EMORY UNIVERSITY | Clinical Trials Audit and Compliance

Clinical Trials Guidebook

Purpose

Clinical trials are the leading catalyst for the advancement of 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 subjects 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 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 of Europe, Japan, and the United States 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. If the sponsor requires GCP, the requirement will usually exist in writing 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 all 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 guidance 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
  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 or Form A/B for Western IRB (visit www.irb.emory.edu for WIRB eligibility requirements)
  - ☐ OCR submission for studies with billable items and services
  - ☐ OSP submission via EPEX for grants and contracts
  - ☐ ORC submission for all sponsor-investigator studies from Winship Cancer Institute
  - ☐ COI submission via eCOI
  - ☐ 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
- ☐ Grady Office of Grant Administration. Seek financial clearance for all studies using Grady as a site.
- ☐ Application of the Form 1572

Note! *If changes to protocol or other study material occurs during IRB submission and before approval submit the revised documentation to OCR and OSP as well to eliminate waiting time in approvals.*

☐ 4. After IRB approval seek the following approvals, if applicable
- ☐ GROC (Grady Research Oversight Committee)
- ☐ VA R&D (Veterans Affairs Research Development Committee)

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

☐ 6. Document study-specific training for each study personnel

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

☐ 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:

GROC:	Apply after IRB approval has been obtained.
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:	Submit proposal in EPEX when the contract is available. If the contract is not available but you have been asked to sign a confidentiality disclosure agreement (CDA), contact OSP to notify them of the study. Do not sign a CDA without first consulting OSP.
VA R&D:	Apply after IRB approval has been obtained.

References

Emory IRB Policies and Procedures; 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.

Training

1. Basic Life Support with Cardiopulmonary Resuscitation (CPR) for Emory University Research Staff who need it for credentialing (www.ocr.emory.edu)

2. 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. (http://www.ehso.emory.edu/training/index.cfm)

3. CITI Certification, Biomedical Focus (www.citiprogram.org)

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

        - CHOA employees are required to take the CHOA Biomedical and Good Clinical Practice Modules

    b. This must be taken prior to IRB approval and must be maintained every 2 years by taking the Biomedical Refresher Course

4. Office for Clinical Research Training (www.ocr.emory.edu)

    a. Investigators: *Key Concepts of Clinical Research*

    b. CRCs and Research Nurses: *How to Conduct Clinical Research at Emory: The Basics*

5. Office for Research Compliance HIPAA Security and Research training (http://www.orc.emory.edu/Training/index.cfm)

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 (www.orc.emory.edu)

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 for each study

    a. Sponsors may provide a training log or you can create your own (Link to CTAC Training Log)

Optional Training at Emory

1. Certification of Research Administration at Emory http://www.osp.emory.edu/communication/training/index.cfm
2. CITI GCP training and additional modules (www.citiprogram.org)
3. eIRB training (www.irb.emory.edu)
4. Emory Research A to Z (ERAZ) (http://www.or.emory.edu/About_Us/ERAZ.cfm)
5. Emory Research Management System (ERMS) (www.ocr.emory.edu)
6. EPEX training (http://www.osp.emory.edu/forms/epex.cfm). After completing the on-line or in-person class, request access to EPEX by completing the EPEX Access form on the OSP website.
7. Export Control (www.orc.emory.edu)
8. Research Matters (www.ocr.emory.edu)

References

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

3 Essential Documentation

Your clinical trial material will consist of many documents referred to as essential documents. These documents demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements. Essential documents should be organized in a 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. The original and all updated versions of the documentation must exist.

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 ORC website (www.orc.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
3. All versions of information given to subjects, 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 eCOI 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 approval letters for initial approval, amendments, continuing reviews, and reportable events
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 of 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. Subject enrollment log
18. Investigational product accountability log
19. Delegation of authority log
20. Records of retained fluid/tissue
21. Training logs
22. Correspondence

Going Green

Study teams with multiple studies may find it difficult to keep essential documentation updated for all studies. One option is to have central binders to maintain department-specific essential documentation with a note in the study regulatory binders that references the location of the central binders. Central binders work well for CVs, licenses, CITI certification, departmental training, and certification and normal ranges for frequently used laboratories. Central binders may also be stored electronically on a departmental shared drive that is easily accessible for all study staff for QA checks or audits.

Study-specific essential documentation (e.g., IRB approval letters and protocols) must be maintained in a study-specific regulatory binder or folder on a secured shared drive.

