, must fully inform the participant of all pertinent aspects of the study including all of the information in the ICF. The investigator should also discuss relevant aspects of the study that may not be described in detail in the ICF (e.g., the schedule of events/procedures for the study, transportation to the study site, additional costs, pill diaries, surveys, and follow-up procedures). Participation in the research study is voluntary and participants must be made aware of alternative therapy options. All questions must be answered to the participant's satisfaction.

The participant should be given the option to take the ICF home to read and discuss with friends and family members. The investigator should encourage the participant to call with further questions.

When a researcher specifically targets individuals that are non-English speaking, the researcher must obtain IRB approval for a fully translated ICF for the participant to sign. When there is not enough time to obtain a fully translated ICF or the researcher expects low accrual of participants of the particular

language, the researcher must seek IRB approval of a short-form that is in the participant's language. For further information on short-form consent or obtaining consent in other special circumstances (e.g., children, cognitively impaired, or participants who are blind or illiterate), visit the IRB website (https://irb.emory.edu/forms/consent/index.html).

**Signing the Informed Consent Form**

When the participant returns to the study site, the investigator will need to again assess the participant's understanding of the study and ask if he/she has questions. If the participant is ready to sign the ICF, he/she must personally sign and date the form. If he/she has already signed the ICF from home, the investigator will need to provide the participant with a new ICF to personally sign and date with the investigator. Do not use the ICF that the participant signed from home. The investigator, or his/her designee, must also personally sign and date the form as the person obtaining informed consent.

If there are optional portions of the ICF, the participant and investigator must also personally sign and date the signature lines. If there are initial lines on each page of the ICF, those should also be completed on all pages.

If a legally authorized representative (LAR) signs the ICF, the person obtaining informed consent should make reasonable attempts to obtain documentation of the authentication of the LAR.

The investigator is required to provide a written copy of the ICF to the participant to keep. The original ICF must remain with the research records at the study site.

**Documentation of the Informed Consent Process**

The informed consent process must also be documented in the research or medical record. A brief note should describe the date and time the informed consent discussion began, whether the participant was given time to read through the ICF and ask questions, who reviewed the ICF with the participant, the date and time the consent was signed, and that a copy was given to the participant to take home.

An informed consent process note template is useful as a reminder of all the items to cover in the informed consent process and how to document. https://www.ctac.emory.edu/resources/trial-tools.html

**Informed Consent Form Revisions and Reconsent**

Whenever there are substantive changes to the protocol or when important new information becomes available, the ICF will be modified. The sponsor will inform the study team of a protocol change or new safety information and updated language for the ICF. If the changes are being initiated by the investigator rather than sponsor, the PI must first seek the sponsor's approval for the ICF changes prior to submitting them to the IRB as an amendment.

When there is new information pertaining to safety, reconsent of participants is almost always appropriate. The investigator should consider obtaining reconsent from active participants and/or

notification to past participants who need to know about the new information (e.g., a newly identified risk of long-term osteoporosis in participants who stopped taking the study drug years earlier). Reconsent must occur at the next meeting between the participant and study team member. The reconsent process must also be documented as for initial consent, with the focus of the reconsent documentation being the reason for reconsent and changes to the ICF.

The IRB and/or sponsor may require reconsent of participants. If the Emory IRB requires reconsent of participants, they will include the requirement in the approval letter of the consent modification. The sponsor may notify study teams of a reconsent requirement via letters, email, or phone. Even if the IRB and/or sponsor do not require reconsent, the investigator should seek reconsent of notification to previous participants when necessary. Revised consent forms and any other written information that will be distributed to participants must receive approval from the IRB in advance of use.

**References**

21 CFR 50, 21 CFR 56, 45 CFR 46, *Emory IRB Policies and Procedures, and International Conference of Harmonization, Efficacy Guidelines, Good Clinical Practice*

## 5 Eligibility

### Determining Eligibility

Ensuring that a participant meets the protocol eligibility requirements is important for participant safety and data integrity of the study. To document eligibility and to ensure compliance with screening requirements, utilize a study-specific eligibility checklist that matches the current version of the protocol. Protocols usually have an inclusion/exclusion list or chart of the eligibility requirements that can easily be copied to a checklist.

Maintain a completed eligibility checklist in the research record for each participant. The checklist should have a signature line for the person completing the checklist and another line for the person verifying eligibility (if it is not the same person completing the form). The person verifying eligibility must be qualified to make the eligibility assessment, IRB-approved to conduct the research, have documented study-specific training, and have eligibility determination activity on the delegation of authority log.

### Eligibility Source Documentation

Just like the rest of the research data, source documentation to support eligibility should be easy to locate in the research record. Consider keeping the supporting eligibility source documents behind the eligibility checklist in the participant electronic or paper chart.

### Maintaining Eligibility

If a participant becomes ineligible while participating in the study, consider holding the study intervention until the participant can be evaluated for safety by a qualified member of the study team. The PI should consult with the sponsor, medical monitor, or data and safety monitoring committee to determine whether the participant should remain in the study. If the sponsor or PI determines that the participant should no longer participate in the study, the participant must be withdrawn.

There are some situations where the participant may have to be withdrawn from the study but the participant may still be able to obtain the drug/device outside of the study. If the drug or device can be obtained outside of the study (e.g., a drug that is already FDA-approved but is being used for another indication for the clinical trial), the PI may consider off-label use for the practice of medicine. If this occurs, data cannot be collected for research.

## 6 Adverse Events

A thorough and prompt assessment of adverse events, as well as appropriate reporting of those events, ensures safety of human participants participating in clinical trials. Each study team member must be knowledgeable of the adverse event reporting requirements to the sponsor and IRB. Those requirements can be located in the protocol, clinical trial agreement, other sponsor correspondence, monitoring reports, and/or IRB policies.

