Principal Investigator (PI) Responsibilities in Human Subjects Research at Emory

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Overview

- Food and Drug Administration (FDA) requirements and guidance
- US Department of Health and Human Services (HHS) and SACHRP recommendations
- PI Responsibilities at Emory
  - Prior to submitting research applications
  - Study conduct, supervision, oversight, and availability/awareness
  - Other scenarios that require additional responsibilities
  - Key takeaways and potential consequences of inadequate oversight
- Steps to take when leaving Emory
- Miscellaneous Updates from the IRB

FDA Guidance – Investigator Responsibilities

- Ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs, including biological products (FDA Form 1572), or agreement for clinical investigations of medical devices (sponsor developed, includes elements of 21 CFR 812.43(c)), the investigational plan, and applicable regulations
- Protecting the rights, safety, and welfare of subjects under the investigator's care
- Controlling drugs, biological products, and devices under investigation (21 CFR 312.60, 21 CFR 812.100)

*Sourced from: Guidance for Industry Investigator Responsibilities — Protecting the Rights, Safety, and Welfare of Study Subjects

FDA Guidance – Investigator Responsibilities

- **Supervision of the Conduct of a Clinical Investigation**
  - It is common practice for investigators to delegate certain study-related tasks to employees, colleagues, or other third parties (individuals or entities not under the direct supervision of the investigator). When tasks are delegated by an investigator, the investigator is responsible for providing adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

FDA Guidance – Investigator Responsibilities

- **Adequacy of supervision by an investigator is assessed by FDA on four major areas:**
  - Individuals who were delegated tasks were qualified to perform such tasks
  - Study staff received adequate training on how to conduct the delegated tasks and were provided with an adequate understanding of the study
  - Adequate supervision and involvement in the ongoing conduct of the study
  - Adequate supervision or oversight of any third parties involved in the conduct of a study to the extent possible

FDA Guidance – Investigator Responsibilities

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

HHS & SACHRP Recommendations

- The HHS 45 CFR 46 Regulation for the Protection of Human Subjects in Research, unlike FDA regulations (312 and 812), does not directly address the roles and responsibilities of investigators involved in human subjects research. Investigators are in the best position to protect participants.
- The Secretary's Advisory Committee on Human Research Protections (SACHRP) offered recommendations on Investigator Responsibilities.

SACHRP Recommendations

§46.104 Responsibilities of Investigators:

- *As appropriate to their role in the research, investigators are responsible for ensuring that research is conducted according to:*
  - *Sound research design and methods;*
  - *The IRB approved study plan (protocol);*
  - *The applicable terms of the grant, contract and/or signed funding agreements, if applicable;*
  - *Applicable laws and regulations, including those for protecting the rights, safety, and welfare of human subjects.*

§46.105 Qualification Standards for Investigators:

- *As appropriate to their role in the research, investigators must be sufficiently qualified by education, training, and experience to assume responsibility for the proper conduct of the research.*
- *Investigators must assure that they have **sufficient time** and **resources** to properly conduct or supervise the research for which they are responsible.*

§46.106 Investigator Records, Reports and Documentation:

- *Investigators are responsible for the safe and secure storage of research data (whether in paper or electronic formats) and for protecting the confidentiality of the data in accordance with the approved protocol.*
- *Investigators are responsible for the accuracy and completeness of study data.*
- *Investigators must maintain records appropriate to the research (e.g., the study plan, consent forms, and correspondence from the IRB) and permit inspection of the research records in accordance with §46.104(j).*
- *Investigators must maintain records for at least three years after the research ends or for the length of time specified in applicable regulations or applicable institutional or sponsor requirements, whichever is longer, and should take measures to prevent accidental or premature destruction of these documents.*
- *Investigators must submit written reports to the IRB as required by the IRB.*

PI Qualifications

- **PI eligibility per school/institutional policies**
  - Emory IRB is no longer involved in assessing whether an individual can serve as PI per the relevant School or EHC policy (which is typically related to grant submissions)
  - Departmental approvers for IRB submissions should alert the investigator if a PI change is needed

What about Requirements at Emory?

- FDA and SACHRP recommendations provide the foundation of Emory Policies that define PI Responsibilities (chapters 5 and 80 in Emory IRB P&Ps).
- PI availability and responsiveness is key in ensuring that the responsibilities are being carried out effectively.
- At Emory, the PI role holds the **ultimate responsibility** for **all study conduct** under an IRB approved protocol.
- The PI is responsible for ensuring complete and accurate information is provided to the IRB which may involve careful review of materials prior to submission. Responsibilities continue until the study is complete and closed with the IRB.

PI Responsibilities at Emory

- Prior to submitting research applications for review and approval the Principal Investigator will:
  - Assure other Investigators and key study personnel are competent and licensed, if applicable, relevant to the scope and complexity of the research conducted;
  - Commit to conduct research in accordance with the ethical principles of The Belmont Report, Federal and State regulations, Institutional policies and procedures, EU IRB policies and procedures, and if applicable, Good Clinical Practice standards.
  - Read, understand and agree to abide by all terms of the Statement of Investigator Responsibilities in conducting Human Subjects Research.