References

International Conference of Harmonization, Efficacy Guidelines, Good Clinical Practice

4 Informed Consent Process

Federal regulations require investigators to obtain informed consent of the subject prior to research interventions. The informed consent form (ICF) must have written IRB approval before implementing with subjects.

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 also been written at an 8th grade reading level and provides the IRB stamping template at the header.

Remember to use 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 because that will increase the chance that you will use an outdated form.

Informed Consent Discussion

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

The investigator, or his/her designee as documented on the delegation of authority log, must fully inform the subject of all pertinent aspects of the trial including all of the information in the ICF. The investigator should also discuss relevant aspects of the trial 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). It is critical that the subject understand that participation in the research study is voluntary as well as all of the alternative therapy options. All questions must be answered to the subject's satisfaction.

The subject should be given the option to take the ICF home to read and discuss with friends and family members. The investigator should encourage the subject to call him/her if he/she has further questions.

Please note that when a researcher specifically targets individuals that are non-English speaking, the researcher must obtain IRB approval for a fully translated ICF for the subject to sign. When there is not enough time to obtain a fully translated ICF or the researcher expects low accrual of subjects of the particular language, the researcher must seek IRB approval of a short-form that is in the subject's language. For further information on short-form consent or obtaining consent in other special circumstances (e.g., children, cognitively impaired, or subjects who are blind or illiterate), see the IRB Policies and Procedures (www.irb.emory.edu).

Signing the Informed Consent Form

When the subject returns to the study site, the investigator will need to again assess the subject's understanding of the study and ask if he/she has questions. If the subject is ready to sign the ICF,

he/she must personally sign and date the form. The investigator, or his/her designee, must also personally sign and date the form as the person obtaining informed consent.

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.

When the subject returns to the study site, if he/she has already signed the ICF previously provided by the study team (to take home and read), the investigator will need to provide the subject with a new ICF to personally sign and date with the investigator. Don't use the ICF that the subject signed from home.

If there are optional further portions of the ICF, the subject 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.

The investigator is required to provide a copy of the signed and dated informed consent to the subject to keep. The original ICF must remain with the research records at the trial 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 subject was given time to read through the ICF and ask questions, who reviewed the ICF with the subject, the date and time the consent was signed, and that a copy was given to the subject to take home.

An informed consent procedure note template may be useful to remind you of all the items to cover in the informed consent process and to document them.

Informed Consent Form Revisions and Reconsent

Whenever there are substantive changes to the protocol or when important new information becomes available you will need to revise the ICF. Often times the sponsor will send ICF changes to the study team with a protocol change or new safety information. 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.

The IRB-approved and stamped version of the ICF must not be altered by the subject or research team.

When there is new information pertaining to safety, reconsent of subjects is almost always appropriate. The investigator should consider obtaining reconsent from subjects actively participating in the study and/or notification to past subjects who need to know about the new information (e.g., a newly identified risk of long-term osteoporosis in subjects who stopped taking the study drug years earlier). Reconsent must occur at the next meeting between the subject and a study team member.

The IRB and/or sponsor may require reconsent of subjects. If the Emory IRB requires reconsent of subjects, they will include the requirement in the approval letter of the consent amendment. 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, it is acceptable for the investigator to notify/obtain reconsent of subjects if he/she deems it necessary. Revised consent forms and any other written information that will be distributed to subjects 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

It is very important to ensure that a subject meets the protocol eligibility requirements. To document eligibility and to help ensure you don't miss any requirements it is a good idea to develop and use a study-specific eligibility checklist that matches the current version of the protocol. Protocols usually have a list or chart of the eligibility requirements, which can easily be copied to a checklist.

You should maintain a completed eligibility checklist in the research record for each subject. 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 properly qualified to make the eligibility assessment, be IRB-approved to conduct the research, have documented study-specific training, and have been delegated by the PI to assess eligibility per 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.

Maintaining Eligibility

If a subject becomes ineligible while participating in the study, consider holding the study intervention until the subject 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 subject should remain in the study. If the sponsor or PI determines that the subject should no longer participate in the study, the subject must be withdrawn.

There are some situations where the subject may have to be withdrawn from the study but the subject may still be able to obtain the drug/device even though not in the trial. If the drug or device can be obtained outside of the trial (e.g., a drug that is already FDA-approved but is being used for another indication for the clinical trial) then the PI may consider maintaining the drug/device as 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 subjects participating in clinical trials. It is critical that each study team member know 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 the 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 subjects shall terminate all investigations within 5 days of the sponsor making this determination.