**Background**

The Investigational New Drug (IND) regulations (21 CFR 312) require that, for serious adverse events (SAE):

- **Investigators:** Except for study endpoints, the **investigator** must *immediately* report to the sponsor all serious adverse events, regardless of whether the investigator believes that they are drug related or anticipated.
    - **Investigator** must include an assessment of causality
    - For nonserious adverse events, the FDA requires that the **investigator** report to the sponsor in accordance with sponsor and protocol requirements, generally on case report forms.
- **Sponsors:** Within 15 days of becoming aware, the **sponsor** must notify the FDA and all participating investigators via IND safety reports of events that are unexpected, caused by the study drug, *and* meet the FDA definition of "serious."

The Investigational Device Exemption (IDE) regulations (21 CFR 812) require that:

- **Investigators** report to the sponsor and IRB all reports of unanticipated adverse device effects (UADE) within 10 days of becoming aware. UADEs are serious, life threatening, or result in death AND unexpected and caused by the device.
- **Sponsors** report to the FDA, all participating IRBs, and all participating investigators all UADEs within 10 working days.
    - **Sponsors** who determine that a UADE presents an unreasonable risk to participants shall terminate all investigations within 5 days of the sponsor making this determination.

The human participants protection regulations (21 CFR 56 and 45 CFR 46) require that the investigator report all unanticipated problems involving risk to participants or others (UP) to IRBs *promptly* (Emory IRB defines "prompt" as 10 business days). UPs are unexpected, caused by the study intervention, and suggest that there is a risk to participants or others. The Emory IRB website has guidance (https://www.irb.emory.edu/guidance/reportable.html) on making UP determinations.

## Adverse Event Scope

The FDA defines an adverse event as any untoward medical occurrence associated with the use of the investigational product in humans, whether or not considered to be related to the investigational product. This is a broad scope. To document assessment of events for SAE, UP, and UADE, and compliance with the regulatory reporting requirements, **the investigator must document real-time assessment of all adverse events**.

The most common places that AEs exist in source documentation are physician notes, nursing/coordinator notes, lab reports (abnormal lab values could be considered adverse events), procedure notes, participant diaries (e.g., pill diaries, daily food logs, and symptom diaries), documentation from phone calls or emails with participants, and adverse event logs.

Document the participant's medical history at the start of the study. Changes in medical conditions that were noted at baseline must be documented as adverse events, e.g., worsening of an existing condition. New events/symptoms that occur to the participant during the study are also adverse events.

## Best Practice to Comply with the Regulations

To demonstrate proper oversight for the trial and real-time adverse event assessment for safety of participants, the PI should document clinical significance, grade, and attribution of the event to the investigational product. The PI may delegate this activity to other qualified investigators; however, the PI is ultimately responsible and must also fulfill his/her regulatory reporting requirements to the sponsor and IRB.

## AE Log

The PI or designee should maintain a system to record AEs on a log. If multiple AEs are expected to occur in each participant because the study either involves a higher risk intervention or an ailing population, generate one AE log for each participant. If few AEs are expected for the study, maintain one AE log in the regulatory binder that will cover all participants. Start with the Emory AE log template (https://www.ctac.emory.edu/_includes/documents/sections/tools/ae_log.docx) and revise it to match the sponsor or protocol terminology (e.g., "Grade 1" vs "mild").

Since AEs exist in multiple source documents but should be recorded to one AE log, the study team must take proactive and prompt measures to obtain the PI's assessment and record onto the AE log. This can be accomplished by tasking one person with reviewing all research and medical records relating to the research visit/event and transcribing them to the AE log. The AE log should be regularly reviewed by the PI, at least weekly, at which time the PI can grade and attribute each AE. Another strategy for documenting PI assessment of AEs is for the PI to document assessment (clinical significance, grade, and attribution) in the electronic medical record and later a research coordinator transcribes the PI's assessment to the AE log. The AE log should contain fields for description of event, start/stop dates, grade, attribution, and PI signature and date.

Throughout the study AEs may recur or change in severity. Each time an AE recurs or changes in severity, close out the initial AE with a stop date and start a new AE with the grade change. For example, if a participant's headache were to change from a grade II to a grade IV record a stop date for the initial grade II headache and record a new AE with a new start date for the grade IV headache. Recording AEs in this manner will provide a more reliable case history versus recording "intermittent headache" or "headache" with no stop date. AE logs may become long in some studies but will keep a more reliable record.

While reviewing the AEs, the PI should consider the criteria for SAE, UP, and UADE and report accordingly.

**External Adverse Event Reports**

Sponsors of multi-site studies are required to send all participating investigators reports of certain adverse events. Upon receipt of these events to Emory investigators, the PI must review and document his/her assessment with regards to UP. If the Emory PI assesses the event as a UP (i.e., Emory participants or others are at a greater risk of harm than previously known), that event must be reported to the IRB within 10 business days. Working with the IRB, the PI should consider taking any of the following measures to protect participants: halt the study until further information is known, notify participants, modify the informed consent, and/or obtain reconsent from active participants.

External AEs will be provided to the PI as described in the protocol, clinical trial agreement, or other sponsor correspondence. Some drugs may have a large volume of these reports, which can be hard to keep up with. Ensure that your site has a system of receipt, review, and documentation of the PI's assessment. If the sponsor requires that the PI download events from a website, ensure that you set frequent periodic reminders to check the system.

The PI can document his/her assessment of external adverse events by completing Emory IRB's Assessment Form for Events (https://www.irb.emory.edu/_includes/documents/sections/reportable_event_assessment_form.docx). Attach the worksheet to the top of each event and have the PI complete the worksheet. If the PI assesses the event as a UP, it must be reported to the IRB within 10 business days of the PI's assessment.