PI Responsibilities at Emory

- **Training and Knowledge:** Ensuring, prior to initiating any Human Subjects Research, that they, and all study staff/key personnel involved in their Research protocol, have acquired the appropriate knowledge and training regarding protections, ethical conduct of Research, and applicable federal regulations, as well as the specific knowledge needed to properly conduct their specific protocol(s).
- **Completion of Required Training Programs:** Ensuring, prior to beginning any Human Subjects Research that they, and all study staff/key personnel involved in their Research protocol, have each completed any training programs mandated by the Emory IRB or by other Emory University departments or committees that have jurisdiction over the Research in which the PI is participating (e.g., CITI Training Course, HIPAA training, radiation safety training, bloodborne pathogens training), including individually, without any assistance from others, attaining a passing score on any required examinations or tests covering the training materials. See the P&P entitled "Investigator Qualifications" for more information.

PI Responsibilities at Emory

- **Knowledge of Protocol and Related Documentation**: Prior to initiating work under any Research protocol, thoroughly reading and understanding the Research protocol and any informed consent document and HIPAA Authorization, and understanding and properly completing the IRB Protocol Application (including all appropriate materials) submitted to the Emory IRB for review and approval. All PIs are also responsible for ensuring that all personnel involved in carrying out the Research protocol are familiar with these documents and also abide by all of these requirements.
- **Regulatory Compliance:** Ensuring that they and all key personnel involved in the Research protocol comply with all Emory IRB P&Ps and determinations (and those of the reviewing IRB, if not Emory IRB), which are an integral part of the University HRPP, as well as all applicable Emory University policies, and all requirements imposed by the FDA Regulations, HHS Regulations, HIPAA Regulations, VA Regulations (for Human Subjects Research that involves the AVAHCS), DOD requirements, and any other applicable laws and regulations. Ensuring that they and all key personnel are operating within the parameters of any Reliance Agreements and cooperate with the Reviewing IRB's requirements for initial and continuing review, record keeping and reporting, and that they provide information requested by the Reviewing IRB in a timely manner.

PI Responsibilities at Emory – additional requirements

DOD Research: For protocols conducted or supported by the DOD, PIs shall insure that they, and the research personnel who work on their studies, complete the training described in the P&P entitled Department of Defense (DOD) Supported Research. The IRB may request written documentation of completion of any required training or certification.

Complete any additional human research ethics or other training required by applicable funding agencies or other entities that oversee the research (e.g. AVAHCS, NIH).

Sponsor-Investigator studies in which an Emory faculty member holds an IND for a drug or an IDE for a device. These require some additional training locally and an entire set of responsibilities related to serving as the sponsor for FDA purposes (beyond the scope of PI).

PI Responsibilities at Emory - Takeaways

- The PI is responsible for continued regulatory oversight and ensuring complete, timely submissions to the IRB (modifications, continuing reviews, reportable new information).
- The PI can delegate tasks to other team members with adequate supervision. Actions taken by delegated team members are ultimately still the PI's responsibility.
- The PI is responsible for any reporting obligations such as any instances of noncompliance and/or unanticipated problems that may occur during study conduct.
- The PI is responsible for updating the IRB when a study is complete by submitting a close-out.
- The PI is responsible for ensuring that the study is conducted according to the approved protocol, SOPs, and all applicable regulations.
- The PI must ensure that documentation of study oversight is done in a timely manner, as required (i.e. sign and date items like the delegation of authority log, adverse event and/or protocol deviation assessments, and ensuring the protocol is being following by routinely monitoring progress)
- The PI is responsible for ensuring that all study data is accurate, complete and verifiable.

Potential Consequences

- When a PI fails to adequately oversee a study there can be consequences. For example:
  - Violation of subject's rights or safety
  - Inaccurate data being generated from a failure to follow the approved protocol
  - Lack of awareness on study progress and regulatory reporting requirements.

Potential Consequences

- Additional Impacts:
  - Approval lapse in an FDA regulated study resulting from a lack of PI response/action may warrant closure. When this occurs, it may require a report to the FDA as a termination of approval.
  - Lack of oversight can lead to major protocol violations or continued violations with no resolution, which may result in a determination of serious and/or continuing noncompliance. The IRB is obligated to report these determinations to federal agencies.
  - If the IRB discovers significant issues resulting from a lack of PI oversight the study can be placed on temporary suspension until issues are resolved.

Leaving Emory?

- As a reminder, if you are currently serving as the PI on one or more active projects at Emory and will be leaving the university, please reach out to the IRB as soon as possible.
  - Each active project will either need to be closed, transferred, or a new Emory PI appointed to continue the project locally.
- The PI Transition Form (Excel file) should be filled out when:
  - Bringing IRB approved studies to the other institution, or
  - Will remain engaged in research to be able to continue the study at Emory/other institution, or
  - If taking a study grant to the other institution. This form should be attached with your submission to the IRB and can also be sent to the IRB listserv (irb@emory.edu) if many studies are involved. An institutional reliance agreement might be required in these cases.

Miscellaneous Updates

- Coming soon: IRB guidance on steps you can take to avoid delays in review/approval.
- If data is being collected/used from international sites prepare for it to take more time, since it involves other offices. See our International Research Q and A page for more information.
- Expect an announcement in the next day or two from Finance about a new **SSN/TIN validation step for new ClinCard use,** that will result in automatic tax withholding for invalid SSN/TIN along with extra $1 fee. Questions should be directed to Emory tax office (contact will be in the announcement).

Please let us know what you think of this webinar by scanning the QR code!

Questions and Contact Information

- For study specific questions, contact the IRB analyst assigned to your study.
- To find IRB staff contact information, go to our website.
- For general questions, contact irb@emory.edu.
- For general reliance questions, contact irb.reliance@emory.edu.
- For questions about reportable new information, expanded access etc., contact the Education and Quality Assurance Team