The human subjects 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 the IRB *promptly* (Emory IRB defines "prompt" as 10 calendar days). UPs are unexpected, caused by the study intervention, and suggest that there is a risk to subjects or others.

The Emory IRB has UP guidance on their website.

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. In order to document assessment of events for SAE, UP, and UADE, as well as document 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 adverse events), procedure notes, subject diaries (e.g., pill diaries, daily food logs, and symptom diaries), documentation from phone calls or emails with subjects, and adverse event logs.

At the start of a study the subject's medical history is collected for a baseline assessment. Changes in medical conditions that were noted at baseline must be documented as adverse events. New events/symptoms that occur to the subject during the course of 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 subjects, 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.

Organization

It is a best practice for the PI or designee to maintain a system to collect AEs onto a 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. While reviewing the AEs, the PI should consider the criteria for SAE, UP, and UADE and report accordingly.

The AE log should contain fields for description of event, start/stop dates, grade, attribution, and PI signature and date.

External Adverse Event Reports

Sponsors of multisite studies are required to send all participating investigators reports of certain adverse events, as described above. Upon receipt of these events to Emory investigators, the PI must review them and document his/her assessment with regards to UP. If the Emory PI assesses the event as a UP (i.e., Emory subjects are at a risk of harm), that event must be reported to the IRB within 10 calendar days. The PI should consider taking any of the following measures to protect subjects: halt the

study until further information is known, notify subjects, amend the informed consent, and/or obtain reconsent from active subjects.

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 Emory IRB has a worksheet that can capture the PI's assessment of external adverse events. 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 calendar 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 Subjects Protection, and OHRP Guidance: Guidance on Reviewing and Reporting Unanticipated Problems Involving Risk to Subjects or Others and Adverse Events*

7 Organizational Logs

Tracking of research data can greatly assist in the successful management of a trial by the investigator, sponsor, and monitor. Clinical trial sponsors will often supply logs or worksheets to the study team to use as supporting documentation to the case report forms or as the actual case report forms (this is often seen with electronic data capture). Sponsors may require study teams to periodically submit logs to them.

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 in case of an audit. Logs should be study-specific with the study title and PI located at the header. Not all logs will apply to every study. You are encouraged to use the logs provided in this chapter and feel free to modify them to fit your needs.

Adverse Event Log

Adverse Events and their documentation are very important for human subject protection as well as data integrity. An AE log serves as the collective source for adverse events that exist in multiple places (e.g., physician notes, nursing notes, lab or procedure reports, pill diaries, or email correspondence with a research subject). AE logs must contain a description of each event, stop and start dates, action taken by the provider (e.g., additional work-up, medication given or investigational product dose modification), grade (according to a pre-defined standard, for example I-IV), and attribution to the investigational product. Including additional checkboxes on the AE log for each event regarding whether the event was reported to the sponsor, IRB, and/or FDA, are helpful as well.

AEs on the log should have supporting source documentation with further detail. Don't forget to report AEs to the sponsor, IRB, and FDA as required by their policies and federal regulations.

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 subjects or others.

For more information on AEs, see the CTAC AE Guidance and IRB website.

Communication log

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

The log can also be used to document communication between study team members and sponsors. Maintain this log with the essential documentation.

Concomitant Medication Log

The concomitant medication log must 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 subject is not taking medication that is prohibited from the protocol. If the subject 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 is one of the most critical logs you will maintain. 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, their 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 certification, eCOI completion, or documented study-specific training. Be sure that all of these requirements occur before the start date on the DOA log. The DOA log can serve as the last point or check point before the study team member starts the research.

Enrollment Log

Your enrollment log will contain the chronologic enrollment of subjects by name and number. It will incorporate the subject's identifier (name or initials), study subject number, and date of enrollment. You may also want to include additional fields such as eligibility, randomization date, and withdrawal date. Remember that the Emory IRB defines enrollment as being the time the subject gives informed consent to participate.

Protocol Deviation Log

The federal regulations do not allow for deviations from the protocol unless there is imminent risk of harm to research subjects. 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 subject. Protocol deviation logs must contain a description of the deviation, date, corrective action taken, and to whom the deviation was reported (e.g., sponsor or IRB) and when. Deviations should be periodically trended over time to look for systemic problems with the study. Problems for the study should have a thoughtful root cause analysis of the problems and a corrective and preventive action (CAPA) plan in place. CAPA plans should be thoughtfully designed, fully implemented, periodically evaluated, and revised as needed to ensure improvement.