**References**

21 CFR 56, 21 CFR 312, 21 CFR 812, 45 CFR 46, *FDA Draft Guidance: Safety Reporting Requirements for INDs and BA/BE Studies, FDA Guidance: Guidance for Clinical Investigators, Sponsors, and IRBs; Adverse Event Reporting Requirements to IRBs—Improving Human Participants Protection, and OHRP Guidance: Guidance on Reviewing and Reporting Unanticipated Problems Involving Risk to Participants or Others and Adverse Events*

## 7 Organizational Logs

Organization of research data, source documents, and regulatory documents is critical as the study progresses through the sponsor, investigators, research coordinators, monitors, and clinical trial participants. Clinical trial sponsors often provide logs and worksheets to use as supporting documentation to the research data (paper case report forms or electronic data capture). Sponsors may require study teams to periodically submit logs.

Investigator-initiated research at Emory, without sponsor-provided logs, should still maintain tracking logs that can be used for trending, data analysis, and data verification. Logs should be study-specific with the study title and PI located at the header. Not all logs will apply to every study; utilize the logs provided in this chapter and modify them to align with the protocol. It's best to use logs at the start of the study. It's much more difficult to get organized months into the study.

**Adverse Event Log**

Documenting adverse events can be challenging since AEs exist in multiple places (e.g., physician notes, nursing notes, lab or procedure reports, pill diaries, or email correspondence with a research participant). An AE log serves as the collective source for adverse events to be tracked and analyzed by the investigator and sponsor. AE logs should contain the following fields:

1. Description of each event
2. Stop and start dates. Resist the temptation to record "intermittent AE xxx" because recalling the history of the AE will be difficult. AEs will start, stop, and change grade periodically; when that happens, close out the AE with a stop date and make a new AE entry on the log with a new start date.
3. Grade (according to a pre-defined standard defined in the protocol, for example I-IV or mild-severe)
4. Action taken by the provider (e.g., additional work-up, medication given or investigational product dose modification)
5. Whether the event was expected given the known risks of the research or investigational product ***and*** the research participant's medical history/comorbidities
6. Attribution to the research/investigational product
7. Whether the event needs to be reported to the sponsor. If it needs to be reported to the sponsor, provide the date it was reported.
8. Whether the event needs to be reported to the IRB and if it was, provide the date
9. Whether the event needs to be reported to the FDA (applicable for sponsor-investigators)

AEs on the log should have supporting source documentation with further detail. Periodically trend AEs to see if they are happening within the expected range of frequency, severity, and duration as described in the informed consent, protocol, and/or investigator's brochure. If the event trends higher than the expected ranges, then it must be reported to the sponsor, IRB, and/or FDA as a potential unanticipated problem involving risk to participants or others.

**Communication log**

The communication log can be used as documentation of discussions between individual research participants and research personnel (e.g., phone conversations or other verbal communication). Maintain the log in the participant's research record.

The log can also be used to document communication between study team members and sponsors. Maintain this log in the regulatory binder.

**Concomitant Medication Log**

The concomitant medication log should contain the name of the medication, start and stop dates, and the reason the medication is being taken. The researcher must refer to the protocol to ensure that the participant is not taking medication that is prohibited by the protocol. If the participant tells the researcher at a later date that he/she has been taking a prohibited medication, consider the protocol requirements and safety profile of the combination of the concomitant medication and the investigational product. Consider the sponsor and IRB's reporting requirements for protocol deviations.

**Delegation of Authority (DOA) Log**

The DOA log documents the PI's delegation of study related activities across the study team. It will be the first thing that an auditor will ask to review when arriving on site. The DOA log provides the names of the study team members, the stop and start dates for the research, signatures, and the study activities that have been delegated to them by the PI.

The DOA log should contain a list of the entire study team that has been approved by the IRB. The start date on the DOA log for each individual should not precede that date of IRB approval for that individual or study, CITI/GCP certification, eDisclose completion, or documented study-specific and protocol training. Ensure that all of these requirements occur before the start date on the DOA log. The DOA log can serve as the final check point before the study team member starts the research.

**Enrollment Log**

Enrollment logs contain the chronologic enrollment of participants by name, study ID number, and date of enrollment. Additional fields such as eligibility, randomization date, and withdrawal date are also useful to include. The Emory IRB defines enrollment as being the time the participant gives informed consent to participate whether or not the participant goes on to participate in the research Studies that record accrual in Oncore don't need a separate enrollment log.

**Protocol Deviation Log**

The federal regulations do not allow for deviations from the protocol unless there is imminent risk of harm to research participants. There are many times though that protocol deviations are unavoidable in clinical trials, whether it be a deviation on the part of the study team or research participant. Protocol deviation logs must contain a description of the deviation, date, corrective action taken, and whether the deviation required reporting to the sponsor or IRB (if so, include the date reported). Deviations should be periodically trended over time to look for systemic problems with the study. Problems for the study should have a thorough root cause analysis and a corrective and preventive action (CAPA) plan. CAPA plans should be thoughtfully designed, fully implemented, periodically evaluated, and revised as needed to ensure improvement (see CAPA chapter in this guidebook for more information).

**Specimen Log**

Information regarding specimens collected and stored for clinical trials should be documented on a log. The specimen log should contain information about what specimen was obtained, method of collection, shipment location (if applicable), and method of storage at Emory (if applicable) including information on the storage conditions (e.g., temperature logs).

**References**

*International Conference of Harmonization, Efficacy Guidelines, Good Clinical Practice*

## 8 Data and Safety Monitoring Plans

To assure the safety and welfare of participants, all greater than minimal risk clinical trials at Emory are required to have a data and safety monitoring plan (DSMP). Sponsors include the DSMP in the protocol. Some clinical trials may have data and safety monitoring boards (DSMB) or committees (DSMC) appointed by the sponsor or investigator.

Emory IRB Policy and Procedure (https://www.irb.emory.edu/_includes/documents/sections/policiesandprocedures.pdf) #50, *Data and Safety Monitoring Plans,* describes the required components of a DSMP. The Emory IRB also provides guidance (https://www.irb.emory.edu/guidance/getting-started/study-submission.html) on how to write a DSMP.