Specimen Log

Information regarding specimens obtained and stored for clinical trials should be documented on a log. The specimen log should obtain information about what specimen was taken, how it was obtained,

where it was shipped to (if applicable), and how it was stored 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 subjects all clinical trials at Emory are required to have a data and safety monitoring plan (DSMP). Sponsors often prescribe the DSMP in the protocol. Some clinical trials may have data and safety monitoring boards (DSMB) or committees (DSMC) that are appointed by the sponsor.

Emory IRB Policy and Procedure #49, *Data and Safety Monitoring Plans,* describes the required components of a DSMP. The Emory IRB also provides guidance 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, must be addressed immediately. Your study team should establish a strong and collaborative working relationship with the monitor while on site.

After the monitoring visit, the PI will need to carefully review the report. The PI should compare old reports to the most recent reports to look for patterns of noncompliance across reports. Patterns of ongoing noncompliance or outstanding issues usually signals problems for the study.

Within 10 days of receiving the monitoring reports, send them to the Clinical Trials Audit and Compliance listserv at ctcompliance@emory.edu or by fax to 2-8580. File the monitoring reports and actions taken in the regulatory binder.

Self-Monitoring

If the study is not being monitored by the sponsor or contract research organization, the PI should consider self-monitoring of the trial. Self-monitoring can be most successfully implemented by someone within the clinical department that is not directly involved with the data collection or entry of the study. Clinical departments are urged to use a buddy system whereby research coordinators or nurses switch off studies to monitor at least twice per year. The Emory University Self Monitoring Tool can be used as a self-monitoring checklist and can be customized for each study.

The FDA regulations require sponsors to monitor trials; thus, if the Emory PI is acting as both a sponsor and investigator (i.e., Sponsor-Investigator), the PI must plan for monitoring. If there is no monitoring provided by the study-supporter, the Sponsor-Investigator must obtain monitoring through a contract research organization or at the very least, perform self-monitoring twice a year. Sponsor-Investigators over a multi-site study may require the sites to perform self-monitoring 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) all information in the IRB applications, amendments 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 research plan except where necessary to eliminate apparent immediate hazards to human subjects. Even with the most cautious and careful research and subject teams, however, meticulous protocol compliance can be difficult to maintain in the increasingly complex clinical trial environment. The studies themselves are highly technical with multiple requirements and the human subjects are research 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 subjects 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 subject safety, report 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 subject charts for quick reference
- Communicate expectations to subjects
- Talk to monitors about common deviations across sites

What to do when a deviation occurs

If you become aware of a deviation that has already occurred, you must first take immediate corrections to protect the rights, welfare, and safety of the subject(s). This may be in the form of a phone call or an office visit with a qualified research team member. The investigator may need to order tests and other procedures to ensure the subject 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 to be reported, as applicable, within 10 business days of becoming aware. You may also need to notify subject(s) of the problem and the IRB will advise you on how to do this (e.g., letter to subjects, phone, or reconsent). Immediate corrections should be focused on **rights, welfare, and safety of subjects and reporting**.

Evaluate risk

After immediate corrections have been made, evaluate the risk of the deviation with regards to severity and frequency. To evaluate severity, a good start is using the Emory IRB reporting requirements, which considers events that adversely affect the rights, welfare, or safety of subjects (among other things) to be major. In general, if you reported the deviation to the IRB, the risk of the event could be severe.

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 subject or other subjects 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, there is a risk of frequency.

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

Corrections

It is important to make a distinction between corrections and corrective actions. Corrections are the immediate steps taken to resolve a problem and involve ensuring **rights, welfare, and safety** of subjects 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 people 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 subject or all subjects 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 absolutely 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, it is now an expectation that CAPAs are 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 subject and future subjects and that the deviation was appropriately reported to the sponsor and IRB. Because you have assessed the **rights, welfare, and safety** of the subject and the root cause is now known, you may consider additional **reporting** to the sponsor and IRB at this time. 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 itself in one or more subjects. 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, addresses urgency and criticality

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; this should be well understood. The CAPA and SOP can be rolled out in stages. The important thing is that you are taking action and documenting it.