### Compliance with the DSMP

The DSMP should define the following:

- Data quality monitoring entity and monitoring frequency (e. g., monitoring visits every 2 months)
- Review of data for safety review (e.g., the DSMB convenes every 2 months to review data)
- Collection, reporting, and review of adverse events

It is the responsibility of the sponsor to provide the monitoring that was agreed upon at the start of the study. It is the PI's responsibility to ensure that the DSMP, as approved by the IRB, is being followed.

### Monitoring

Sponsors are required to secure compliance when noncompliance is found. Deviations noted in monitoring reports are often findings of noncompliance (with the protocol requirements or federal regulations) and thus, should be addressed promptly. Study teams should establish a collaborative working relationship with study monitors.

After the monitoring visit, the monitor will send the study team a written report of findings. The PI and study team should carefully review the report and assign tasks. Compare old reports to the most recent reports to look for patterns of noncompliance across reports. Send all monitoring and other quality assurance reports to the Clinical Trials Audit and Compliance listserv at ctcompliance@emory.edu within 10 days of receipt. File the monitoring reports and actions taken in the regulatory binder.

### Self-Assessments

If the study is not being monitored by the sponsor or contract research organization, the PI should consider performing self-assessments. Self-assessments are best implemented by someone within the clinical department that is not directly involved with the data collection or entry. Clinical departments

are urged to use a buddy system whereby research coordinators or nurses switch off studies to review at least twice per year. The Emory University Self Assessment Tool can be used. Self-assessments may be part of an IRB-approved DSMP for moderate and high complexity category B studies as defined by the Emory IRB. The Emory IRB does not allow self-assessments for high-complexity studies (Phase I, II, and III under an IND/IDE, high risk due to procedures involved or trials comparing two or more standard of care interventions for comparative effectiveness). Emory investigators acting as both sponsor and investigator (Sponsor-Investigators) must obtain monitoring through a contract research organization.

Sponsor-Investigators over a multi-site study may require the sites to perform self-assessments along with periodic collection of protocol deviation forms, to ensure compliance across all sites.

**References**

*IRB Policies and Procedures and NIH Policy on Data and Safety Monitoring*

## 9 Corrective and Preventive Action Plans

The IRB-approved research plan includes all information submitted and approved by the IRB, including 1) the scientific protocol, 2) information in the IRB applications, modifications and reported events, and 3) any other study-specific IRB determination or requirement. The federal regulations and Good Clinical Practice guidelines do not allow deviations from the IRB-approved plan except where necessary to eliminate apparent immediate hazards to human participants. Even with the most cautious and careful research and participant teams, however, protocol compliance can be difficult to maintain in the increasingly complex clinical trial environment. Studies are technical with multiple requirements and the human participants are volunteers with individual medical and life situations that may influence compliance.

The investigator and research team members must make a concerted effort to comply with the protocol and educate participants on the requirements through the continuing informed consent process. When deviations from the IRB-approved research plan occur, the investigator must act quickly to ensure participant safety and reporting to sponsor and/or IRB when necessary.

**How to prevent deviations**

- All study team members must be trained on the protocol before starting the research
- Ask the sponsor about confusing wording in the protocol
- Keep the protocol, or significant sections, handy with the participant charts for quick reference
- Communicate expectations to participants
- Talk to monitors about common deviations across sites

**What to do when a deviation occurs**

If study team members become aware of a deviation that has already occurred, taking immediate corrections will protect the rights, welfare, and safety of the participant(s). Immediate corrections may include a phone call or an office visit with a qualified research team member. The investigator may choose to order tests and other procedures to ensure the participant is safe. Document the deviation, reason it occurred, and immediate corrections taken. Consider the reporting requirements of the sponsor and IRB; report appropriately. Do not wait to report—if there isn't time to complete an electronic application then report by phone and finish the application when time allows. The Emory IRB requires noncompliance and deviations meeting reporting criteria to be reported within 10 business days of becoming aware. The study team may also need to notify participant(s) of the problem; the IRB will advise on how to do this (e.g., letter to participants, phone, or reconsent). Immediate corrections should focus on **rights, welfare, and safety of participants and reporting**.

**Evaluate risk**

After immediate corrections have been taken, evaluate the risk of the severity and frequency of the deviation. To evaluate severity of a problem, start by using the Emory IRB reporting requirements, which considers events that adversely affect the rights, welfare, or safety of participants (among other things) to be major.

To evaluate frequency, consider recurrence of the problem in the future and history of the problem in the past. For future assessment, consider the risk of the event recurring in the same participant or other participants in the study. For past assessment, review the protocol deviation log for other occurrences of the event. If there is a risk of the problem recurring in the future or if you notice it becoming a pattern on the protocol deviation log, the risk of frequency is apparent.

If there is a risk of severity and/or frequency, continue to investigate the problem through root cause analysis. If there is no risk of severity or frequency, the immediate corrections taken initially should resolve the problem. Lastly, document the deviation, corrections, and risk assessment and continue to monitor the protocol deviation log for patterns.

**Immediate Corrections**

There are distinct differences between immediate corrections and corrective actions. Corrections are the immediate steps taken to resolve a problem and ensure the **rights, welfare, and safety** of participants and **reporting**. Corrections may resolve minor deviations, but they will not effectively resolve more significant noncompliance (reminder: risk = severity + frequency). Corrective actions are developed and implemented for more significant or systematic noncompliance once the root cause is known.

**Root Cause Analysis**

When significant deviations or noncompliance occur in research, it is important to identify the causes of the problem so that they can be resolved to prevent further noncompliance. There can be multiple reasons or causes that contribute to one single problem. Conversely, there may be multiple methods to resolve each cause. The root cause is the initiating, most basic cause of a problem that may or may not lead to a chain of causes or other problems. Eliminating the root cause should prevent recurrence of the problem.

A root cause analysis (RCA) is the process of identifying and documenting the root cause and the downstream effect on the causal chain. RCA should focus on identifying underlying problems that contribute to error rather than focusing on mistakes made by individuals.

Steps

1. Identify the problem
    a. A problem statement should include
        i. Description of the problem
        ii. Where and when it happened

iii. Weight/magnitude of the problem
iv. Requirements that were not met
v. Evidence to show that requirements weren't met

2. Interview those impacted by the problem
3. Interview those responsible for the problem, if applicable

Questions to identify root causes

1. What happened? What is the problem?
2. Why and how did the problem occur? What were the steps?
3. Who was affected by the problem? Was it one participant or all participants in the study?
4. What is the magnitude of the problem? Is it in one study or does the problem exist in all studies under this PI or even in an entire clinical department?
5. Keep asking "why" and "how" until you reach the root cause

Once the root cause has been identified, the next step is to develop a corrective and preventive action plan to eliminate the root cause.

**Corrective and Preventive Action (CAPA) Plans**

The FDA indicates that corrective and preventive actions (CAPAs) are necessary to resolve problems and noncompliance in clinical investigations. Corrective actions are those taken to resolve a problem and preventive actions are those actions that keep the problem from recurring. Although investigators have implemented CAPAs for decades, federal agencies, sponsors and IRBs now expect CAPAs to resolve problems in research. CAPAs must be thoroughly documented, implemented, and evaluated over time for effectiveness.

Corrective actions

The first and most critical corrective action is to ensure that the immediate corrections previously taken removed any risk of harm or further harm to the participant and future participants and that the deviation was appropriately reported to the sponsor and IRB. When study teams have assessed the **rights, welfare, and safety** of the participant and the root cause is known, they may consider additional **reporting** to the sponsor and IRB. Ensure that the report to the sponsor and IRB is accurate and thorough and that the CAPA is included.

Preventive actions

Preventive actions are necessary to ensure that the problem does not repeat in one or more participants. Preventive actions should be based on **process.** Create and document a process or standard operating procedure (SOP). Train on the process, implement the process, evaluate the process, and amend the process as necessary. Consider revising the protocol or informed consent as necessary.

CAPAs must be thorough (SMART CAPA)

**Specific:** Compliant with regulations, addresses the full observation or root cause, accountable to named individual or role

**Measurable:** Action can be measured to demonstrate whether it is adequate to address root cause

**Achievable:** Addresses all implicated processes and levels

**Realistic:** Plan can be carried out given resources, knowledge and expertise

**Time-bound:** Assigned to a person or role who can accomplish action in a given time period

CAPAs must be implemented

Ensure that the CAPA is well documented and that all study team members have been trained and understand their roles and responsibilities for successful CAPA implementation. The CAPA and associated SOP may be relevant only for the study or it may need to be implemented systematically across the clinical department. The CAPA and SOP can be rolled out in stages. The important thing is to take action and document it.

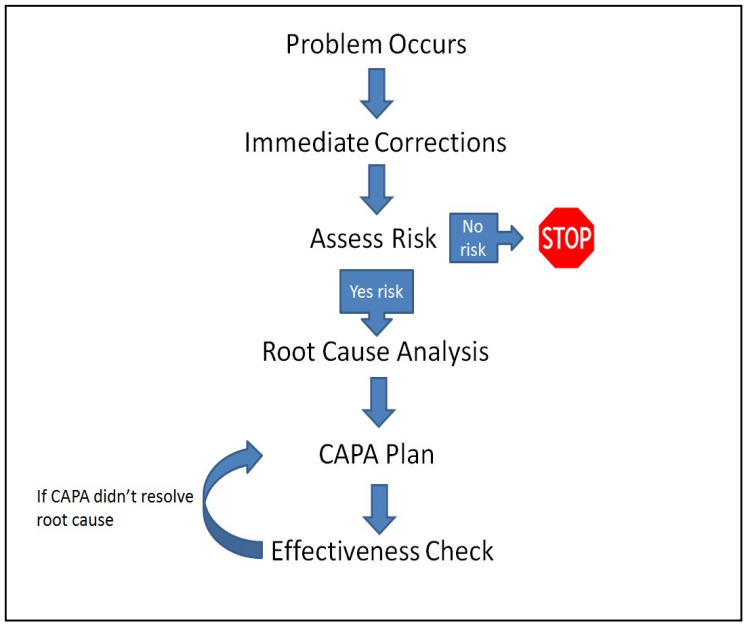
CAPAs must be evaluated over time

Effectiveness check is the final step of the CAPA process. Ensure that the CAPA has addressed the root cause and that the problem has not recurred. If the CAPA has not addressed the root cause, amend the CAPA as necessary, train on the process, implement the process, and re-evaluate.

CAPA must be well documented

Documenting the CAPA

- Action type (corrective or preventive)
- Action description
- Owner
- Due date
- Plan for effectiveness check
- Effectiveness check outcome




**References**

*IRB Policies and Procedures #73*

## 10 Reporting Requirements

Each sponsor has unique reporting requirements for events that occur during the clinical trial and need to be reported to the sponsor by individual site PIs. These reports are in addition to those that a study team must make to the IRB. The PI is ultimately responsible for ensuring that the sponsor's reporting requirements are followed; however, the study team must be knowledgeable of the sponsor's reporting requirements to ensure compliance. The sponsor's reporting requirements are located in the protocol, clinical trial agreement, or other sponsor correspondence.

The sponsor will define which events need to be reported to the sponsor and at what frequency. The sponsor should also provide instructions for reporting (e.g., electronic entry on a sponsor's website or via electronic data capture system). The sponsor's time frame for reporting should be taken seriously and reported to the IRB as noncompliance if it is not followed.

### Adverse Events

Adverse events (AEs) must be recorded locally and then considered for sponsor and/or IRB reporting. All AEs don't need to be reported to sponsors and IRBs; thus, the number of AEs recorded locally will be greater than the number of AEs reported. Sponsors may require reporting of AEs of specific grade or severity and/or interest to the sponsor or FDA (usually called adverse events of special interest (AESI). AESIs will be defined in the protocol and are events that the sponsor or FDA are monitoring for importance. CTAC recommends transcribing all adverse events to an AE log with each entry graded, attributed, signed, and dated by the PI or medically qualified designee. The AE log could include a column listing the date the event was reported to the sponsor and/or IRB.