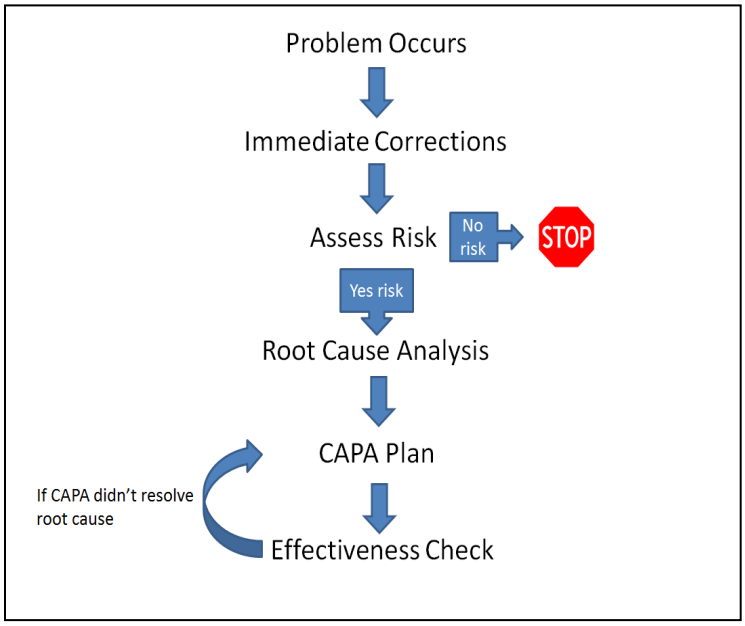
CAPAs must be evaluated over time

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

10 Reporting Requirements

Each sponsor has unique reporting requirements for events that occur during the clinical trial and that 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 will generally be 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 the means to do the reporting (e.g., electronic entry on a sponsor's website or faxing a paper form). The sponsor's time frame for reporting should be taken seriously and reported to the IRB as noncompliance if it is not followed appropriately.

Adverse Events

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. Paper copies of reports made to the sponsor should be kept with the research records.

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.

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. Generally speaking, the most stringent documented requirement (that err on the side of more reporting) should be followed. If the monitor asks the PI to report something to the IRB that does not fall within the documented sponsor reporting requirements, talk to the monitor about the Emory and Western IRB reporting requirements. If the monitor or sponsor is persistent about reporting to the IRB, then the study team must submit the report to the IRB.

11 Case Report Forms

Research data is ultimately submitted to the sponsor and/or analyzed by the Emory Investigator by either paper case report forms (CRFs) or by electronic data capture (EDC). For the purpose of this Guidebook, the term CRF encompasses both paper CRF and EDC. Case report forms are arguably the most important documentation in a clinical trial since they are the last point of data entry, which ultimately influences the outcome of a study. CRFs must be organized, understandable, reproducible, reliable, updated, and verified for accuracy by the PI.

CRF Completion

- The CRF must be completed by authorized site personnel, as documented on the delegation of authority log. Ensure that all CRF pages are signed and dated by the person completing the form
- Ensure data entries are consistent with the source data (usually the subject's medical record)
- Always write clearly ensuring that the entries are legible to others
- Avoid abbreviations and acronyms, unless they are standard medical abbreviations or known to be acceptable
- Ensure that you 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 put a 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 amendment.
- Do not record incomplete dates (e.g., if you know the month and year, 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

Verification of CRFs

The investigator should ensure the accuracy, completeness, legibility, and timeliness of the CRF 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 CRF page or multiple CRFs at defined periodic time points. Some sponsors may have the PI sign an attestation page at the end of CRF completion, which will document the PI's verification that the data is 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 subject or entire study. For investigator-initiated research, best practice is for the PI to sign CRFs at visit completion.

Maintenance and Storage of CRFs and Source Documentation

CRFs should be promptly completed after the data is collected. A backlog of CRF entries compromises the data integrity. You may not be able to recall the data later. Once the study is complete, CRFs should be kept either via paper copy or on a CD-ROM. Don't ever lose sight of your CRFs and don't rely on the sponsor to give them to you in case of an audit.

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 for CRFs

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

11 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 subjects of the study team changes if the research team contact information will change for the subjects. Letters or other materials that will be distributed to all subjects 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 Amendment for the new PI. Consider revising the protocol and informed consent form, as appropriate. Also consider notifying current subjects; correspondence sent to all subjects 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

ACTSI	Atlanta Clinical and Translational Science Institute
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
CIN	Clinical Interactions 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
ORC	Office of Research 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 required approvals at Emory and does not describe, in detail, the functions of every department. For further information, follow links to departmental websites.