### Protocol Deviations and/or Noncompliance

CTAC recommends transcribing all protocol deviations to a log with each entry signed and dated by the PI or designee. The log could include a column listing the date the event was reported to the sponsor and/or IRB. Report deviations to the sponsor within the sponsor's required time frame. Periodically review the log for patterns of similar deviations that could represent a problem.

### Monitoring Reports

The sponsor may require study teams to report adverse events or deviations found on routine monitoring visits that do not meet the IRB's reporting requirements. It is important for the study team to be knowledgeable of the sponsor's reporting requirements included in the protocol, clinical trial agreement, or other sponsor's correspondence. The more stringent reporting requirement should be followed.

## 11 Research Data

Research data are submitted to the sponsor and/or analyzed by the Emory Investigator on paper case report forms (CRFs) or by electronic data capture (EDC). EDCs are software that stores research and patient data collected in clinical trials. EDCs are becoming the standard for Industry and DHHS-supported clinical trials because they offer quick access to data, security, accuracy, and query management. EDCs are also available for investigator-initiated clinical trials. Emory offers the REDCap platform for investigator-initiated studies.

**Data Entry**

- EDCs are designed to imitate paper forms, capture clinical trial information, and promote data standards
- Data must be entered by authorized site personnel, as documented on the delegation of authority log
- EDC entry must be consistent with source data from the participant's medical record, source worksheets, and/or participant questionnaires
- If the study uses paper CRFs, entries must be legible
- Abbreviations and acronyms should be avoided unless they are standard medical abbreviations or known to be acceptable
- Complete the header information on each page consistently. Complete every field on each CRF page, unless otherwise indicated. If something is not done, unknown, or not applicable make a comment (ND/UK/NA) and strike through the field so it is obvious the item has not just been missed.
- Do not write outside of the designated boxes. Write comments on the comments section/page.
- Complete each box using leading zeros
- To amend incorrect data on a CRF page:
    - Score through the error with a single line,
    - Do not obscure the original entry (do not use correction fluid),
    - Write the correct data nearby, and
    - Initial and date each change.
- Do not record incomplete dates (e.g., if the month and year are known, but not the day, record-04/NK/05).
- Record dates in the requested format (e.g., 11/04/05; 04/11/05; 11 APR 05; 11 APR 2005)
- Use the correct or consistent unit for weight, height, lab results, etc.
- Ensure AEs are consistent through visits, as applicable. If events are new at cycle/visit 1 but continue through cycle/visit 2, make sure it is documented at cycle/visit 2 as well. This can be best accomplished by recording AEs on an AE log which includes start date, stop date, grade of AE, attribution (relation to study drug), and action taken. Ensure that a qualified study team member, who has been given AE activity on the delegation of authority log, assesses and documents the clinical significance, grade, and attribution of the AE.

- If a medication was given for an adverse event, document the drug, start/stop dates, and response

**Source Data Verification**

The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data. This can be accomplished and documented either electronically or by paper. For electronic data capture, the sponsor may ask the PI to electronically sign each page or multiple pages at defined periodic time points. Some sponsors may have the PI sign an attestation page at the end of EDC completion, which will document the PI's verification that the data are complete and accurate. For paper CRFs, the PI may sign and date each page or sign an attestation page at the completion of all CRFs for a certain participant or entire study.

**Data Review and Queries**

Sponsors periodically review data in the EDC, termed "centralized monitoring," during the study to verify and analyze data. When sponsors suspect an error with data entry, they will issue a query for the study team to review, clarify, and/or correct data. Sponsors send queries by email, notification in the EDC, or through a sponsor system requiring study teams to log-in to view and correct queries. Sponsors have time requirements resolving data queries to ensure high quality data.

**EDC and Source Documentation Organization**

Data should be entered promptly after the research or clinical encounter. A backlog of EDC entry compromises data integrity. Emory requires research records be stored for 10 years after study closure or termination. For studies involving children, in-vitro specimens, or pregnant women, Emory requires storage of research records for 25 years. The FDA requires that investigators and sponsors retain records for 2 years following the date a marketing application is approved for the drug/device for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified. The sponsor may have further record retention policies. A good rule of thumb is to store the records for the longest period of time across Emory, FDA, and the sponsor.

**Abbreviations**

| | |
|---|---|
| CRF | case report form |
| LE | late entry |
| NK | not known |
| ND | not done |
| NA | not applicable |
| NAD | no abnormalities detected |
| AE | adverse event |

SAE serious adverse event

UNK unknown

**References**

*Emory University Records Management Policy and International Conference of Harmonization, Efficacy Guidelines, Good Clinical Practice*

## 12 Study Team Changes

**Exiting Study Team Member**

Prior to departure from a study, the exiting study team member should complete the following:

- Outstanding data entry and/or data queries
- Incomplete source documentation
- Notification to the sponsor of the study team changes
- Notification to the active participants of the study team changes if the research team contact information will change for the participants. Letters or other materials that will be distributed to all participants must have IRB approval prior to sending.
- Provide a list of study-specific contacts (e.g., sponsor, monitor, OCR analyst)
- Provide a list of outstanding issues

**Incoming Study Team Member**

Prior to starting the research, the incoming study team member should complete the following:

- All required training/certification items mentioned in Chapter 2, Emory Training Requirements, of this Guidebook.
- Notification to the sponsor of the study team changes

**Change in Principal Investigator**

If there is a change in PI, the following documents need to be revised and completed;

- Seek approval from the sponsor for the PI change
- Seek IRB approval via eIRB modification for the new PI. Consider revising the protocol and informed consent form, as appropriate. Also consider notifying current participants; correspondence sent to all participants must be approved by the IRB.
- Update the Form FDA 1572 (drug studies) or the Investigator Agreement (device studies)
- Update the DOA log
- Ensure that the new PI has completed the Emory required training and study-specific training

**Documentation of Study Handover**

The exiting and incoming study team member should document the study handover in a note to file or other documentation for the regulatory binder. The note should contain some of the items above and the date of the handover. The incoming study team member should obtain documented study-specific training and any required approvals prior to being added to the delegation of authority log.

**Abbreviations**

| | |
|---|---|
| GCTSA | Georgia Clinical and Translational Science Alliance |
| AE | Adverse Event |
| AREF | Atlanta Research and Education Foundation |
| AVAMC | Atlanta Veterans Affairs Medical Center |
| CAPA | Corrective and Preventive Action |
| CFR | Code of Federal Regulations |
| CHOA | Children's Healthcare of Atlanta |
| CRN | Clinical Research Network |
| CITI | Collaborative Institutional Training Initiative |
| COI | Conflict of Interest |
| CRC | Clinical Research Coordinator |
| CRF | Case Report Form |
| CTAC | Clinical Trials Audit and Compliance |
| CTRC | Clinical and Translational Research Committee |
| DOA | Delegation of Authority |
| DSMB | Data and Safety Monitoring Board |
| DSMC | Data and Safety Monitoring Committee |
| DSMP | Data and Safety Monitoring Plan |
| EDC | Electronic Data Capture |
| EPEX | Emory's Proposal Express System |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practice |
| GROC | Grady Research Oversight Committee |
| HIPAA | Health Insurance Portability and Accountability Act |

| | |
|---|---|
| IATA | International Air Transportation Association |
| ICF | Informed Consent Form |
| ICP | Informed Consent Process |
| ICH | International Conference on Harmonization |
| IDE | Investigational Device Exemption |
| IND | Investigational New Drug |
| IRB | Institutional Review Board |
| NIH | National Institutes of Health |
| OCR | Office for Clinical Research |
| ORIC | Office of Research Integrity and Compliance |
| OSP | Office of Sponsored Programs |
| P&P | Policies and Procedures |
| PI | Principal Investigator |
| RCA | Root Cause Analysis |
| RCR | Responsible Conduct of Research |
| RSC | Radiation Safety Committee |
| SAC | Scientific Advisory Committee |
| SAE | Serious Adverse Event |
| SAS | Safety Advisory Subcommittee |
| SOP | Standard Operating Procedure |
| UADE | Unanticipated Adverse Device Effect |
| UP | Unanticipated Problem Involving Risk to Participants or Others |

**Appendix 1, Study Start Up Required Approvals**

*The list below represents a brief description of approvals at Emory and does not describe, in detail, the functions of every department. For further information, follow links to departmental websites.*

**Georgia Clinical and Translational Science Alliance (GCTSA):** Any research investigator with an appointment at Emory, Morehouse, Georgia Tech, or University of Georgia is eligible for GTCSA support. The Georgia CTSA Clinical Research Centers (GCRCs) is a service center focused on supporting and streamlining new clinical trials. The GCRC offers inpatient and outpatient research units, specialized staff, space, equipment, coordinator support, help with study initiation, budgets and more. For more information and GCTSA application visit their website.

**Biosafety:** The investigator is required to submit a Notice of Intent (NOI) to the Biosafety office when the proposed research involves any of the following:

1. Experiments involving the deliberate transfer of recombinant DNA or RNA, or DNA or RNA derived from recombinant DNA into one or more human participant;
2. Experiments utilizing live, recombinant, or attenuated microorganisms for the purposes of vaccination of one or more human participants; or
3. Experiments involving use of investigational vaccine containing recombinant DNA in humans.

For more information on the Biosafety requirements or to download forms, visit the Biosafety website at https://www.ehso.emory.edu/guidance/programs/research-safety.html

**Protocol Review and Monitoring Committee (PRMC).** For cancer clinical trials, in any department, the investigator must apply to the PRMC prior to seeking IRB approval. The PRMC form can be found at https://winshipcancer.emory.edu/research/clinical-trials-office/protocol-review-monitoring-committee.html. The PRMC is available on Winship intranet (Sharepoint) and is done electronically The Investigator may submit the application in eIRB while awaiting PRMC approval. Once the PRMC has given approval, a PRMC administrator will move the study in eIRB to the IRB Inbox (i.e., the study won't electronically go to the IRB until the PRMC administrator moves the study after PRMC approval).

**Conflict of Interest (COI):** The investigator and anyone named by the PI who is responsible for the design, conduct, or reporting of research must complete eDisclose

for the study. Visit the RCRA website for more information and the link to the eDisclose system is https://rcra.emory.edu/coi/ecoi.html **Emory Healthcare Office of Quality:** For studies being conducted at an Emory Healthcare (EHC) facility, or that have a procedure or test done in an EHC facility, study teams must complete the applicable Office of Quality Checklists and submit to the Office of Quality. The IRB will not distribute the stamped informed consent and HIPAA authorization forms until the Office of Quality has given final sign-off. The Office of Quality Checklists are located on the IRB website at https://irb.emory.edu/guidance/research-types/clinical-studies.html

For drug and device studies, Emory Healthcare also requires study teams to complete a Key Points Summary that will be placed in the participants' Emory electronic medical record Epic so that EHC

providers taking care of patient participants can have information on the study drug/device, eligibility criteria, and emergency contact information for the researcher.

The Key Points Summary must be uploaded with the initial eIRB application in the Data and Safety Monitoring Plan section. The Summary can be located on the IRB website at https://irb.emory.edu/guidance/research-types/clinical-studies.htmlFor studies involving sensitive and stigmatizing information, inclusion of study information into the medical record may discourage participants from participating. For such studies, the research team can request a *sensitive* determination by the IRB by completing the Request for Sensitive Study Status Worksheet and Sensitive Studies Summary in place of the Key Points Summary.