Atlanta Clinical and Translational Science Institute (ACTSI): The Clinical Interaction Network Scientific Advisory Committees (SAC) are responsible for completing scientific and resource review of all protocols requesting resource support from the Clinical Interaction Network (CIN). The SAC meets monthly and protocols must be submitted three weeks in advance of any SAC meeting. Meeting dates and protocol submission instructions can be found at http://www.actsi.org/areas/cin/protocol_submission/index.html

At the time of the SAC submission, protocols will also be submitted for review by the Safety Advisory Subcommittee (SAS) of the ACTSI. The CIN staff will submit to the SAS on behalf of the Investigator. The SAS will provide their review/comments to the SAC prior to final approval.

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 subjects;
2. Experiments utilizing live, recombinant, or attenuated microorganisms for the purposes of vaccination of one or more human subjects; 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 http://www.ehso.emory.edu/programs/research/index.cfm

Clinical and Translational Research Committee (CTRC): For cancer clinical trials, in any department, the investigator must apply to the CTRC prior to seeking IRB approval. The CTRC form can be found at http://winshipcancer.emory.edu/research/WinshipContentPage.aspx?nd=720

The Investigator may submit the application in eIRB while awaiting CTRC approval. Once the CTRC has given approval, a CTRC administrator will move the study in eIRB to the IRB Inbox (i.e., the study won't electronically go to the IRB until the CTRC administrator moves the study after CTRC approval).

Conflict of Interest (COI): The investigator and anyone named by the PI who is independently responsible for the design, conduct, or reporting of research must complete eCOI for the study. The web address for eCOI is https://www.ecoi.emory.edu/

Visit www.coi.emory.edu for eCOI instructions.

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 notifies them that the checklist has been completed. The Office of Quality Checklists are located on the IRB website at http://www.irb.emory.edu/researchers/formstools/formstools.cfm

Completed checklists should be sent to Laura Deane in the Office of Quality at ldeane@emory.edu

For drug and device studies, Emory Healthcare also requires study teams to complete a Key Points Summary that will be placed in the subjects' Emory electronic medical record so that EHC providers taking care of patient subjects 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 http://www.irb.emory.edu/researchers/formstools/formstools.cfm

For studies involving sensitive and stigmatizing information, inclusion of study information into the medical record may discourage subjects 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 http://www.irb.emory.edu/researchers/formstools/formstools.cfm

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: http://www.irb.emory.edu/researchers/formstools/formstools.cfm

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 subjects.

Institutional Review Board (IRB): IRB approval is required before the research can start. The investigator must submit to the Emory or Western 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 http://www.irb.emory.edu/researchers/eresearch/getacct.cfm

Studies that are eligible to go to WIRB and instructions for applying to WIRB can be found on the Emory IRB website at http://www.irb.emory.edu/researchers/wirb/wirb.cfm

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. For studies requiring OCR review (below), OCR 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.

For studies that do not require OCR review, the PI must contact Susan Rogers at IDS at (404) 712-7485 or sroger2@emory.edu and submit to her the written protocol, Investigational brochure (IB), budget request and IRB number, if available upon initial contact to 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

Office of Research Compliance (ORC): ORC offers counseling to all Emory investigators acting both as Sponsor and Investigator (i.e., "Sponsor-Investigators"), as defined by the FDA. However, ORC review is mandatory for all Winship Cancer Institute Sponsor-Investigator studies prior to enrolling subjects. ORC 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. www.orc.emory.edu

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 course of 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 for Procedures with Human Subjects form. If the research involves nuclear medicine procedures, the investigator must submit the Human Studies Application for Radionuclide Use form. Both forms are located on the Radiation Safety webpage of the Environmental Health and Safety Office website at http://www.ehso.emory.edu/programs/radiation/radiation-forms.cfm

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 subjects.

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 web-site 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//vaww.gateway.research.va.gov/eRRRP

Researchers must submit to the R&D the protocol, IRB approval, and other pertinent documents specific to the research project.

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)	
OCR training for Investigators (Key Concepts of Clinical research)	
OCR training for Coordinators/Research Nurses (How to Conduct Clinical Trials at Emory)	
ORC training (HIPAA Privacy and Security)	
IATA training (International Air Transportation Association)	
ERMS training (Emory Research Management System)	
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