The Request for Sensitive Study Status Worksheet and Sensitive Studies Summary must be uploaded with the initial eIRB application in the Data and Safety Monitoring Plan section. The Summary can be located on the IRB website at https://irb.emory.edu/guidance/research-types/clinical-studies.html

**Grady Office of Grant Administration:** All studies using Grady as a site must obtain financial clearance through OGA. This approval can be obtained while the IRB approval is pending. Contact Amaka Wright in Grady OGA at (404) 616-1828 or awright3@gmh.edu

**Grady Research Oversight Committee (GROC):** All studies using Grady as a site must seek GROC approval after IRB approval. The GROC application form can be found on the IRB website at: https://irb.emory.edu/forms/eirb/how-to.html under Overview and Ancillary Research tab. The investigator must complete the GROC application and submit it to GROC, along with the IRB approval letter, stamped informed consent and HIPAA authorization forms, and the lay summary. Further instructions are located on the GROC application. Grady researchers must obtain both IRB and GROC approval before starting research with human participants.

**Institutional Review Board (IRB):** IRB approval is required before the research can start. The investigator must submit to the Emory or external IRB, the following documents when applicable to the study: initial application, the investigator's brochure, protocol, informed consent form, HIPAA authorization form, questionnaires, study advertisements, and relevant FDA correspondence.

Instructions on obtaining an eIRB account can be found on the IRB website at https://irb.emory.edu/forms/eirb/how-to.html Studies that are eligible for external IRB review and instructions can be found on the Emory IRB website at https://irb.emory.edu/guidance/research-types/collaborative.html**Investigational Drug Service (IDS):** Investigational drugs and FDA-approved drugs that are provided by the sponsor or paid for by the grant are required to be stored in the Emory IDS, for research conducted at Emory facilities. The Office for Clinical Research will initiate discussion with IDS regarding charges for drug storage and dispensation; these charges will be included in the budget for the trial. The PI must provide the sponsor with the address of the IDS.

**Office for Clinical Research (OCR):** OCR review is required for studies with billable items and services. Complete an OCR routing package by emailing the following documents to the OCR listserv at

OCR@emory.edu: Request for Prospective Reimbursement Analysis and Budget Development Form, protocol, clinical trial agreement/contract, Investigator Effort Calculations Report, draft budget, informed consent drafts, and recent FDA correspondence.

For more information on the OCR application requirements, visit their website at http://www.ocr.emory.edu

**Research integrity and Compliance (ORIC):** ORIC offers assistance to all Emory investigators acting both as Sponsor and Investigator (i.e., "Sponsor-Investigators"), as defined by the FDA. ORIC advises contacting the office early in the approval process. Contact Margaret Huber (404-727-2233 or mhuber@emory.edu) in the ORC for more information. https://rcra.emory.edu/oric/index.html

**Office of Sponsored Programs (OSP):** OSP assists researchers with funding applications, proposal development, budget preparation, proposal processing with the sponsor, funding negotiation, and awards acceptance. To get started, route the proposal and budget through Emory Proposal Express (EPEX). www.osp.emory.edu

After Emory has received the award, the Data Management Group will send the PI the electronic notice of award (eNOA) and SmartKey. During the study, the PI will work with the Office of Grants and Contracts for the fiscal activity of the trial.

**Office of Technology Transfer (OTT):** OTT assists researchers with material transfer agreements (MTA), intellectual property rights, and negotiate license arrangements for intellectual properties. www.ott.emory.edu

**Radiation Safety:** Emory University Radiation Safety Committee (RSC) approval is required for studies that involve imaging procedures that utilize ionizing radiation, such as x-rays, CT scans or Nuclear Medicine Imaging scans. Procedures such as Echocardiogram or MRI do not involve ionizing radiation and thus do not require Radiation Safety Committee review.

The investigator must submit to the RSC the Radiation Summary and the Human Studies Application for Radiation Use forms. Both forms are located on the Radiation Safety webpage of the Environmental Health and Safety Office website at https://www.ehso.emory.edu/guidance/programs/radiation-safety.html)

**VA Research and Development Committee (R&D):** All studies using the Atlanta VA Medical Center as a site must seek VA R&D approval after IRB approval has been obtained. VA researchers must obtain both IRB and R&D approval before starting research with human participants.

To complete the R&D Application, the investigator must have an account with the Atlanta Research and Education Foundation (AREF). To create a new account, log into the AREF website at www.atlaref.org With an AREF account, you can log in to the electronic Request to Review Research Proposal (eRRRP) from a VA computer using your AREF Online credentials at https://www.va.gov/atlanta-health-care/research/research-credentialing-and-training/

Researchers must submit to the R&D the protocol, IRB approval, and other pertinent documents specific to the research project. See website https://www.va.gov/atlanta-health-care/research/for-investigators/

## Appendix 2, Emory Training Tracking Sheet

Employee name: _____

Job title: _____

*See CTAC Guidebook Chapter 2 for optional versus required training. Attach relevant training documentation, as applicable.*

| Course Title (complete training applicable for your job title/description) | Date Completed and Initials |
|---|---|
| CITI certification (Biomedical Focus) | |
| CITI certification (GCP module) | |
| Investigator training (New Faculty Training) if hired after Jan. 2023 SOM Orientation | |
| Clinical Research Orientation (if new to Emory, re-hire or promotion (https://www.ocr.emory.edu/resources/training/orientation.html ) | |
| ORC training (HIPAA Privacy and Security) | |
| IATA training (International Air Transportation Association) | |
| Oncore Training (Emory Clinical Trial Management System) (CTMS) | |
| CPR training (Basic Life Support with Cardiopulmonary Resuscitation) | |
| EHSO training (Bloodborne Pathogens for Research) | |
| VA research training | |
| eIRB training | |
| EPEX training | |
| Study specific training, specify: | |
| Other, specify: | |
| Other, specify: | |
| Other, specify: | |

Training verified by:

_____ _____

Supervisor signature and date Supervisor print name